Pneumomediastinum and Pneumopericardium as Uncommon Complications of COVID-19 Infection: A Review Article

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Abstract

There is an emerging body of literature describing an increasing incidence of pneumomediastinum and, to a lesser extent, pneumopericardium as a complication of COVID-19. However, the literature lacks information regarding patients’ characteristics and a general view of this unusual condition. The purpose of this paper is to summarize the current literature on this phenomenon. In this study, we summarize the risk factors/etiology, imaging modalities, management, and prognosis of known cases in the literature. In total, 48 articles were included in the study, ranging from case reports to case series. Most patients were male (85.5%). The overall mortality rate was 27.1% and the recovery rate was 62.5%.

Introduction And Background

Late in 2019, a new respiratory infectious disease emerged throughout the world, which was then called coronavirus disease 2019 (COVID-19). COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. Human-to-human transmission can occur from aerosols or during medical procedures [2]. Symptoms may occur between two days to two weeks after being exposed to the virus. The most common symptoms are fever, cough, shortness of breath, fatigue, headache, loss of taste or smell, sore throat, nasal congestion, runny nose, nausea or vomiting, and diarrhea [3].

The severity varies from asymptomatic to severe and life-threatening [4]. Serious complications may develop such as pneumothorax [5], pneumopericardium, and pneumomediastinum as reported by Hazariwala [6]. Pneumomediastinum refers to the presence of air in the mediastinum. In spontaneous pneumomediastinum (SPM), there is no known cause, while the etiology in secondary pneumomediastinum is identified [7]. Pneumopericardium occurs when air enters the pericardial sac through a defect near the ostium of the pulmonary veins [8]. This review is intended to provide information on the reports of pneumomediastinum and pneumopericardium that developed in patients with COVID-19 infection. This study examined the risk factors, possible etiologies, imaging modalities, management, prognosis, and characteristics of reported cases.

Review

Methods

An extensive literature review was conducted using PubMed, EMBASE, and Google Scholar databases to find all relevant cases. Articles that were published from inception to 1 December 2021 were included in the review. The obtained search strategy comprises the following keywords and MeSH terms “COVID-19”, “COVID-19”, “SARS-CoV-2”, “SARS-CoV-2”, “SARS-CoV”, “novel coronavirus”, “pneumopericardium”, “PP”, “pneumomediastinum”, “SPM”, and “mediastinal emphysema”. Animal studies and non-English investigations were excluded from our search.

The analysis of the current study was conducted using IBM SPSS version 23 for Mac (IBM Corp., Armonk, NY), in which patients’ demographical data, past medical history (known comorbidities), intubation requirement, diagnosis, radiological modality, and outcomes were calculated. Descriptive analysis was used for presenting the data; categorical variables were demonstrated as frequencies and percentages, while continuous variables were demonstrated as mean ± standard deviation.

