

# Re-evaluation of Nucleic Acid Retested Positive Cases in the Recovered COVID-19 Patients: Report from a Designated Transfer Hospital in Chongqing, China

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## Abstract

Since the outbreak of coronavirus disease 2019 (COVID-19) in Wuhan, Hubei province, China,<sup>1</sup> the epidemic has spread rapidly in Hubei province and other regions in China. A total of 80,552 patients confirmed with COVID-19 have been reported in the main land China up to March 5th, 2020.<sup>2</sup> They included a huge number of patients discharged from hospital. A total of 53726 cases have met the discharge criteria (one of the criteria includes two continued negative result of nucleic acid test with repeated interval period of at least 1day or 24 hours.) in mainland China up to March 5th, 2020. Previous studies have paid more attention to the epidemic situation of COVID-19 and patient's diagnosis and treatment. Closely attention should be paid to the discharged patients. Surprising, previous follow-up reported that some patients nucleic acid retest result was positive again after discharge.<sup>3</sup> Impact factors should be further investigated. Since the first confirmed case was diagnosed in our hospital (Chongqing Emergency Medical Center, the designated transfer hospital) on February 4th, we have confirmed a total of 17 cases. All the patients infected with the novel coronavirus have been transferred to a designated hospital in Southwest China's Chongqing by ambulance with an inbuilt negative-pressure chamber.<sup>4</sup> In the follow-up of these patients, all patients accepted RT-PCR tests again after having discharged from designated hospital 3 days later. Four of them showed recurrence of positive results after few days of discharge. Thus, we reported these cases aiming to provide information on policy formulation and modification of discharge plans.

## Introduction

The first confirmed case of imported COVID-19 appeared in Chongqing on January 21st, 2020, and a total of 576 cases had been confirmed in Chongqing up to March 5th, 2020. However, during follow up, some recovered patients had recurrence of RT-PCR positive. On

February 25th, the center for disease control and prevention (CDC) in Guangdong province reported that 14% of discharged patients in the province had this phenomenon. We have followed up the patients discharged from designated hospital who were diagnosed in our transfer hospital,<sup>4</sup> and four of them had similar conditions. Thus, we report the four series of cases.

## Methods

Data were collected from medical records of these patients with novel coronavirus pneumonia confirmed by Chongqing Emergency Medical Center. Their families, center of disease control and prevention of Yuzhong District, Chongqing, and the designated hospital were contacted directly. We further analyzed the epidemiological history, clinical symptoms and multiple RT-PCR test results of virus nucleic acid after diagnosis and recovery.

All of the cases reported were confirmed in our hospital by the trial version 5 of new coronavirus pneumonia diagnosis and treatment program.<sup>5</sup> They were then transferred to the designated hospital to accept treatment and met the criteria of discharge.<sup>5,6</sup> Their discharge decisions were made by a panel of experts associated with COVID-19. The patients were quarantined sequentially and the nucleic acid was examined 3 days after discharge. All were followed up by telephone.

This study was approved by the medical ethics committee of the Chongqing Emergency Medical Center (No. 2020-06). Written informed consent for emergency medical rescue of public health emergencies was waived According to the relevant provisions of national medical ethics.

## Results

Three patients showed nasopharyngeal swabs result positive after three days of

discharge. The remaining one showed anal swab result positive after three days of discharge. However, the symptoms and manifestations of CT were not exacerbated for the latter. Therefore, three patients returned to the designated hospital for quarantine again. Two patients have been discharged again from the hospital on March 2nd, 2020, and the nucleic acid is still negative after having discharged up to now. The other (case 4) is still under medical observation. The case 3 was quarantined in our hospital due to positive results of anal swab.

Case 1: A 29-year -old male, He is working in a service industry. The specific exposure history is unknown. The first case of a family cluster might be associated with the COVID-19. He lives with his parents, and all of them were identified infected with the novel coronavirus. He had symptom of fever and cough at onset on Jan 27, and presented to our hospital 3 days later. Due to positive nucleic acid test, he was confirmed as having the novel coronavirus disease. After 14 days of treatment, he met the criteria of discharge on Feb 15. The nasopharyngeal swab was positive 3 days after discharge, but it was negative four times after that until March 5th, 2020.

