ISSN: 1607-8322, e-ISSN: 2220-5799 **Anaesthesia, Pain & Intensive Care**
Vol 26(3); June 2022 DOI: 10.35975/apic.v26i3.1905

CASE SERIES **INTENSIVE CARE / COVID-19**

Pneumothorax in COVID-19 patients on non-invasive ventilation: a case series

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Abstract

COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and the disease mainly affects the lungs. A rare complication reported in these patients has been pneumothorax, whether spontaneous or iatrogenic in ventilated patients. Sudden desaturation or acute deterioration in clinical conditions should immediately raise a suspicion of pneumothorax, and the clinicians must take appropriate measures without any delay.

We present a series of 7 cases of COVID-19 admitted to our ICU who developed primary spontaneous pneumothorax. All these patients were on non-invasive ventilation (NIV). They did not have any history of underlying lung disease before the existing ailment, and all of them were non-smokers.

Abbreviations: SARS-CoV-2 - acute respiratory syndrome coronavirus-2; NIV - non-invasive ventilation; ARDS - acute respiratory distress syndrome; COVID – coronavirus disease; RT-PCR - Reverse Transcription Polymerase Chain Reaction test; ROSC - return of spontaneous circulation; Pplateau – plateu pressure

Key words: COVID-19; Pneumothorax; Non-invasive ventilation; NIV

Citation: Yadav I, Lakhanpal M, Aggarwal A, Kumar R. Pneumothorax in COVID-19 patients on non-invasive ventilation: a case series. Anaesth. pain intensive care 2022;26(3):410-415. **DOI:** 10.35975/apic.v26i3.1905

Received: April 19, 2022**; Reviewed:** April 22, 2022**; Accepted:** April 24, 2022

1. Introduction

Coronavirus disease 2019 (COVID-19) is a communicable disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The most common symptoms of COVID-19 are fever, cough, muscular weakness and shortness of breath.

Apart from antiviral drugs and immunomodulators, the primary mode of treatment includes oxygen supplementation, non-invasive ventilation (NIV), prone positioning, and mechanical ventilation. [1] Barotrauma causing pneumomediastinum and pneumothorax are common complications in mechanically ventilated patients of acute respiratory distress syndrome (ARDS), with a reported rate of up to 15% in some multicenter randomized controlled trials. [2] Spontaneous pneumothorax was reported as a complication of severe acute respiratory syndrome (SARS), caused by SARS-CoV-1, with a frequency of 1.7% in hospitalized patients. [3]

Here we present a case series comprising of seven patients, who suffered from pneumothorax during their stay in the ICU. Patients admitted to ICU between October 2020 to May 2021 were reviewed for the presence of pneumothorax. A total of 90 COVID-19 patients were admitted to ICU during the study period. Out of these, 42 were on NIV or mechanical ventilators. Seven patients developed pneumothorax, and five patients were discharged from ICU. The other two

expired due to other complications related to COVID-19.

In this case series, we will discuss this unusual complication of COVID-19 infection, i.e., spontaneous pneumothorax

2. Case Report 1

Our first patient was a 73-year-old female with diabetes and bronchial asthma, who presented with a history of dyspnea, fever, sore throat, and dry cough for the last one week. On examination, she was febrile but not tachypneic, nor in distress. Reverse transcription Polymerase Chain Reaction (RT-PCR) test was positive. Her oxygen saturation (SpO_2) was 80% on room air. Based on the examination, she was categorized as a severe case. She was put on non-rebreather mask (NRBM) with a flow of 12 L/min O_2 maintaining a saturation at 94%. On admission, a chest X-ray (CXR) demonstrated infiltrates in the left lower zone. The patient was prescribed antibiotics e,g, inj. piperacillin, tazobactum, and clindamycin, anticoagulant (inj. heparin as well as inj. dexamethasone, guided by the institutional protocol. Two days later, she desaturated and her SpO_2 fell to 82%, and was put on non-invasive ventilation (NIV) support with the following settings; FiO_2 = 0.6, PEEP = 6 cmH_2O, and P support = 12 6 cmH_2O. Repeat CXR showed worsening of the bilateral infiltrates. Her oxygen requirement and NIV pressure support progressively increased to FiO_2 = 1, PEEP = 10 cmH_2O, P support = 16 cmH_2O). The next day, a repeat CXR showed right-sided pneumothorax (Figure 1).

