

# The second wave of desaturation in coronavirus disease 2019

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## Abstract

After a complete symptomatic recovery from coronavirus disease 2019 pneumonia, the second phase of desaturation is a new phenomenon that is being increasingly observed. Two possible mechanisms behind it can be a continued subclinical infection and lung fibrosis. We have presented a case with the former mechanism, who responded well to steroids.

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## Introduction

In late 2019, a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was identified in humans and led to a pandemic [1]. Understanding the spectrum of this disease, its prevention and its optimal clinical management is the current focus of physicians and researchers around the globe. Many drugs have been and are being investigated for their role in the management of coronavirus disease 2019 (COVID-19). Remdesivir has shown potential in decreasing hospital stay among patients with COVID-19 [2]. Dexamethasone has shown a mortality benefit in severe COVID-19 [3]. However, the current management of SARS-CoV-2 pneumonia and acute respiratory distress syndrome focuses mainly on providing supportive measures [4].

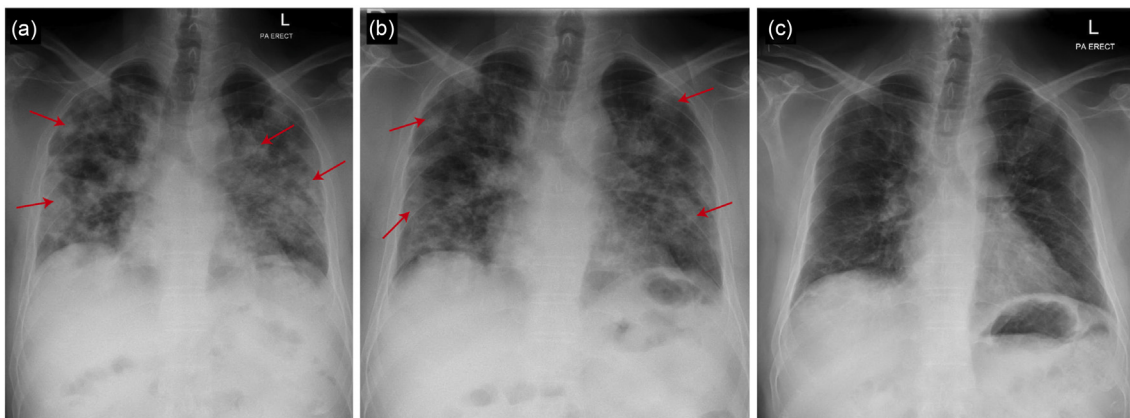
The clinical course in COVID-19 varies from asymptomatic disease to fulminant acute respiratory distress syndrome [5]. There is anecdotal evidence about persisting dyspnoea following treatment of COVID-19. Post-COVID pulmonary fibrosis is hypothesized to be one of the aetiologies behind this phenomenon [6]. Also, post-treatment; an asymptomatic

patient may develop a subclinical infectious process. This subclinical infection may lead to a second phase of desaturation. There are currently no guidelines on the treatment of this second phase of desaturation. We present a case in which we monitored the response to steroids in a patient who had desaturation secondary to an ongoing residual subclinical inflammation after he was treated for COVID-19 pneumonia. Our patient had an excellent response to steroids; hence we postulate that steroids could be a potential treatment for such patients.

## Case presentation

A 53-year-old gentleman with a past medical history of diabetes mellitus, hypertension and dyslipidaemia presented to the hospital with a 1-day history of dyspnoea. He was treated for COVID-19 pneumonia and was discharged 1 day before his readmission. His initial presentation was with dyspnoea, fever, fatigue and a dry cough. Investigation revealed a positive SARS-CoV-2 RT-PCR test with bilateral infiltrates on chest X-ray (Fig. 1a).

Initially he required 3–4 L of oxygen to maintain saturation, but the requirement increased in the subsequent days and reached up to 13 L of oxygen via a non-rebreather mask. He was treated with favipiravir and dexamethasone for 10 days, according to the local guidelines at the time. The patient gradually improved, and his oxygen requirement decreased. He



**FIG. 1.** Chest X-rays of patient: (a) at the time of COVID-19, showing bilateral infiltrates, (b) at the time of second admission, showing similar changes, (c) in follow-up clinic with improvement in infiltrates.

was discharged from the hospital in an asymptomatic condition, with 100% saturation on room air. His repeated SARS-CoV-2 RT-PCR test was negative.

One day after discharge, the patient presented with a new-onset shortness of breath at rest and exertion. He was requiring 2–3 L of oxygen to maintain oxygen saturation ( $SpO_2$ ) above 94%, and was tachypnoeic (26 breaths per minute). He was afebrile and did not have any other symptoms. Chest examination revealed bi-basal crackles, with the rest of the physical examination unremarkable.

Chest X-ray was repeated and did not show significant changes compared with the previous one (Fig. 1b). A CT pulmonary angiography showed no evidence of pulmonary embolism. However, it was significant for extensive bilateral patchy areas of ground-glass opacities and patchy areas of consolidations with air bronchograms (Fig. 2).

