# The Long-Lasting Persistence of SARS-CoV-2 Nucleic Acid in COVID-19 Patients

**Shan Li**
Jiangsu Province Hospital and Nanjing Medical University First Affiliated Hospital
https://orcid.org/0000-0003-4330-6280
**Chaojie Wu**
Jiangsu Province Hospital and Nanjing Medical University First Affiliated Hospital
**Mingshun Zhang**
Nanjing Medical University
**Lianzheng Zhou**
Changzhou No.2 People's Hospital
**Jie Xiang**
Wuhan Jinyintan Hospital
**Wei Zhang**
Jiangsu Province Hospital and Nanjing Medical University First Affiliated Hospital
**Yuan Ma**
Jiangsu Province Hospital and Nanjing Medical University First Affiliated Hospital
**Wenqiu Ding**
Jiangsu Province Hospital and Nanjing Medical University First Affiliated Hospital
**Zhengxia Wang**
Jiangsu Province Hospital and Nanjing Medical University First Affiliated Hospital
**Mao Huang**
Jiangsu Province Hospital and Nanjing Medical University First Affiliated Hospital
**Ningfei Ji** ( jiningfei@163.com )
Jiangsu Province Hospital and Nanjing Medical University First Affiliated Hospital

**Case Report**

**Keywords:** SARS-CoV-2, COVID-19, Convalescent, Nucleic acid test, Long-lasting

**Posted Date:** March 31st, 2021

**DOI:** https://doi.org/10.21203/rs.3.rs-354369/v1

# The long-lasting persistence of SARS-CoV-2 nucleic acid in COVID-19 patients

Shan Li[1*], Chaojie Wu[1*], Mingshun Zhang[2], Lianzheng Zhou[3], Jie Xiang[4,5], Wei Zhang[6], Yuan Ma[1], Wenqiu Ding[1], Zhengxia Wang[1], Mao Huang[1¶], Ningfei Ji[1¶]

¶ Correspondence to: Mao Huang, hm6114@163.com; Ningfei Ji, jiningfei@163.com;

* Contribute equally

**Abstract**

**Background:**

Although recurring cases of COVID-19 have been sporadically reported, the long-persistence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is still arguable. We aimed to provide the evidences of recovered COVID-19 patients with long-lasting positive SARS-CoV-2 RNA tests in a Chinese hospital.

**Case presentations:**

We reported 4 discharged patients with COVID-19 patients relapsed during the period of self-quarantine, leading to an extended disease course. All of four patients were historically healthy without known underlying diseases (diabetes, hypertension, cancer, i.e.) which may influence the disease course.

**Conclusion:**

The persistent course of SARS-COV-2 nucleic acid test positive in these 4 cases was prolonged, which provided some ideas for the long-term existence

of SARS-COV-2 RNA in convalescent patients.

**Keywords:**

SARS-CoV-2; COVID-19; Convalescent; Nucleic acid test; Long-lasting

## Background

The current pandemic of COVID-19 which caused by a novel coronavirus (SARS-CoV-2) is unprecedented. It has exhibited distinctive features from prior coronavirus related diseases. Compared with SARS and MERS, COVID-19 shows higher infectivity [1]. What's more, it is concerned that the global epidemic situation of COVID-19 has not been effectively controlled currently.

With effective prevention and control in China, the number of discharged cases has increased significantly. Recently, during the follow-up of discharged patients, cases with repeated positive nucleic acid tests have been reported sporadically[2-5], which draw people's attention to the discharged COVID-19 patients. The explanation for this phenomenon is inconclusive currently, it raises the concern that discharged COVID-19 patients may be at risk of viral reactivation and be considered potential transmission of SASRS-CoV-2 infection.

Some previous research of COVID-19 discharged patients nucleic acid re-positive lasted within 2 months[6-8], presently, the persistent course of the 4 cases we are about to show lasts more than 3 months. This may provide an idea for long- lasting positive SARS-CoV-2 RNA tests in recovered COVID-19 patients.