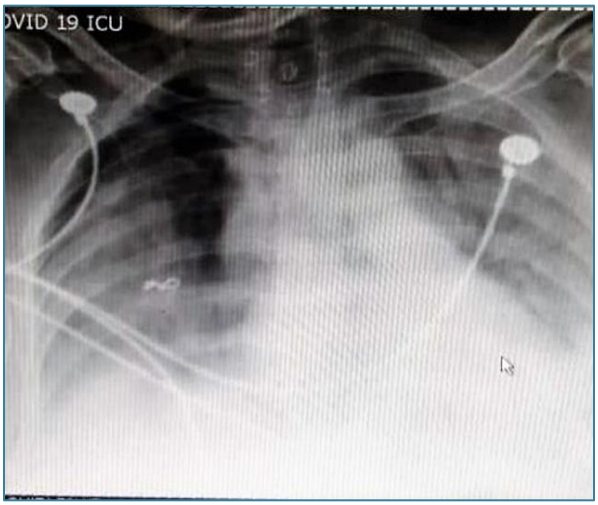

Figure 1: X-ray shows right pneumothorax

A right chest tube was inserted. A follow-up chest radiograph showed a resolution of the pneumothorax. Her condition deteriorated on NIV, so she was put on mechanical ventilation with a FiO_2 = 0.8, PEEP = 8 cmH_2O, tidal volume = 350 ml, RR = 18/min, maintaining SpO_2 at 94%. Her condition remained critical despite best possible ventilator adjustment (FiO_2 = 1, PEEP = 12 cmH_2O). Proning was done but still no improvement. She suddenly developed bradycardia and hypotension (on noradrenaline infusion) and went into asystole. Full protocol of ACLS was started. Despite 30 min high-quality CPR, return of spontaneous circulation (ROSC) could not be achieved, so the patient was declared dead.

3. Case Report 2

A 71-year-old man presented with a short history of fever, dry cough, headache, and dyspnea. The patient was febrile, tachypneic (RR = 30/min), COVID test was positive, and he was categorized as a severe case. His oxygen saturation was 78% on room air, so the patient was put on NIV with FiO_2 = .6, PEEP = 6 cmH_2O, and P support = 12 cmH_2O. His SpO_2 was 94% on these settings. The laboratory test showed raised CRP. The initial CXR showed diffuse patchy infiltration. He received inj. piperacillin-tazobactum, inj. clindamycin, inj. dexamethasone, and inj. heparin. A few days later, he complained of shortness of breath and developed hypoxia. NIV settings were changed to FiO_2 = 1, PEEP = 8 cmH_2O, and P support = 12 cmH_2O. A repeat CXR showed bilateral pneumothorax. He was managed with bilateral thoracostomy and chest tube insertion (Figure 2). Three days later, the patient's COVID report came out to be negative. He was transferred to the non-COVID ICU at another hospital.

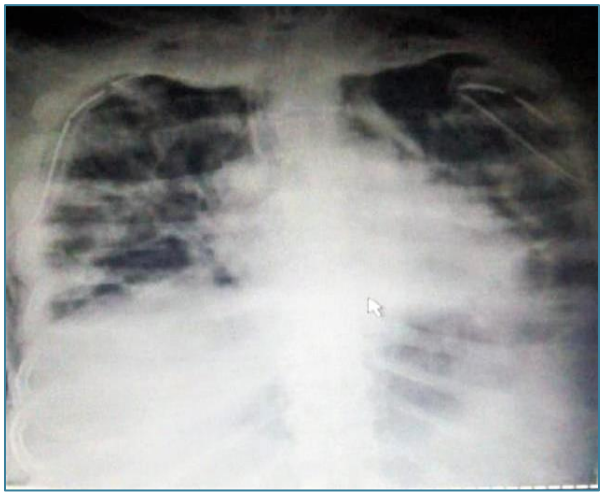

Figure 2: X-ray shows bilateral pneumothorax with a bilateral chest tube in situ.

4. Case Report 3

An 86-year-old woman presented with a two weeks history of dry cough, fever and fatigue. On presentation, she was febrile, tachypneic, and hypoxic (SpO_2 = 56%).