Results

A total of 48 articles have been found reporting cases of pneumomediastinum and pneumopericardium in patients with COVID-19 (Table 1). The majority of cases were reported among male patients. The minimum age reported was 17 years, and the maximum was 82 years (mean 55.3 ± 14.5). Intubation was not required in more than half of the patients. The outcome of the patients varied, in which 31.25% of the cases died, while 64.58% of them achieved recovery. (Mean recovery time was 19.8 ± 13.5 days.)
| No | Reference | Age (years) | Sex | Known comorbidities | Clinical symptoms at presentation | Intubation requirement | Diagnosis | Radiological modality | COVID-19 management | PM/PP management | Outcome |
|----|-----------|-------------|-----|---------------------|-----------------------------------|------------------------|-----------|----------------------|-------------------|------------------|---------|
| 1  | Singh, et al. [9] | 33 | M | NKC | 13 days of fever, body aches, SOB, cough, headache, and chest pain | No | PM and PP | Chest CT | Oxygen via nasal cannula, oral azithromycin | Conservative | Recover after 6 |
| 2  | Li, et al. [10] | 68 | M | Hypertension, GERD, and acute anuric renal failure | 2 weeks of fever, chills, cough, and SOB | Yes, before diagnosis | PM and PP | CXR and chest CT | NA | Conservative | Recover after 1- days |
| 3  | Hazariwala, et al. [6] | 57 | F | Asthma, HTN, and obesity | 17 days of severe cough and progressive SOB | Yes, after diagnosis | PM and PP | CXR and chest CT | HPNC, hydroxychloroquine, zinc, azithromycin, methylprednisolone, LMWH | ECMO | Died at 30 day |
| 4  | Hazariwala, et al. [6] | 55 | M | Asthma, DM, HTN, hyperlipidemia, obesity, smoking | Cough, fevers, and progressive dyspnea | Yes, after diagnosis | PM and PP | CXR and chest CT | HPNC, hydroxychloroquine, zinc, azithromycin, methylprednisolone | Conservative | Died at 50 day |
| 5  | Ghods, et al. [11] | 82 | M | NA | Dyspnea, cough, fever, and malaise | No | PM | CXR and chest CT | NA | Echocardiography-guided catheter insertion | Died at days |
| 6  | Sahu, et al. [12] | 61 | M | HTN | 7 days of fever and SOB | Yes, after diagnosis | PM and PP | CXR | Tocilizumab | Conservative | Died at 7 days |
| 7  | Rashedi, et al. [13] | 55 | M | Marginal B-cell lymphoma and mildly overweight | 15 days of dry cough, myalgia, and SOB | Yes, after diagnosis | PM and PP | CXR and chest CT | NIV, broad-spectrum antibiotics, remdesivir, methylprednisolone | Conservative | Died al days |
| 8  | Scacciavillani, et al. [14] | 61 | M | NKC | Fever and worsening dyspnea | Yes, before diagnosis | PM and PP | CXR and chest CT | Two prone positioning sessions, and a tracheostomy on day 14 | Conservative | Recover after 4- days |
| 9  | Behzadnia, et al. [15] | 24 | F | NKC | Fever, myalgia, fatigue, body aches, and headache | No | PM and PP | Chest CT | NIV, dexamethasone, melatonin, LMWH, famotidine, vitamin D3, methylprednisolone, CytoSorb sessions, meropenem, Targocid, vitamin C, aspirin | Conservative | Recover after 1- days |
| 10 | Baburao, et al. [16] | 62 | F | DM | 2 days of cough, fever, and SOB | Yes, after diagnosis | PM and PP | CXR and chest CT | IV remdesivir, IV methylprednisolone, IV piperacillin, and tazobactam | Conservative | Died followi multi-o failure |
| 11 | Bistre, et al. [17] | 70 | F | NKC | 7 days of SOB, palpitations, and fever | Yes, after diagnosis | PP | CXR | Bipap | Conservative | Died at 21 day |
| 12 | Pimenta, et al. [18] | 54 | M | NA | 14 days of SOB, fever, and fatigue | Yes, before diagnosis | PM and PP | CXR and chest CT | Antibiotics (not specified) | Conservative | Recover after 5- days |
| No. | First Name, Last Name, et al. [Ref] | Age | Gender | Conditions | Symptoms | Experiencing Symptoms | Imaging | Treatment | Outcome |
|-----|----------------------------------|-----|--------|------------|----------|----------------------|--------|-----------|---------|
| 13  | Polistina, et al. [19]           | 70  | M      | HTN, resolved pericarditis, and Parkinson’s disease | 7 days of fever, chills, and SOB | No PM and PP | HRCT chest, chest CT | HFNC, IV corticosteroids, and remdesivir | Conservative | Recovered after 7 days |
| 14  | Elhakim, et al. [20]             | 63  | M      | DM and HTN | 2 days of SOB, fever, and fatigue | No PM | CXR and chest CT | Supplemental oxygen, ceftriaxone, azithromycin, methylprednisolone, LMWH, and remdesivir | Conservative | Recovered after ~7 days |
| 15  | Khan, et al. [21, 22]            | 17  | F      | Drug abuse | 3 days of abdominal pain, nausea, vomiting, and diarrhea | No PM and PP | CXR and chest CT | Normal saline IV, ketorolac, famotidine, and ondansetron | Conservative | Recovered after 7 days |
| 16  | Kipourou, et al. [23]            | 62  | M      | NKC | 9 days of progressive SOB | No PM | CXR and chest CT | HFNC, remdesivir, IL-1 receptor antagonist, and methylprednisolone | Conservative | Recovered after 11 days |