## Case presentations

**Case 1** A 35-year-old man with a history of COVID-19 contact presented with cough, fever and short of breath. With ground glass opacities (GGO) chest

computed tomography (CT), he was clinically diagnosed with common COVID-19. After 28 days supportive treatment and complete symptoms relief, he was discharged from the hospital and quarantined in a hotel. In the hotel, his throat swab test was positive for SARS-CoV-2 (Day 54 from disease onset). And the asymptotic patient was readmitted into the hospital. With full supportive therapy, the patient was still positive for SARS-CoV-2 in throat swab and sputum on day 70, day 76, and day 92. He was positive for SARS-CoV-2 IgM and IgG (Day 76). On day 93 and 94, he turned negative for SARS-CoV-2 and was discharged from the hospital. SARS-CoV-2 infection lasted at least 92 days in patient #1.

**Case 2** A 64-year-old woman with a history of COVID-19 contact presented with fever and fatigue. Without significant improvement in private clinic, she was admitted into the hospital. Her throat swab test was positive (Day 33 from disease onset) and she was diagnosed with common COVID-19. With supportive therapy, her symptoms were relieved and pulmonary GGO was almost absorbed (Day 53). The patient was discharged. However, she was tested positive again in throat swab (Day 64). After the re-admission into hospital, the patient was asymptotical but positive for SARS-CoV-2 nucleic acid and IgG, negative for SARS-Cov-2 IgM (Day 67). PCR test in throat swab was still positive in Day 90. On day 91 and 92, the repeated SARS-CoV-2 nucleic acid tests were negative. She was discharged from the hospital. SARS-CoV-2 lasted at least 90 days in patient #2.

**Case 3** A 56-year-old woman presented with fever, chest tightness, short of breath and chest X-ray showing pneumonia. Her throat swab test was positive (Day 14 from disease onset) and she was diagnosed with common

COVID-19. With supportive therapy, her symptoms disappeared and pulmonary GGO was largely absorbed (Day 33). After 13 days from her discharge, her throat swab test was positive and re-admitted into the hospital (Day 46). She was empirically treated and discharged again from the hospital (Day 65) after the nucleic acid tests turned negative. During the self-quarantine, she was again positive in throat swab test and re-re-admitted into the hospital (Day 81). She was without evident symptoms. The patient was positive for SARS-CoV-2 specific IgG but negative for SARS-CoV-2 specific IgM. At Day 92, she was still positive in throat swab nucleic acid test but negative in blood and feces nucleic acid tests. In the repeated nucleic acid tests in different samples at Day 93/94, she was negative. Therefore, the patient was discharged at Day 95. SARS-CoV-2 persisted at least 92 days in patient #3.

**Case 4** A 60-year-old man with a history of COVID-19 contact presented with fatigue, fever and dyspnea. Chest CT showed GGO and he was diagnosed with severe COVID-19 (Day 9). With empirical therapy, he was relieved and self-quarantined in home. In the community test, his throat swab test was positive and re-admitted into the hospital (Day 25). With supportive therapy, his nucleic acid tests were still repeatedly positive (Day 52). And the patient was given thymalfasin to boost the immune system. At Day 60, he was discharged with negative nucleic acid tests. During the isolation, the patient turned repeatedly positive for SARS-CoV-2 nucleic acid (Day 72). He was re-re-admitted into the hospital. He complained cough, sputum production, and chest tightness. Chest CT showed interstitial pneumonia. Sera tests indicated the patient was positive for SARS-CoV-2 IgG but negative for virus specific IgM. With full supportive therapy, his nucleic acid tests finally turned negative at Day

109. And the patient was discharged at Day 111. SARS-CoV-2 persisted at least 108 days in patient #4.

## Discussion

The estimated time for COVID-19 varied, ranging from 15.6 days to 49.4 days[9]. In the present study, we reported 4 cases of COVID-19 with extended disease duration.