He was tested again for COVID-19, but the RT-PCR result was negative, ruling out a possibility of reinfection. The sepsis workup did not reveal any bacterial growth (including *Mycoplasma pneumoniae*, *Legionella pneumophila* and *Chlamydia pneumoniae*). Nasopharyngeal PCR tests for common respiratory viruses (including influenza virus, parainfluenza virus, respiratory syncytial virus and Middle East respiratory syndrome coronavirus) were negative. A bronchoscopy performed to rule out tuberculosis, eosinophilic pneumonia or pulmonary haemorrhage revealed none of these.

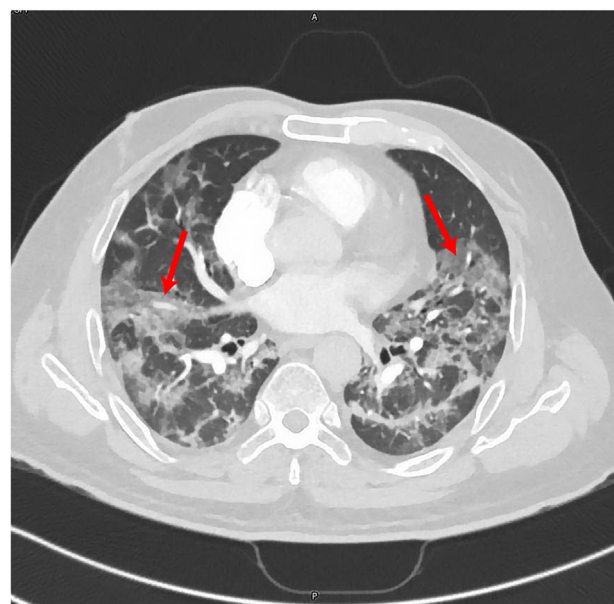
As the patient continued to have desaturation, a multidisciplinary team decided to start a trial of 60 mg prednisolone for 2 weeks. He responded very well, and oxygen requirement decreased. He was off oxygen at rest in 2 days and was discharged with a follow up in the pulmonary clinic.

Repeated chest X-ray 2 weeks after discharge showed significant regression on bilateral infiltrate (Fig. 1c). Pulmonary function test was performed, which showed a restrictive

pattern with decreased diffusing capacity for carbon monoxide (Fig. 3). A 6-minute walking test showed a clear improvement compared with his previous condition, when was not able to complete more than 3 minutes of walking.

## Discussion

Infection with SARS-CoV-2 has a wide spectrum of clinical course and can involve various organs. Lungs are the most common organs involved. Presenting complaints include a dry cough, fever, myalgias, headache, dyspnoea, sore throat, diarrhoea, vomiting, ageusia and anosmia [7]. Most cases of SARS-



