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Subcutaneous Emphysema and Pneumomediastinum in COVID-19 Non-mechanically ventilated Patients, a case series study

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ABSTRACT

Background: Subcutaneous emphysema and pneumomediastinum are unusual consequences in severe acute respiratory syndrome but in COVID-19 patients increased frequency was found, especially in advanced stages with considerable mortality which may represent a prediction of poor prognosis in this group of people.

Objective: Follow the course and outcome of COVID-19 patients with subcutaneous emphysema and/or pneumomediastinum who were not subjected to mechanical ventilation and detect their outcome.

Patients and Methods: observational case series study from April 2020 to October 2020 where thirty-four covid-19 positive patients developed spontaneous subcutaneous emphysema and/or pneumomediastinum. They were investigated properly for the cause with close follow up for the progress and outcome.

Results: We observed increased occurrence of subcutaneous emphysema/ pneumomediastinum in COVID-19 positive patients, even in non-ventilated cases. None of our patients were vaccinated against corona virus yet. Pneumomediastinum/ subcutaneous emphysema mostly were not associated with pneumothorax that happened only in three patients (8.8%) of the study group as late occurrence. Of the 34 patients in our study, only six patients (17.65%) survived, twenty-eight patients (82.35%) died, the main causes were multi-organ dysfunction syndrome (MODS), septic shock and Respiratory failure.

Generalized subcutaneous emphysema/pneumomediastinum and the requirement of invasive ventilation have a very poor prognosis and high mortality in covid-19 patients.

Conclusions: Development of subcutaneous emphysema and/or pneumomediastinum is predictor of mortality in COVID-19 patients. We observed increase in pneumomediastinum/subcutaneous emphysema in non-vaccinated, non-ventilated COVID-19 positive patients. Persistent severe cough, high transpulmonary pressure and fragility of the airways and lungs could explain the cause.

Keywords: COVID-19, Pneumomediastinum, Pneumothorax, Subcutaneous Emphysema.

INTRODUCTION

In December 2019, a respiratory virus from Wuhan, China, designated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was discovered to cause an illness known as coronavirus disease 2019. SARS-CoV-2 was proclaimed a pandemic on March 11, 2020,

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following its recognition as a worldwide public health emergency [1].

Acute respiratory distress syndrome (ARDS) due to hypoxemic respiratory failure is the most common COVID-19 consequence [2]. Both invasive and non-invasive positive pressure ventilation (PPV) has become a vital life-saving therapy for COVID-19 ARDS, despite the fact that PPV induces barotrauma in around 1% to 2% of patients [3].

Barotrauma develops as a result of elevated intra-alveolar pressure, high tidal volume, or intrinsic positive end-expiratory pressure (PEEPi), which causes dynamic hyperinflation and is more common with invasive ventilation than non-invasive ventilation (NIV) [4].

In our study, we observed that subcutaneous emphysema (SE) and pneumomediastinum occurred spontaneously, without invasive or non-invasive mechanical ventilation, that means there were other causes for these complications. This study aimed to follow the course and outcome of COVID-19 patients with subcutaneous emphysema and/or pneumomediastinum and detect what are their possible causes.

PATIENTS AND METHODS

This is an observational case series study which was performed in two corona centers (New Najran General Hospital, Khamis Mushait General Hospital). Between April 2020 and October 2020, thirty-four patients were diagnosed as covid-19 positive by Polymerase chain reaction developed spontaneous subcutaneous emphysema and/or pneumomediastinum. They were investigated properly for the cause and close follow up and monitoring was done to observe their progress, course and the outcome. Informed written consent from all patients (or next of kin) was taken and the ethics committee in our institutions approved the study.

Patients were included in our study based on clinical basis by the presence of SE, laboratory basis by confirmed diagnosis of COVID-19 based on their positive reverse transcriptase-polymerase chain reaction (RT-PCR) assay and radiological basis by chest X-ray (CXR) or computed tomography (CT) scan chest findings suggestive of subcutaneous emphysema/pneumomediastinum. Patient who developed subcutaneous emphysema or pneumomediastinum after invasive or noninvasive ventilation or secondary to pneumothorax were excluded from the study.