As the main entry route, pulmonary involvement was the main manifestation in patients with COVID-19. An autopsy pathological study of a ready-for discharge COVID-19 patient who succumbed to sudden cardiovascular accident revealed that SARS-CoV-2 remained in lung cells and caused lung lesions[10]. Chest X-ray maybe not as sensitive as CT to detect small but significant pulmonary exudates; thereby some patients with COVID-19 may be prematurely released before the full and true recovery. The second explanation for the early discharge was that the RT-PCR test may be false negative[6, 7]. Repeated tests in different samples before the discharge may decrease the risk of false negative results. In our study, RT-PCR tests were positive in sputum and throat swab but negative in blood, anal swabs or feces, which was different from other reports[11, 12]. We recommended testing multi-site specimen for virus surveillance in the re-admitted patients. The third but less likely cause for RT-PCR test positive results was due to the re-infection. There is still no direct evidence that recovered COVID-19 patients autonomously acquire complete immunity

against SARS-CoV-2. In the present study, however, all patients with COVID-19 were quarantined, significantly reducing the risk of re-exposure to SARS-CoV-2.

The RT-PCR test positive results in the discharged patients with COVID-19 may be from the true virus or less likely from virus fragments. In the 4 patients with extended duration of COVID-19, 3 patients were positive for SARS-CoV-2 specific IgG. In theory, the virus hidden in the body[10] may escape from the immune responses by mutation, which would increase the risk of re-emergence of new serotype of SARS-CoV-2 in future. In a recent study[8], RT-PCR of pharyngeal swabs and IgM/IgG antibodies against SARS-CoV-2 were negative for close contacts of discharged COVID-19 patients, they hold on prolonged presence of viral nucleic acid in clinically recovered COVID-19 patients was no associated with effective infectiousness. Besides, a recent study describe evidence that SARS-CoV-2 RNA reverse-transcribed and integrated into the human genome[13], however, the result is controversial currently.

This study is hampered by some limitations. First, whether the re-admitted patients with COVID-19 were asymptotic virus carrier[14] was not answered. Though virus may be hardly isolated in the late samples[15], virus culture should be explored to test the infectivity of RT-PCR positive respiratory samples. Second, the potential causes for the RT-PCR test positive results in recovered COVID-19 patients were unexplored. Third, the disease course of

COVID-19 in these patients may still develop. We should keep following these patients and better understand the disease course of COVID-19. SARS-CoV-2 persistence in the asymptotic populations would pose new challenges to global COVID-19 prevention and control strategies.

## Conclusion

In summary, we showed that the persistent course of SARS-COV-2 nucleic acid test positive in these 4 cases was prolonged, which provided some ideas for the long-term existence of SARS-COV-2 RNA in convalescent patients.

## List of abbreviations

SARS-CoV2: Severe acute respiratory syndrome coronavirus 2; COVID-19: Coronavirus disease 2019; RT-PCR: Reverse transcription-polymerase chain reaction; IgM: Immunoglobulin M; IgG: Immunoglobulin G.

## Acknowledgments

Not applicable.

## Authors’contributions

NJ and MH had the idea for and designed the study and had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. SL, CW, MZ, LZ, JX, WZ, YM, WD, and ZW collected the data. NJ, SL and CW analyzed the data and drafted the paper. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

## Funding

This study was funded by the Jiangsu Provincial Key Research and Development Program (BE2020616). We thank all patients involved in the study.

## Availability of data and materials

The datasets used during the current study are available from the corresponding author on reasonable request.

## Ethics approval and consent to participate

This study was conducted in accordance with the ethical committee of The First Affiliated Hospital of Nanjing Medical University (approval number 2020-SR-120).

## Consent for publication

Written consent was obtained from the patients for publication.

## Competing interests

All authors declare no conflict of interest.