| 17  | Kafle, et al. [24]               | 44  | M      | NKC | 5 days of fever, cough, and 2 days of SOB | Yes, before diagnosis PM | HRCT chest, CT chest | Antibiotics, remdesivir, dexamethasone, LMWH, antihistamines, and antipyretics | Conservative | Recovered after 20 days |
| 18  | Volpi, et al. [25]               | 52  | M      | DM and asthma | Dyspnea, fever, and cough | Yes, before diagnosis PM and PP | CXR and chest CT | CPAP, co-amoxiclav and doxycycline, epoprostenol, and meropenem | Conservative | Recovered |
| 19  | Volpi, et al. [25]               | 68  | M      | HTN and hypercholesterolemia | Dyspnea, myalgia, and cough | Yes, before diagnosis PM | CXR and chest CT | CPAP, co-amoxiclav, and doxycycline | Conservative | Recovered |
| 20  | Volpi, et al. [25]               | 66  | M      | HTN, obesity, and chronic kidney disease | Fever and acute confusion | Yes, before diagnosis PP | CXR | CPAP and antibiotics (not specified) | Conservative | Recovered |
| 21  | Suresh, et al. [26]              | 66  | M      | HTN, chronic kidney disease, and migraine | Cough and SOB | Yes, after diagnosis PM and PP | CXR, chest CT | HFNC, dexamethasone IV, remdesivir IV, ceftriaxone IV, and IV azithromycin | Conservative | Transferred after 11 days |
| 22  | Suresh, et al. [26]              | 47  | F      | SLE, Sjogren’s syndrome, Hashimoto’s thyroiditis, and GERD | SOB, nausea, and vomiting | Yes, after diagnosis PM and PP | CXR and chest CT | HFNC, remdesivir IV, dexamethasone IV, vancomycin, piperacillin-tazobactam, heparin IV | Chest tube | Died at 25 day |
| 23  | Suresh, et al. [26]              | 33  | M      | Asthma | Worsening SOB | Yes, after diagnosis PM | CXR and chest CT | NIV, remdesivir, methylprednisolone, azithromycin, ceftriaxone, tocilizumab, dexamethasone, heparin infusion | Conservative | Transferred after 11 days |
| 24  | Machiraju, et al. [27]           | 51  | M      | HTN and DM | 8 days of fever, myalgia, and dry cough | Yes, before diagnosis PM, PP | CXR and chest CT | Meropenem, Targocid, and itraconazole | Conservative | Died at 10 day |
| 25  | Machiraju, et al. [27]           | 77  | M      | HTN | 7 days of SOB | Yes, before diagnosis PM, PP | CXR and chest CT | High-flow oxygen, dexamethasone, LMWH, remdesivir, meropenem, Targocid | Conservative | Died at 17 day |
| Case | Author(s) | Age | Sex | Comorbidities | Duration of Symptoms | Initial Symptoms | Initial Investigations | Initial Treatments | Outcome | Additional Notes |
|------|-----------|-----|-----|---------------|---------------------|------------------|----------------------|-------------------|--------|------------------|
| 26   | Machiraju, et al. [27] | 53  | F   | DM and dyslipidemia | 5 days of fever and headache | No PM | CXR and chest CT | Oxygen via nasal prongs, dexamethasone, remdesivir, LMWH | Conservative | Recovered after 1 days |
| 27   | Kalpaxi, et al. [28] | 49  | M   | obesity | Fever, chest pain, and dry cough | No PM | Chest CT | HFNC, corticosteroid, LMWH antibacterial, antiviral (not specified) | Conservative | Recovered after 2 days |
| 28   | Kalpaxi, et al. [28] | 66  | M   | HTN, dyslipidemia, and obesity | 3 days of fever, dyspnea, and dry cough | Yes, after diagnosis | PM and PP | Chest CT | Oxygen via Venturi mask, corticosteroid, LMWH, antibacterial, and antiviral (not specified) | Conservative | Recovered after 3 days |
| 29   | Kalpaxi, et al. [28] | 44  | M   | NKC | 5 days of fever, dyspnea, and dry cough | No PM and PP | Chest CT | HFNC, corticosteroid, LMWH antibacterial, antiviral (not specified) | Conservative | Recovered after 1 days |
| 30   | Chowdhary, et al. [29] | 71  | M   | DM and HTN | 8 days of fever, productive cough, and SOB | No PM | CXR and chest CT | BiPAP, remdesivir, LMWH, clarithromycin, dexamethasone, ivermectin, zinc, piperidone acetylcysteine, piperacillin and tazobactam, methylprednisolone, nebulization of levosalbutamol, ipratropium, and budesonide | Conservative | Recovered after 6 days |
| 31   | Chowdhary, et al. [29] | 61  | M   | DM and HTN | 9 days of fever, non-productive cough, SOB, and weakness | Yes, after diagnosis | PM and PP | CXR and chest CT | NIV, remdesivir, meropenem, LMWH, doxycycline, dexamethasone, ivermectin, zinc, piperidone, nebulization of levosalbutamol, ipratropium, and budesonide | Conservative | Died after 5 days |
| 32   | Chowdhary, et al. [29] | 30  | M   | NKC | 5 days of fever, productive cough, and SOB | No PM | Chest CT | NIV, remdesivir, meropenem, LMWH, doxycycline, dexamethasone, ivermectin, zinc, nebulization of levosalbutamol, ipratropium, and budesonide | Conservative | Recovered after 11 days |
| 33   | Protkia, et al. [30] | 56  | F   | Chronic lymphocytic leukemia | 7 days of fever, cough, SOB, headache, and nausea | No PM | CXR and chest CT | Supplemental oxygen, azithromycin, corticosteroids, LMWH, IV paracetamol | Conservative | Recovered after 3 days |

