# Severe, Symptomatic Reinfection in a Patient with COVID-19

VIJAIRAM SELVARAJ, MD; KARL HERMAN, MD; KWAME DAPAAH-AFRIYIE, MD


## ABSTRACT

To date, there have only been a few reports of reinfections in COVID-19 patients. The possibility of being reinfected with COVID-19 is poorly understood. In this case report, we describe an individual who was initially diagnosed in April 2020 with COVID-19. Seven months later, he presented again to the hospital with shortness of breath and was found to have COVID-19 reinfection. We also summarize a list of all known cases of COVID-19 reinfection at this time.


**KEYWORDS:** SARS-CoV-2, COVID-19, reinfection, secondary infection, antibodies

## INTRODUCTION

Reinfection with COVID-19 is rare, with only a handful of cases reported among the 42 million cases worldwide. The susceptibility of previously infected patients to reinfection is not well understood. Reports of COVID-19 reinfection have been reported in Hong Kong, The Netherlands, Belgium, Ecuador, Israel and Australia.[1,2,3] The first case of reinfection in the United States was recently reported in a patient in Reno, Nevada.[4] We describe an individual with two instances of COVID-19 infection with distinct illnesses.

## CASE PRESENTATION

A male in his 70s tested positive for SARS-CoV2 in early April 2020. Twelve days later, he presented to the hospital with worsening shortness of breath. His past medical history was significant for obesity, chronic low back pain, neuropathy, asthma, obstructive sleep apnea, and hypertension. His home medications included Albuterol, Umeclidinium, Symbicort-Formoterol, Loratadine, Montelukast, Tamsulosin, and Valsartan-hydrochlorothiazide. On physical exam, he was tachypneic and unable to complete full sentences. His C-Reactive Protein (CRP), LDH, and ferritin were noted to be 19mg/L (0–10mg/L), 130IU/L (100–220IU/L), and 337ng/ml (22–322ng/ml). X-ray imaging showed mild, patchy mid- and lower-lung airspace disease bilaterally. He was able to maintain his oxygen saturation levels above 90% while ambulating on ambient air. He was given albuterol, antitussives, and discharged home from the Emergency Department. Follow-up X-ray imaging done three weeks later showed resolution of airspace disease and no acute process.

Nearly seven months later, he presented to the hospital again with shortness of breath and subjective fever. He reported no symptom relief despite using his nebulizer and completing a course of azithromycin. He reported that his wife and daughter tested positive for SARS-CoV-2 ten days prior to his admission. He tested negative for SARS-CoV-2 one week before admission. He also endorsed body aches, nausea, and malaise. On physical exam, he was noted to be hypoxic while ambulating, reaching 87% on ambient air. Lung examination revealed rales at bases. He was hospitalized and started on supplemental oxygen via nasal cannula.

The respiratory viral panel came back only positive for SARS-CoV-2. Immunoglobulin levels were normal. SARS-CoV-2 antibodies, including IgG at the time of admission were negative. His CRP, LDH, and ferritin were noted to be 77mg/L, 256IU/L, and 1,478ng/ml. D dimer level was 269ng/ml (0–230ng/ml). X-ray imaging showed multifocal airspace disease, greatest at the left lung base. He received Dexamethasone, Remdesivir and enrolled in a placebo-controlled Monoclonal Antibody study. He did not require negative SARS-CoV-2 antibodies before enrollment in the study since most cases are new infections. Presumably, a case of reinfection implies a lack of or inadequate serum antibodies to the virus. In view of initial concern for presumed bacterial infection, he also received two doses of ceftriaxone.

CRP trended down to 35.34mg/L at the time of discharge. He was eventually discharged home on 3 Liter/min supplemental oxygen after being hospitalized for three days.

## DISCUSSION

The human body has innate and adaptive immunity. When any viral infection occurs, IgM antibodies typically appear within one to two weeks. These antibodies subsequently mobilize against the virus and then begin to disappear slowly after that. A few weeks after an infection has cleared, IgG antibodies appear. Typically, IgG levels persist for many years, especially in cases of certain childhood viruses such as varicella. However, this is not the case with coronavirus infections.