She was put on NIV support, with FiO_2 = 1, PEEP = 12 cmH_2O, and P support = 16 cmH_2O. She maintained saturation at 96%. Her blood laboratory reports showed lymphopenia and elevated inflammatory markers. Chest X-ray showed diffuse infiltrates, hence, she was categorized as a severe COVID-19 case. She was started on broad-spectrum antibiotics, corticosteroids, and anticoagulants. A few days later, the patient became more hypoxic with increased work of breathing, requiring mechanical

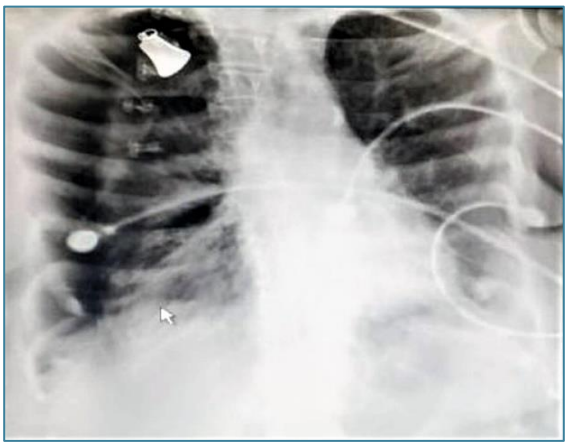

Figure 3: X-ray shows right-side pneumothorax

ventilation. She was kept on volume control mode with: RR = 18 bpm, TV = 400 ml, FiO_2 = 0.6, and PEEP = 10 cmH_2O. Her peak inspiratory pressure (PIP) and plateau pressures ($P_{plateau}$) were 27 and 23 cmH_2O respectively. Eight days later, her PCR report came negative. On 13th day she was extubated following proper weaning protocol and put on NIV FiO_2 0.5, PEEP = 8 cmH_2O, and P support = 12 cmH_2O, maintaining saturation of 93%. On 15th day, the patient was noted to be more hypoxic, requiring high FiO_2 on the NIV. Her CXR revealed right side pneumothorax (Figure 3). A chest tube was inserted. Her pneumothorax resolved within two days. She was later transferred to the ward and discharged in good condition with a follow-up plan.

5. Case Report 4

A 54-year-old woman, with a history of diabetes and hypothyroidism, presented with seven days history of dry cough and fever. On presentation, she was febrile, tachypneic, and hypoxic (SpO_2 = 74%), requiring NIV support with FiO_2 = 0.8, PEEP = 8 cmH_2O, and P support = 12 cmH_2O maintaining saturation at 93%. Her blood laboratory reports showed elevated inflammatory markers. X-ray showed bilateral infiltrates. She was started on broad-spectrum antibiotics, corticosteroids, anticoagulation, and inj. heparin. On the 10th day, the patient was put on NIV with FiO_2 = 1, PEEP = 12 cmH_2O, and P support = 16 cmH_2O because of low PO_2. But seeing no improvement in her PO_2 levels despite high NIV support and increased breathing rate, the patient was put on mechanical ventilation, with the following settings; volume control mode (VCV), RR = 18 bpm, TV = 400 ml, FiO_2 = 0.6, and PEEP = 10 cmH_2O. Her PIP and $P_{plateau}$ were 26 and 24 cmH_2O, respectively. CXR revealed left pneumothorax (Figure 4). A left-sided chest tube was placed. Her pneumothorax resolved within two days. On 15th day, on the family's request, the patient was shifted to a higher center for further management.

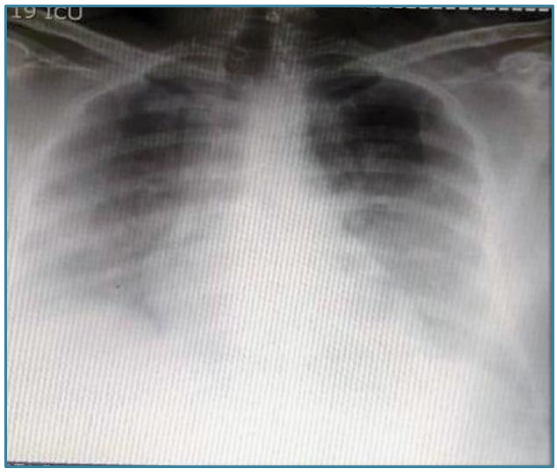

Figure 4: X-ray shows left side pneumothorax.