All patients were closely observed, their data were collected, including demographic data, clinical symptoms at presentation to the hospital, timing of hospital presentation after the onset of symptoms, associated co-morbidities, oxygen saturation and ventilator requirement on presentation and during management, radiological findings at first presentation and its progress, treatment received, total hospital stays, ICU length of stay and mortality.

Statistical analysis:

The data was input and analyzed using Microsoft Excel software. The data was then examined using SPSS version 20 software. Qualitative data is provided as numbers and percentages, whereas quantitative continuous groupings are presented as mean ± SD. A P value of less than 0.05 in a two-tailed test indicates a statistically significant outcome.

RESULTS

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Thirty-four patients were diagnosed as covid-19 positive by Polymerase chain reaction developed subcutaneous emphysema and/or pneumomediastinum before any invasive or NIV all of them were admitted in ICU at a stage of their hospital management. Three patients needed direct ICU admission from emergency department (ED) and the others were admitted in high dependency unit (HDU) then shifted to ICU during the same hospitalization. Their demographics and baseline clinical data are shown in Table (1). Hypertension was the most common associated comorbidity (73.53%). None of the 34 patients included in our study received COVID vaccination before being infected. BMI were calculated for all patients and classified as in Table (1).

Table (1): Demographics and baseline clinical data

Variable		Value	Percentage
Age	Range	40-79	
	Mean ± SD	58± 2.51	
Sex	Male	23	67.65%
	Female	11	32.35%
HTN	Hypertensive	25	73.53%
	Non hypertensive	9	26.47%
DM	Diabetic	5	14.71%
	Non diabetic	29	85.29%
IHD	IHD	3	8.82%
	Non IHD	31	91.18%
Smoking	Smoker	10	29.41%
	Non smoker	24	70.59%
BMI	<25	3	8.82%
	25-29.9	8	23.53%
	30-34.9	14	41.18%
	>35	9	26.47%
COVID Vaccine	Vaccinated	0	0%
	Non vaccinated	34	100%

SD, Standard Deviation; DM, diabetes mellitus; HTN, hypertension; IHD, ischemic heart disease; BMI, body mass index.

The most common presenting symptoms were persistent severe cough, dyspnea, sore throat which were present in all patients (100%) followed by fever that was present in 25 patients (73.5%). The timing between the onset symptoms and first presentation to hospital was 8.11 days (range 3–18 days). At presentation to the hospital, there was a different degree of hypoxia Table (2). Thirty patients (88.24%) required PPV, either NIV or invasive mechanical ventilation (IMV) after developing subcutaneous emphysema or pneumomediastinum during their management course; the other four patients (11.76%) required just oxygen therapy.

Table (2): Oxygen saturation on hospital presentation

Oxygen Saturation	Number of patients	Percentages
90-95%	14	41.18%

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80-90 %	11	32.35%
70-80%	8	23.53%
Less than 70%	1	2.94%

CXR was performed on every patient at admission and on a regular basis thereafter. Every CXR was thoroughly investigated for the existence of SE, pneumomediastinum, or pneumothorax, and the degree of lung affection was measured using a severity score based on lung opacities. The six-point scoring method was utilized to objectively quantify lung opacities according to lung zones [5]. Both lungs were separated into three zones: upper, middle, and lower, with one point awarded for opacity in each zone for a total score of six.

Chest X-ray of all patients on arrival to the hospital showed neither surgical emphysema nor pneumomediastinum, but they had different degrees of diffuse bilateral patches and airspaces opacities (figure 1). Follow up CXR was done daily and the progress of the severity of opacities was documented.