*DM: Diabetes Mellitus, HTN: Hypertension, NKC: Non-kleine cell anemia, CXR: Chest X-ray, CT: Computed Tomography, HFNC: High Flow Nasal Cannula, PM: Pulse Oximetry, PP: Pulse Pressure, SOB: Shortness of Breath, BiPAP: Bilevel Positive Airway Pressure, NIV: Non-invasive Ventilation, IV: Intravenous*
| No. | Authors            | Age | Gender | Diagnosis                        | Symptoms                                                                 | PM   | Chest and CT | Other Treatments                                                                                     | Outcome                      |
|-----|--------------------|-----|--------|----------------------------------|---------------------------------------------------------------------------|------|--------------|------------------------------------------------------------------------------------------------------|------------------------------|
| 34  | Protrka, et al.    | 67  | M      | HTN                              | Fever, cough, and dyspnea                                                 | No   | PM           | LMWH, corticosteroids, antibiotics (not specified)                                                   | Died at 14 days              |
| 35  | Protrka, et al.    | 74  | M      | HTN, prostate and bladder cancer | 10 days of fever, SOB, and cough                                          | No   | PM           | HFN, LMWH, corticosteroids, antibiotics (not specified)                                              | Thoracic drainage catheter   |
| 36  | Kooblall, et al.   | 41  | M      | Asthma and obesity               | Myalgia, pyrexia, dyspnea, and cough                                      | No   | PM           | CPAP, tocilizumab, steroids, and antibiotics (not specified)                                        | Recovered after 2 days       |
| 37  | Kooblall, et al.   | 52  | M      | Asthma                           | Dyspnea and chest pain                                                   | No   | PM           | CPAP, tocilizumab, steroids, and antibiotics (not specified)                                        | Conservative                |
| 38  | Kong, et al.       | 62  | M      | Bronchitis                       | 14 days of fever, dry cough, SOB, wheezing, myalgia, nausea, and vomiting | No   | PM           | Oxygen nasal cannula                                                                                | Died at 1 hours              |
| 39  | Urigo, et al.      | 54  | M      | HTN and DM                       | 10 days of cough and 4 days of SOB                                       | No   | PM           | Oxygen nasal cannula                                                                                | NA                           |
| 40  | Chaudhry, et al.   | 52  | M      | Morbid obesity, allergies, and HTN| 7 days of fever, malaise, cough, and dyspnea                              | No   | PM           | HFNC, steroids, IL-6 inhibitors, plasma, remdesivir                                                  | Conservative                |
| 41  | Yiğit, et al.      | 23  | M      | Asthma                           | 7 days of cough, SOB, and chest pain                                      | No   | PM           | Low-flow nasal oxygen, favipiravir, LMWH, prednisolone, and levofloxacin                             | Recovered                   |
| 42  | Hayrabedian, et al.| 59  | M      | NA                               | NA                                                                         | Yes  | before diagnosis | Chest CT                                                                                          | Airway pressure release ventilation Died at 13 hours |
| 43  | Pooni, et al.      | 56  | M      | DM, HTN, and seasonal asthma     | 14 days of a non-productive cough, dyspnea, and fever                     | No   | PM           | CPAP, antibiotic (co-amoxiclav and clarithromycin) which was escalated to piperacillin, and tazobactam on the fifth day | Conservative                |
| 44  | Malekpour, et al.  | 54  | M      | HTN and previous right kidney transplant surgery | 7 days of dry cough, SOB, nausea, vomiting, and decreased appetite | No   | PM           | Ceftriaxone, remdesivir, and methylprednisolone                                                     | Conservative                |
| 45  | Malekpour, et al.  | 71  | M      | Hypothyroidism                   | 3 days of fever, dry cough, headache, and sore throat                    | No   | PM           | Ceftriaxone and levofloxacin                                                                        | Recovered after 5 days       |
TABLE 1: Case reports of pneumomediastinum and pneumopericardium developed in patients with COVID-19 infection.