Coronaviruses have been known to cause reinfections, similar to other to other viral causes of upper respiratory

tract infections. It appears that coronaviruses are adept at ensuring that the body's long-term response to the virus is not that powerful. Previous studies of MERS and SARS-CoV infections have shown that total binding and neutralizing antibodies decrease slowly over 1 to 3 years.[5,6] Everyone previously infected will have limited or no ability to protect themselves from reinfection. Studies have also shown that patients with more severe illness and prolonged viral shedding had higher antibody titers present for a longer duration of time.[7]

Most infected patients with SARS-CoV-2 begin to have detectable antibodies 10–14 days after symptom onset, though antibody levels in patients with mild disease may be low or undetectable[8]. There is a paucity of information about the degree to which this immune response provides protective immunity towards subsequent infections and this protection's longevity. A Chinese study showed that forty percent of asymptomatic individuals became seronegative and 12.9% of symptomatic individuals became seronegative in the early convalescent phase (eight weeks after infection).[9] In our case, it is unclear if the patient developed any antibodies following his initial infection or if he became seronegative over time. His SARS-CoV-2 antibodies were negative, although it also remains unknown if he specifically developed antibodies to the spike Receptor Binding Domain (RBD).

Similar to observations from prior case reports, our patient showed increased symptom severity during his reinfection.[1,2,3,4] Patients with mild or asymptomatic disease appear more likely to get reinfected. Postulated mechanisms include a higher dose of the virus, greater virulence, or antibody-dependent enhancement.[4,10] We could not assess if he was infected with phylogenetically different strains as virus samples from his first SARS-CoV-2 infection were not retained. Our patient did not suffer from any immunological disorders and was not taking any immunosuppressive medications that would facilitate his reinfection. His immunoglobulin levels were normal. There have been other case reports of reinfections where patients have also remained mostly asymptomatic or shown decreased symptom severity, implying some degree of immunity from their first infection (**Table 1**).

Our case has implications for the role of monoclonal antibody and vaccination in patients infected with SARS-CoV-2. Based on prior reports of reinfection, it is evident that the body's innate immunity will not provide lifelong protection. There is also an apparent paradox between declining antibody levels and low incidence of reinfection, implying many immune mechanisms at work, including T lymphocytes. Specific questions remain unanswered. The first question is how long will innate, monoclonal antibody-mediated, or vaccine-mediated immunity last. The second question is will one vaccine be sufficient to cover all SARS-CoV2 variant strains. Lastly, will the administration of monoclonal antibody to patients with mild or asymptomatic disease prevent or reduce reinfection rates. Given increased symptom severity during reinfection, our case also highlights the need to monitor these patients more closely on a short-term and long-term basis. As more cases of reinfection arise, we will need more research to better understand the mechanisms that drive it in order to control and reduce infection rates worldwide.

**Table 1.** Current Cases of COVID-19 Reinfection Worldwide

| Countries | Number of Cases | Status | Severity of Reinfection |
|---|---|---|---|
| India | 6 | Confirmed | Mild |
| Spain | 4 | Confirmed | Mild, Serious |
| Qatar | 4 | Confirmed | Mild |
| The Netherlands | 4 | Confirmed | Mild, Serious |
| United States | 3 | Confirmed | Serious |
| Belgium | 3 | Confirmed | Mild |
| Mexico | 3 | Presumed | Unknown |
| Hong Kong | 1 | Confirmed | Mild |
| Ecuador | 1 | Confirmed | Serious |
| Israel | 1 | Confirmed | Mild |
| Sweden | 1 | Confirmed | Mild |
| Brazil | 1 | Confirmed | Serious |
| Pakistan | 1 | Presumed | Serious |
| Australia | 1 | Presumed | Mild |

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## Authors

Vijairam Selvaraj, MD, Division of Hospital Medicine, The Miriam Hospital; Warren Alpert Medical School of Brown University, Providence, RI.

Karl Herman, MD, Division of Hospital Medicine, The Miriam Hospital; Warren Alpert Medical School of Brown University, Providence, RI.

Kwame Dapaah-Afriyie, MD, Division of Hospital Medicine, The Miriam Hospital; Warren Alpert Medical School of Brown University, Providence, RI.

## Correspondence

Vijairam Selvaraj, MD
The Miriam Hospital
164 Summit Ave, Providence, RI, 02906
413-271-0421
vijairam.selvaraj@lifespan.org