## Author details

[1]Department of Respiratory and Critical Care Medicine, The First Affiliated Hospital of Nanjing Medical University, Nanjing 210029, China

[2]Key Laboratory of Antibody Techniques of National Health Commission, Department of Immunology, Nanjing Medical University, Nanjing 211166, China

[3]Department of Respiratory and Critical Care Medicine, The Affiliated Changzhou No.2 People's Hospital of Nanjing Medical University, Changzhou

213003, China

[4]Diagnosis and Treatment Research Center of Wuhan Infectious Disease of Chinese Academy of Medical Sciences, Wuhan 430023, China

[5]Department of laboratory, Wuhan Jinyintan Hospital, Wuhan 430024, China

[6]Department of Radiology, The First Affiliated Hospital of Nanjing Medical University, Nanjing 210029, China

## Reference

1. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72314 Cases From the Chinese Center for Disease Control and Prevention. JAMA.2020 2020-04-07;323(13):1239-42.

2. Lan L, Xu D, Ye G, Xia C, Wang S, Li Y, et al. Positive RT-PCR Test Results in Patients Recovered From COVID-19. JAMA.2020 2020-04-21;323(15):1502-3.

3. Xing Y, Mo P, Xiao Y, Zhao O, Zhang Y, Wang F. Post-discharge surveillance and positive virus detection in two medical staff recovered from coronavirus disease 2019 (COVID-19), China, January to February 2020. Euro Surveill.2020 2020-03-01;25(10).

4. Qu YM, Kang EM, Cong HY. Positive result of Sars-Cov-2 in sputum from a cured patient with COVID-19. Travel Med Infect Dis.2020 2020-03-01;34:101619.

5. Chen D, Xu W, Lei Z, Huang Z, Liu J, Gao Z, et al. Recurrence of positive SARS-CoV-2 RNA in COVID-19: A case report. INT J INFECT DIS.2020;93:297-9.

6. Xiao AT, Tong YX, Zhang S. False negative of RT-PCR and prolonged nucleic acid conversion in COVID-19: Rather than recurrence. J MED VIROL.2020 2020-10-01;92(10):1755-6.

7. Li Y, Hu Y, Yu Y, Zhang X, Li B, Wu J, et al. Positive result of Sars-Cov-2 in faeces and sputum from discharged patients with COVID-19 in Yiwu, China. J MED VIROL.2020 2020-10-01;92(10):1938-47.

8. Hong K, Cao W, Liu Z, Lin L, Zhou X, Zeng Y, et al. Prolonged presence of viral nucleic acid in clinically recovered COVID-19 patients was not associated with effective infectiousness. Emerg Microbes Infect.2020 2020-12-01;9(1):2315-21.

9. Sun J, Xiao J, Sun R, Tang X, Liang C, Lin H, et al. Prolonged Persistence of SARS-CoV-2 RNA in Body Fluids. EMERG INFECT DIS.2020 2020-08-01;26(8):1834-8.

10. Yao XH, He ZC, Li TY, Zhang HR, Wang Y, Mou H, et al. Pathological evidence for residual SARS-CoV-2 in pulmonary tissues of a ready-for-discharge patient. CELL RES.2020 2020-06-01;30(6):541-3.

11. Ling Y, Xu SB, Lin YX, Tian D, Zhu ZQ, Dai FH, et al. Persistence and clearance of viral RNA in 2019 novel coronavirus disease rehabilitation patients. Chin Med J (Engl).2020 2020-05-05;133(9):1039-43.

12. Wu Y, Guo C, Tang L, Hong Z, Zhou J, Dong X, et al. Prolonged presence of SARS-CoV-2 viral RNA in faecal samples. Lancet Gastroenterol Hepatol.2020 2020-05-01;5(5):434-5.

13. Zhang L, Richards A, Khalil A, Wogram E, Ma H, Young RA, et al. SARS-CoV-2 RNA reverse-transcribed and integrated into the human genome. bioRxiv.2020 2020-12-13.
14. Zhang J, Du Y, Bai L, Pu J, Jin C, Yang J, et al. An Asymptomatic Patient with COVID-19. Am J Respir Crit Care Med.2020 2020-06-01;201(11):1428-9.
15. Wolfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Muller MA, et al. Virological assessment of hospitalized patients with COVID-2019. NATURE.2020 2020-05-01;581(7809):465-9.