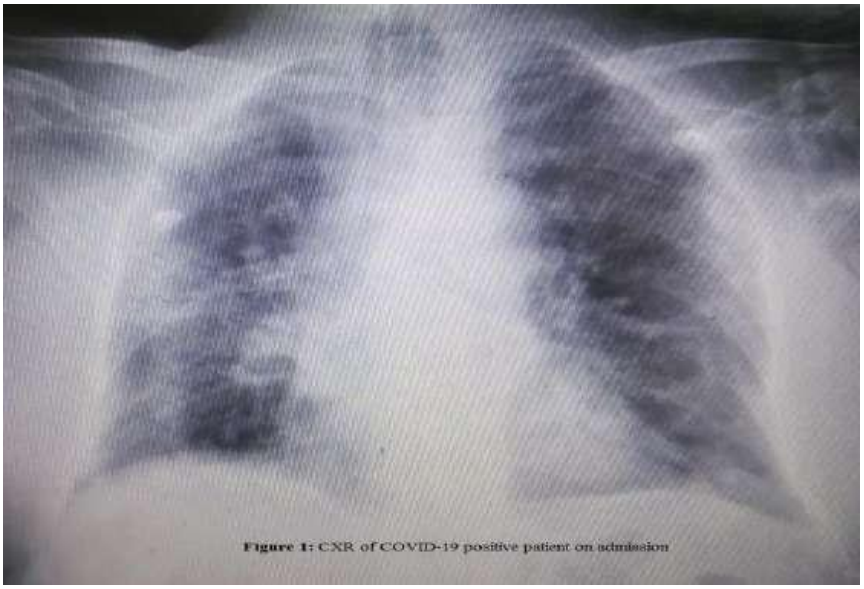

Figure 1: CXR of COVID-19 positive patient on admission

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The average of CXR's lung severity scoring was 3 out of 6 on admission and 4.5 out of 6, at the time of development of SE/ pneumomediastinum which means affection of most of the lung parenchyma at the time of development of SE/pneumomediastinum.

CT chest was done with the beginning of subcutaneous emphysema or pneumomediastinum (figure 2) then followed up if there is any new events or patient deterioration.

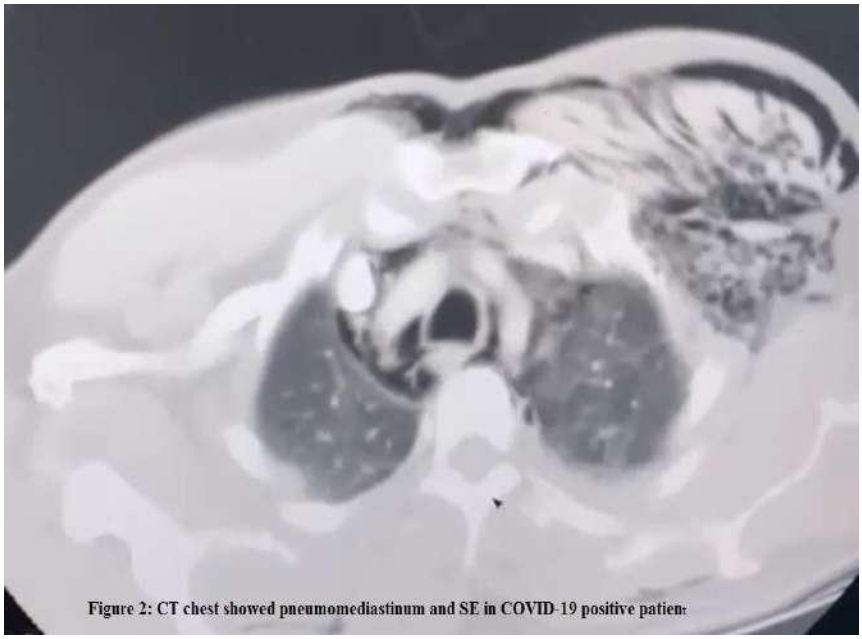

Figure 2: CT chest showed pneumomediastinum and SE in COVID-19 positive patien:

Twenty-three patients (67.65%) developed subcutaneous emphysema at first (six at the first week (17.65%), twelve during the 2nd week (35.3%) and five (14.7%) developed at the 3rd week of admission). Only two patients out of the 23 had pneumothorax at the 2nd week of admission on both sides for which bilateral chest tubes were inserted (figure 3). Fifteen patients (44.1%) developed pneumomediastinum secondary to subcutaneous emphysema.