6. Case Report 5

A female patient 42 y old, came with a history of dyspnea and cough for one week with a COVID positive report. On examination, she was febrile, tachypneic, and had a saturation of 82% on room air, so she was labeled as a severe case of COVID pneumonia. She was put on NRBM support @ 15 L/min oxygen. Since she did not maintain saturation, she was put on NIV with FiO_2 = 0.7, P support = 12 cmH_2O, and PEEP 6 cmH_2O. She was given institutional protocol

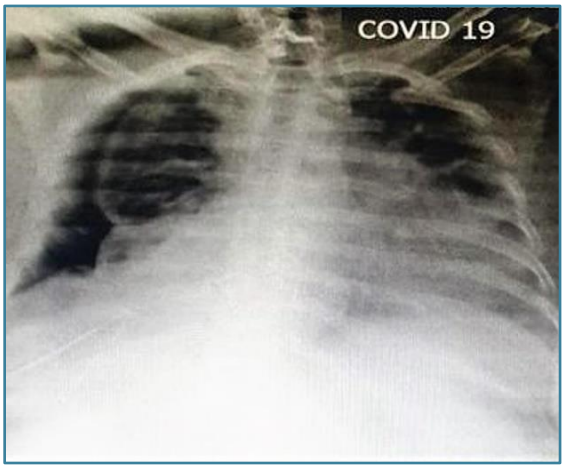

Figure 5: X-ray shows right-side pneumothorax.

antibiotics, antivirals, anticoagulants, and steroids. Her oxygen demand gradually decreased to 7 L oxygen on face mask and saturation improved to 96-97%. On Day 5, her condition deteriorated, and saturation dropped to 80%, for which urgent CXR was done, which revealed right-sided pneumothorax (Figure 5). An immediate right chest tube was inserted, after which the patient's condition improved. Over a period of three days, her oxygen demand dropped to 4 L. Once the requirement came down to 2 L and after a COVID negative report, she was transferred to a non-COVID facility on Day 17.

7. Case Report 6

A 64 y old female presented with a history of dyspnea, fever, and cough for five days, with a COVID positive report. On examination, she was febrile, tachypneic, with labored breathing, and with SpO_2 of 55% on room air, so she was categorized as a severe case of COVID pneumonia. She was put on NIV with FiO_2 = 1 and P support of 14 cmH_2O. The patient did not show any clinical improvement, so she was intubated and put on VCV, FiO_2 = 1, PEEP = 10 cmH_2O, RR = 25/min, and TV= 400 ml. Even on these settings, her SpO_2 remained 70-75%. Antibiotics, antivirals, steroids, and anticoagulants were started. Gradually saturation improved to 88-90%. On Day 4, her condition further deteriorated, and saturation dropped to 50%. Urgent CXR was done, which showed right-sided pneumothorax (Figure 6). An immediate right sided chest tube was inserted. However, the patient's condition didn't improve, and she went into cardiac arrest and could not be revived.

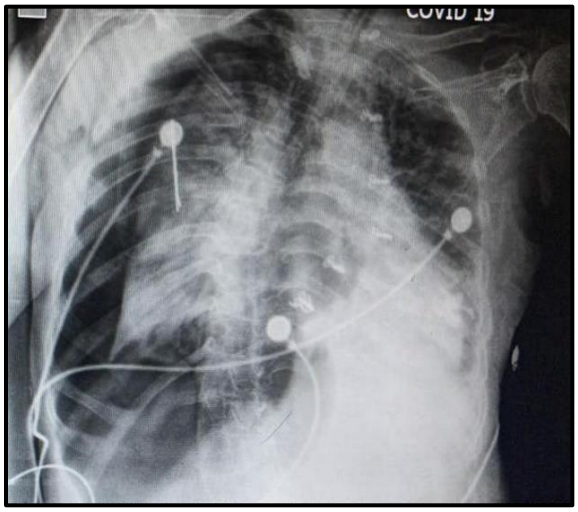

Figure 6: X-ray shows right-side pneumothorax

8. Case Report 7

A male patient, 38 y, came with a history of cough, dyspnea, and fever for four days with a COVID positive report. On examination, he was febrile and tachypneic with a saturation of 78% on room air. He was categorized as a severe case of COVID pneumonia. He was put on NIV with FiO_2 0.9, PEEP = 6 cmH_2O, and P support =12 cmH_2O, on which he maintained a saturation of 96-97%. Antibiotics, antivirals, steroids, and anticoagulants were started. On Day 13, his condition deteriorated with RR 40-45/min and SpO_2 = 75%. His urgent CXR showed left-sided pneumothorax