**FIG. 2.** CT pulmonary angiogram, showing post-infection changes.

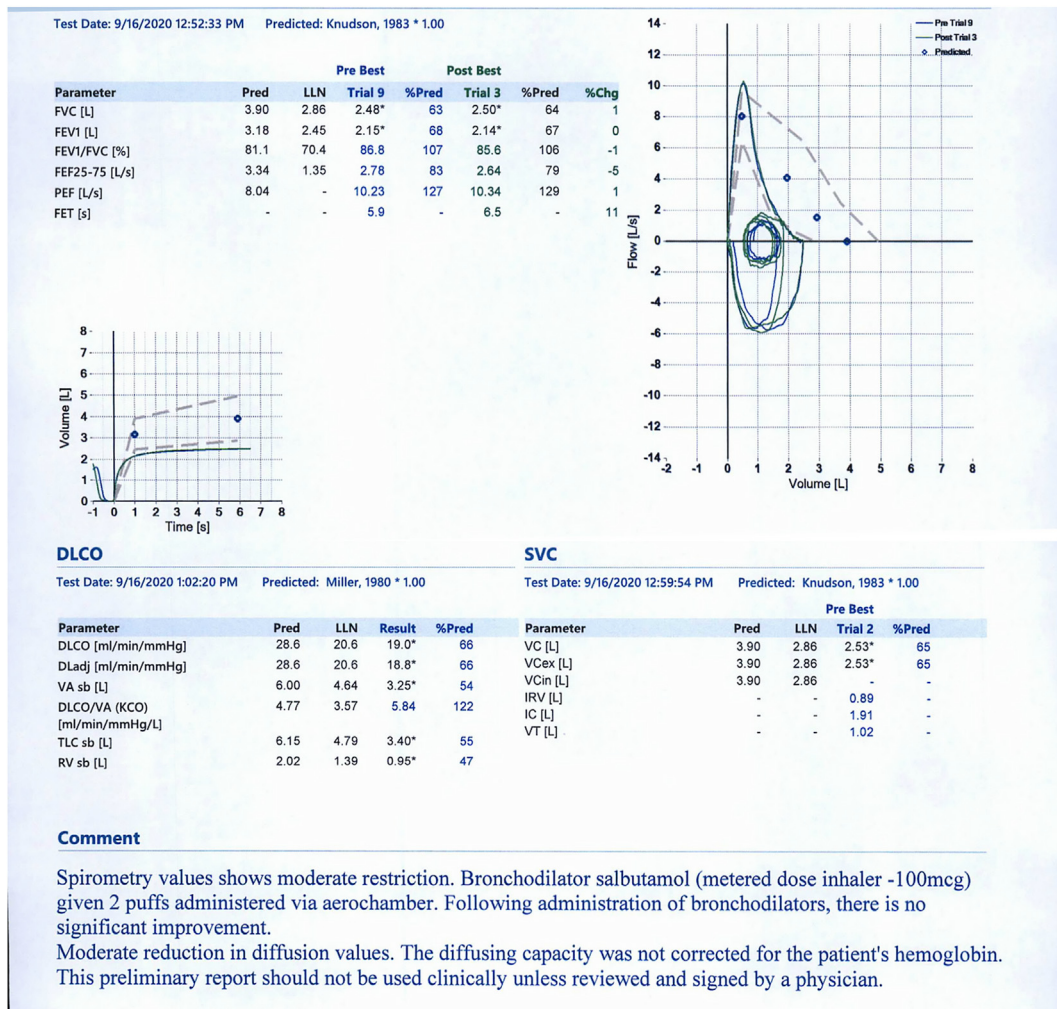


FIG. 3. Pulmonary function test (PFT), revealing a restrictive pattern with decreased diffusing capacity for carbon monoxide (DLCO).

CoV-2 infection are mild to moderate, whereas around 20% progress to severe and critical illness. The long-term respiratory sequelae of COVID-19 remain unclear, and may depend on disease presentation [8].

The greater part of research related to SARS-CoV-2 focuses on its management. To date, the treatment is largely supportive. Many drugs have been and are being investigated for this purpose, including hydroxychloroquine, interleukin-6 pathway inhibitors such as tocilizumab, convalescent plasma, remdesivir and dexamethasone [2,3,9-11]. Among all the tested treatment modalities, the most promising results are from remdesivir and dexamethasone, as the preliminary reports show a reduction in hospital stay from the former and a reduced mortality with the latter.

The RECOVERY trial is investigating the role of dexamethasone in SARS-CoV-2 infection. Initial results show a decreased 28-day mortality in the treatment arm. However, this effect is seen only in the subset of patients requiring invasive and non-

invasive mechanical ventilation [3]. Consequently, current guidelines recommend the use of dexamethasone only in moderate to severely ill patients [12].

In some patients, a second phase of dyspnoea is seen after an interval asymptomatic recovery phase in patients successfully treated for COVID-19 pneumonia or acute respiratory distress syndrome. We propose two possible mechanisms behind this, post-infection fibrotic changes in the lungs or a continued subclinical infective process, which becomes symptomatic again after some time. Fibrotic lung changes are reported in survivors with COVID-19 pneumonia and abnormalities in lung function have been detected in patients with COVID-19 shortly after their discharge from hospital [6,13]. Our patient had ongoing lung damage despite viral clearance and symptomatic recovery. This resulted in chronic lung changes as the pulmonary function test revealed a restrictive pattern with decreased diffusion capacity.

Pulmonary fibrosis usually occurs secondary to dysregulated healing processes. Chronic inflammation can lead to fibrosis. The changes in the cellular and molecular environment in the lung tissue secondary to viral infection, as found in COVID-19, are the key factors behind the fibrosis [14].

The ongoing damage takes place in the tissues secondary to the inflammation, leading to an over expression of inflammatory cytokines, including transforming growth factor- $\beta_1$ , tumor necrosis factor- $\alpha$ , interleukin-1 and interleukin-6. This in turn stimulates the proliferation of type 2 alveolar cells and increased fibroblast recruitment [15,16]. Eventually, the cascade can lead to an increase in the production and deposition of extracellular matrix, impairing gas exchange and leading to hypoxaemia [16].

The long-term reversible and irreversible respiratory sequelae of COVID-19 remain obscure, as does the patient population at high risk of developing them. Our patient had an excellent recovery with steroids. Authors are of the view that a large-scale randomized controlled trial is required to establish the efficacy of steroids in post-COVID-19 recurrent dyspnoea.

## Conclusion

A second wave of desaturation after resolution of symptoms post-COVID-19 treatment is a rare phenomenon. It can be secondary to an ongoing subclinical infection or due to fibrosis. The role of steroids is not studied in this scenario. Our patient had a dramatic response to steroids, indicating a possible role in reducing the post-infection inflammation. Larger studies are needed to investigate the management of post-COVID-19 desaturation.

## Ethics approval

The case was approved by Medical Research Centre Qatar before submission, and written informed consent was obtained from the patient for publication of this case report and accompanying images.

## Availability of data and materials

Not applicable.

## Conflict of interest

All authors declare no potential conflicts of interest related to the publication of this case series.

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None.

## Authors' contributions

Mohd A obtained the patient consent; and the literature was reviewed by FA, AB, ZY, Mohd A, Mousa A, AE and AA. The manuscript was written by FA, ZY and Mohd A; the radiology section, both writing and images, was by AB; critical review and modifications were made by FA, ZY, AE and AA; and the final review and approval were by FA, AB, ZY, Mohd A, Mousa A, AE and AA.

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