| Reference | Type of study | Prevalence, n (%) | Place |
|-----------|---------------|-------------------|-------|
| Juárez-Lloclla, et al. [42] | Case series study | 12 | Peru |
| Mart, et al. [43] | Cohort study | 5 (5.4%) | Tennessee |
| Wall, et al. [44] | Case series study | 5 | United Kingdom |
| Cut, et al. [45] | Case series study | 11 | Romania |
| Haberal, et al. [46] | Cohort study | 7 (0.02%) | Finland |
| Hamouri, et al. [47] | Cohort study | 15 (0.81%) | Jordan |
| Kumar, et al. [48] | Cohort study | 15 (7.56%) | India |
| Loffi, et al. [49] | Cohort study | 6 (5.56%) | Italy |
| Kabi, et al. [50] | Case series study | 4 | India |
| Gorospe, et al. [51] | Case series study | 4 | Iran |
| Gandolfio, et al. [52] | Case series study | 11 | Italy |
| Adhikary, et al. [53] | Case series study | 12 | India |
| Kangas-Dick, et al. [54] | Cohort study | 34 (10%) | United States |
| Miyakawa, et al. [55] | Cohort study | 13 | United States |
| Agrawal, et al. [56] | Case series study | 4 | India |

Table 2 summarizes the cases of pneumomediastinum and/or pneumopericardium found in large cohorts and case series studies. Different countries around the world have documented the occurrence of these complications in the literature. The number of cases reported in each county varied between 4 and 34 cases. Interestingly, India has the highest reporting rate among all countries.
**Discussion**

**Etiology**

Many predisposing factors have been associated with SPM. They include cough, obesity, preexisting lung disease, and Valsalva maneuver. However, most are idiopathic [57-59]. The pathophysiology of SPM and PP is explained by the Macklin phenomena. It asserts that air following alveolar rupture dissects through the peri-bronchial vascular sheath and into the mediastinum and pericardium, leading to SPM and PP, respectively [60]. Alveolar rupture may result from a large pressure gradient between the marginal alveoli and the lung interstitium [54].