Case 2: A 49-year-old female (the mother of case1) was exposed to her infected son. She had symptoms of cough and the confirmation test was made by a combination of exposure history and positivity of nucleic acid. She also received antiviral treatment for 14 days ,until discharge on February 16th. Three days after discharge, nasopharyngeal swab test result was positive. From then, negative results were tested four times until March 5th, 2020.

Case 3: A 12-year -old female, was exposed to her infected mother. Thus, she was asked to visit our hospital to collect oropharyngeal swabs for the RT-PCR test and to undergo a chest computed tomography (CT) examination. Mild COVID-19 was diagnosed due to RT-PCR tests result positive. Antiviral treatment with arbidol, interferon and traditional

Chinese medicine were obtained in the designated hospital in the next 15 days. Then, she was met the criteria of discharge (2 negative RT-PCR test results at least 1 day apart). In addition, she was asymptomatic and, the finding CT scan was negative, The nucleic acid tested of anal swab was positive after three days of discharge. It was still positive for the next two times until March 5th, 2020.

Case 4: A 38-year-old male was exposed to his friends who returned from Wuhan when dining with them. Three of the table were infected COVID-19. He presented with fever, fatigue, cough 8 days. He was diagnosed with novel coronavirus pneumonia on January 30th, 2020 according to the typical respiratory symptom, positive oropharyngeal swab result and radiological ground-glass opacification. He was transferred to the designated hospital, and was treated for 27days. The nasopharyngeal swab was positive 3 days after discharge , but became negative 2 days later on March 4th, 2020.

## Discussion

The COVID -19 outbreak in China is the third coronavirus outbreak in the 21st century and has already infected more people than SARS<sup>7</sup> and MERS(a total of 2519 cases at Jan 31,2020).<sup>8</sup> With the intensive surveillance measure which have been taken to prevent and control of epidemic by Chinese government, good impact has been achieved on the spread and treatment of COVID-19 in Wuhan and the whole country. No new cases have been confirmed in Chongqing for 10 days consecutively until March 5th, 2020.<sup>9</sup> However, a follow-up of the recovered patients showed a recurrence of RT-PCR positive in some patients. According to the report in JAMA,<sup>3</sup> although all 4 patients were positive in the RT-PCR retest, there were no typical symptoms or chest computed tomography (CT) images of COVID-19. Our patients also had no clinical manifestations to support recurrence of this disease. In addition, some patients turned negative when they repeated tests for the

COVID-19 nucleic acid.

Does the patient's with nucleic acid detection positive have infectivity? SARS and MERS, both coronavirus infections, had not previously reported to reoccur again .<sup>10</sup> Further monitoring revealed that no further transmission to others have occurred in our patients, the same as JAMA report.<sup>3</sup>

Why does this happen? In general, specimens such as alveolar lavage fluid deposited deep in the lungs have a higher positive rate than that of oropharyngeal swab<sup>6</sup> and turn negative more slowly. If the patient was discharged after two negative results of oropharyngeal swab test separated by the least 24 hours, there may be a persistent virus in the lung. When the patient immunity declined, the RT-PCR test of oropharyngeal swab may be positive again. Thus it is recommended that saliva should be collected if possible, while it has been emphasized that the specimens of lower respiratory tract (saliva or airway extract) has more accuracy for RT-PCR test.<sup>6</sup> In addition, virus-free cells may be collected due to improper site and insufficient depth, which will also cause "false negative" .<sup>11</sup> This phenomenon also may be due to the biological characteristics of the novel coronavirus .<sup>12</sup>

Positive nucleic acid results of anal swab of case 2 for 3 times were shown after discharge. Positive results of anal swab nucleic acid test do not mean that there is live virus in the stool of the patient. Secondly, the removal rate of viral RNA in the stool of the patient is slower than that of the oropharyngeal swab. So the positive duration of anal swabs or stool samples during recovery are relatively long.<sup>13</sup>

According to current discharge criteria ,<sup>6</sup> recovered patients should stay at home for 14 days in quarantine, which would prevent most of these patients from re-infecting others. We also suggest whether negative result of the virus nucleic acid test of anal sample

should be included in the discharge criteria.

There are several limitations in our observation. Patients were confirmed in our hospital and transferred to the designated hospitals for treatment. Virus nucleic acids of different samples were tested in the two hospitals and CDC, and samples were collected from different medical professionals of above mentioned settings. Furthermore, different batches of kits from different manufacturers were used, as this is a novel virus, and we are still learning about it.

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