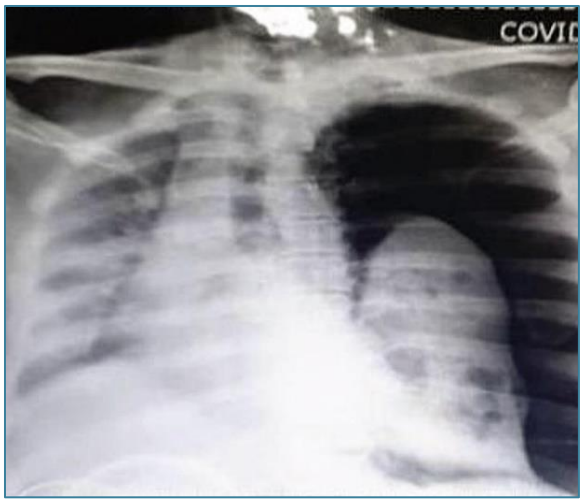

Figure 7: X-ray shows left side pneumothorax.

(Figure 7). Immediate left sided chest tube was placed, and saturation improved to 92-93%. NIV support was reduced. On Day 14 patient was shifted to a non- COVID facility after obtaining a COVID negative report.

9. Discussion

Pneumothorax is the presence of air in the pleural cavity, and it could be spontaneous (primary or secondary) or traumatic. Traumatic pneumothorax occurs due to some trauma or while performing central line insertion and pacemaker insertion procedures. Spontaneous pneumothorax can further be classified as primary or secondary. Primary pneumothorax occurs in the absence of any noticeable lung disease whereas a secondary pneumothorax occurs due to underlying lung pathology. It usually develops spontaneously in COVID-19 patients. [4]

Retrospective studies of patients with COVID-19 suggested that pneumothorax might occur in 1% of those requiring hospital admission, 2% in patients requiring Intensive Care Unit (ICU) admission, and 1% of patients dying from the infection. [5,6] More recently, the rate of barotrauma, comprising both pneumothorax and pneumomediastinum. in ventilated patients, has been reported as 15%. [7, 8]

We received 42 COVID-19 patients on NIV or mechanical ventilators. Out of these, seven patients developed primary spontaneous pneumothorax. This

constitutes a rate of 16.66%. All these seven patients were on NIV with high PEEP and pressure support. None of the cases had any pre-existing lung disease, and all were non-smokers. Most of them had positive outcomes after conservative management and chest tube insertion.

The association of pneumothorax with COVID-19 can be due to multiple mechanisms. Initially, it was thought to be because of barotrauma due to high PEEP and high pressure support. Later on, many case reports and studies showed that even patients who were not on NIV or mechanical ventilator, could also develop spontaneous pneumothorax, thus suggesting that there are other contributing factors to it.

Cyst or pneumatocele formation has been documented as a radiological consequence of COVID-19 soon after the initial outbreak, which can be another cause of pneumothorax. [9, 10] Previously reported cases found that cyst formation was not restricted to patients receiving positive-pressure ventilation, suggesting that barotrauma alone cannot be accounted for these findings. [10]

Other possible factors for pneumothorax in COVID-19 may be persistent coughing resulting in increased intrathoracic pressure in underlying pleural abnormalities or alveolar damage from COVID-19 pneumonia-related inflammation or ischemic parenchymal damage. [11]

Methylprednisolone, which is a part of the treatment of COVID 19, was thought to affect lung healing. The presence of a higher peak serum LDH and peripheral leucocyte count indicated a greater extent of lung injury, thus raising the risk of a pneumothorax. [12]

Pulmonary embolism was reported in some cases of COVID 19, and related infarction can result in parenchymal cavitation with subsequent pleural rupture leading to a pneumothorax.[13]

None of the patients on a mechanical ventilator with high PEEP developed pneumothorax in our case series. It only developed in patients with NIV, which adds on as one of the contributory factors indicating multiple confounding and contributory factors causing pneumothorax, barotraumas being just one of them.

10. Conclusion

Spontaneous pneumothorax is a rare complication of COVID-19 viral pneumonia. It may occur at any time during the disease. Patients with baseline ground-glass opacities and consolidations and those on NIV appear to be at a high risk. Sudden desaturation or acute deterioration in clinical conditions should raise a suspicion of pneumothorax. Early detection can save the patient with a simple and bedside chest tube insertion procedure. Thus clinicians should be vigilant about the diagnosis and treatment of this complication.

11. Conflict of Interest

None declared by the authors.

12. Financial Disclosures

No institutional or industry funding was involved in the study.

13. Consent of patients

Written consent was obtained from every patient to use his data and picture in this case series for educational purposes.

14. Authors' contribution

All authors contributed in the management of the patients mentioned in this case series, as well as preparation of the manuscript.

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