Currently, no obvious pathophysiological etiology of PM and PP in COVID-19 patients exists. Although PM and PP occurred in almost all age groups, most of the cases (73%) were above 50 years old (Table 1), suggesting that age may play a role in this condition. Furthermore, most of the reported cases were male patients (83.3%) (Table 3), raising the possibility that gender might be a predisposing factor. The number of reported cases is still small, and a comprehensive epidemiological study would be necessary to draw definitive conclusions. Hypertension, diabetes, asthma, and obesity were common comorbidities in many cases. Hypertension was the most common, indicating that it might be a predisposing factor. SPM may also occur following cytokine storm-induced diffuse alveolar damage that increases the probability of alveolar rupture [44]. The use of mechanical ventilation with high positive end-expiratory pressure (PEEP) was suggested to develop PM and PP in COVID-19 patients [17,47].

| Variable                  | Frequency | %   |
|---------------------------|-----------|-----|
| Gender                    |           |     |
| Male                      | 40        | 83.33% |
| Female                    | 8         | 16.66% |
| Intubation requirement    |           |     |
| Not required              | 27        | 56.25% |
| Required before diagnosis | 10        | 20.83% |
| Required after diagnosis  | 11        | 22.92% |
| Diagnosis                 |           |     |
| PM                        | 25        | 52.08% |
| PP                        | 2         | 4.16% |
| PM and PP                 | 21        | 43.75% |
| Radiological modality     |           |     |
| Chest CT only             | 14        | 29.16% |
| CXR only                  | 3         | 6.25% |
| Chest CT and CXR          | 31        | 64.58% |
| Died                      | 15        | 31.25% |
| Outcome                   |           |     |
| Recovered                 | 31        | 64.58% |
| Transferred to another care-center | 2 | 4.16% |

**TABLE 3: Summary of case reports included in this review.**

CT, computed tomography; CXR, chest x-ray; PM, pneumomediastinum; PP, pneumopericardium.

**Imaging Modalities**

In imaging, COVID-19 pneumonia appears as multifocal opacities with a ground-glass appearance (GGO) [61]. Most often, it appears bilaterally in the peripheral and lower area of the lung [5]. The chest x-ray (CXR) is the initial imaging study in patients with COVID-19 due to its availability and affordability. Furthermore, it is the only imaging method available for critically ill patients in the ICU [62]. Factors such as poor inspiration and positioning may lead to inaccurate interpretation [63]. In the event of unexplained clinical deterioration in COVID-19 patients, imaging is essential to diagnose possible complications such as PM and PP [37]. Chest computed tomography (CT) is a valuable tool in screening for complications and ruling out coexisting conditions [28]. The most common CT finding is peripheral, multifocal, bilateral, and GGO with or without consolidation. In addition, cavitation, nodule formation, interlobular septal thickening, and pleural effusion can be seen in rare cases [64]. Moreover, CT can detect the Macklin effect, which helps diagnose PM and PP [60].

**Management and Treatment**
The mainstay of managing hospitalized COVID-19 patients is monitoring the vital signs and providing symptomatic relief. The use of corticosteroids should be reserved for patients receiving supplemental oxygen or those on ventilator support. In addition, remdesivir is recommended for severe cases or for those who have a high risk of disease progression. Immunomodulatory drugs, such as baricitinib or tocilizumab, can be considered for patients with rapidly declining oxygen levels [65]. The decision to start empiric antibiotic therapy may be considered sometimes, as it is difficult to clinically distinguish between COVID-19 infection and community or hospital-acquired bacterial pneumonia. Further, if bacterial pneumonia co-infection is suspected, starting empirical antibiotic therapy is also recommended [66,67].

Most cases of PM and PP are benign and self-limiting [9]. Nonetheless, close monitoring is always recommended due to the possibility of serious circulatory and respiratory complications [20]. Behraemia et al. [15] reported a case of concurrent PM and PP that required ICU admission. Despite the unfavorable progression, they successfully managed their patient with conservative measures only. To date, no clinical guidelines have been developed for the management of PM and PP in COVID-19 patients. For this reason, physicians must determine the appropriate management approach on a case-by-case basis.

The literature describes several approaches to managing PM in COVID-19 patients. In several cases, conservative management was sufficient in treating patients (Table 3). Surgical decompression was required for tension PM via thoracotomy [10]. Li et al. [50] reported two cases where they used a pigtail catheter to decompress the mediastinum. Moreover, Wali et al. [44] used subcutaneous and intrapleural chest drains. In the retrospective study by Kangas-Dick et al. [54], there was no significant difference in the mortality rates between patients who were managed conservatively or by surgical measures. For this reason, a conservative approach is recommended to be the mainstay of management in the absence of compressive symptoms. Patients with asymptomatic PP can be managed conservatively, while those with tension PP should be managed with a pericardial aspiration to avoid possible hemodynamic deterioration. A drainage tube placement into the pericardial sac may be necessary if the PP is persistent or recurring [19]. Ghods et al. reported a case of tension PP that required emergency echocardiography-guided catheter placement [11].

The use of mechanical ventilation with high PEEP was hypothesized to be one of the etiologies for developing PM and PP in COVID-19 patients [14]. A recent case series described five patients with COVID-19 pneumonia who developed PM shortly after being mechanically ventilated [44]. Singh et al. [9] avoided the use of mechanical ventilation to prevent further barotrauma. Interestingly, their patient achieved full recovery after six days with only supplemental oxygen. To reduce the risk of barotrauma in mechanically ventilated patients, physicians are challenged with the dilemma of achieving optimal oxygenation in the lowest ventilatory setting possible. Strategies to lower the required PEEP settings, such as treating reversible causes and applying for a proning position, should be considered [25]. In their case series, Suresh et al. [26] applied a protocol that involves prone positioning for 18 hours a day to enhance oxygenation in their patients. Interestingly, frequent proning in mechanically ventilated patients was suggested to cause barotrauma, leading to the development of PM [44]. These findings warrant further investigation to determine the safety of such intervention.

**Prognosis**

Out of 48 patients in our review, 40 (83.3%) were male. It is not clear if this disparity is because of the relatively few reported cases or if gender predisposes the development of such pathologies. Further, 72.9% (35 patients) had chronic illnesses that varied from diabetes mellitus, hypertension, heart failure, chronic kidney disease, obesity, asthma, and drug abuse. The incidence of PM and PP in COVID-19 patients is still unknown. Multiple studies with a relatively small-sized population reported widely variable results between 0.02% and 10% (Table 2). While PM is considered a benign condition, its occurrence in patients with SARS infection resulted in worse outcomes, with 38% requiring intubation and a 31% mortality rate [68]. In COVID-19 patients, developing PM is a bad prognostic indicator, indicative of extensive damage to the alveoli [69]. The total mortality rate in our review was 51.25% (15 patients), while 64.58% (31 patients) achieved full recovery, and 4.16% (2 patients) were transferred to another care facility for further management (Table 3).

Air leaks can occur spontaneously, as seen in COVID-19 patients, or secondary to barotrauma from mechanical ventilation [17]. In the present review, more than half of the cases occurred spontaneously, without mechanical ventilation. Barotrauma increases the risk of mortality and length of hospital stay [27]. Its prevalence in mechanically ventilated COVID-19 patients was 15%, compared to 0.5% in mechanically ventilated patients for other etiologies [69]. Thus, COVID-19 infection on its own can predispose individuals to develop barotrauma. Patients with COVID-19 pneumonia who are mechanically ventilated have a poor prognosis, with estimated mortality rates between 40% and 60.4% [70,71]. Mechanical ventilation can lead to severe complications, namely tension pneumomediastinum and tension pneumopericardium, which can result in a rapid deterioration of hemodynamic status [6].

**Conclusions**

Patients with COVID-19 may experience unusual complications, such as PM and PP. Our literature review identified 48 cases. Various clinical presentations were associated with these complications; however, radiological findings were predominantly similar in all cases. PM and PP have been reported in nearly all age groups, but most patients were older than 50 years and mostly males. Clinical outcomes were influenced by comorbid conditions such as hypertension, diabetes, asthma, and obesity. Several surgical approaches have been described in the literature for managing PM and PP; however, most patients had a full recovery with only conservative measures.
Identifying and treating these complications promptly is essential to improve the survival rates. Small numbers of case reports and cohort studies have been published on this topic; more research is needed to determine the pathophysiology and risk factors and to establish evidence-based management guidelines.

**Additional Information**

**Disclosures**

**Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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