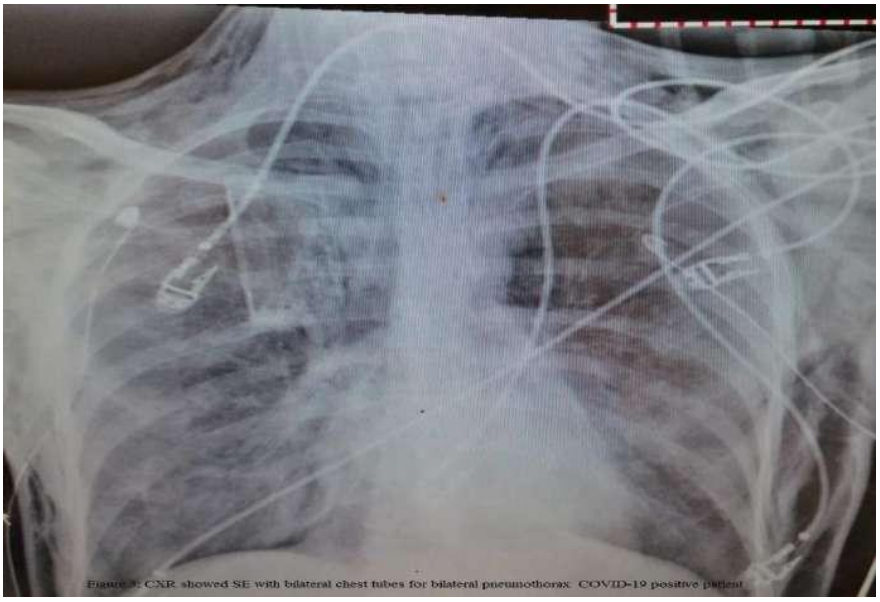

Figure 3: CXR showed SE with bilateral chest tubes for bilateral pneumothorax COVID-19 positive patient

The other eleven patients (32.35%) developed pneumomediastinum at first (two in the first week (5.89%), five in the 2nd week (14.7%), and four (11.8%) in the 3rd week of admission). Of them one patient had left pneumothorax during the 2nd week of admission that needed chest tube insertion. Secondary to the pneumomediastinum all of the eleven patients developed subcutaneous emphysema.

Thirteen out of the 34 patients (38.24%) developed localized subcutaneous emphysema in the neck and upper part of the chest, while 21 patients (61.76%) had generalized emphysema from face till the thigh and knee with variable degree and severity.

From the thirty- four patients included in our study, six patients survived (17.65%) (4 males and 2 females) and twenty-eight patients died (82.35%) (19 males and 9 females) all of them had invasive or NIV, 7 had localized subcutaneous emphysema, 21 had generalized subcutaneous emphysema and three had pneumothorax which was managed by chest tube insertion. The cause and timing of death is shown in table (3).

Table (3): Cause and Timing of death from admission

Cause of death	2nd week	3rd week	4th week	Total Number	Percentage
RF and hypoxia	2 (7.1%)	3 (10.71%)	3 (10.71%)	8	28.57%
MODS		5 (17.86%)	6 (21.4%)	11	39.29%
Septic shock		4 (14.28%)	5 (17.86%)	9	32.14%
Total	2 (7.1%)	12(42.85%)	14(50%)	28	100%

MODS, Multi-organ dysfunction syndrome; RF, Respiratory failure.

From the six survivors, four did not have invasive or NIV and two had NIV and all of them had localized subcutaneous emphysema without pneumomediastinum or pneumothorax.

All patients in our study group had a prolonged ICU and hospital stay with an average of 21 days (range 9−30 days) ICU stay and average 26 days (range 13−35 days) hospital stay.

Overall, we observed increase in the incidence of pneumomediastinum/subcutaneous emphysema in covid -19 patients even in non-ventilated patients which excludes barotrauma as a cause, but most likely, the cause refers to persistent severe cough, high transpulmonary pressure and the fragility of the airway not only the lung as most of the pneumomediastinum/subcutaneous emphysema were not associated with pneumothorax and pneumothorax occurred in only three patients of the study group, late in their course.

None of our patients was vaccinated for COVID-19 which may signify a risk of poor consequences in non-vaccinated patients regarding our condition of concern.

Of the 34 patients in the study group twenty-eight patients (82.35%) died which may signify that subcutaneous emphysema/pneumomediastinum has a poor prognosis and can be considered as a determinant of poor outcome in covid-19 patients.

Generalized subcutaneous emphysema, pneumomediastinum and the requirement of invasive ventilation are associated with high mortality.

DISCUSSION

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SE is often a non-life-threatening illness that responds well to conservative treatment. Death from SE is uncommon, but we should be concerned when the volume of air is significant or fast growing, since this can create severe compression on the airway and be life-threatening, as documented by **Byun et al.** [6] in patients with recently established SE, lethal pathologies such as pneumothorax, esophageal rupture, and necrotizing infections should be evaluated based on clinical data and findings.

SE and pneumomediastinum are generally caused by the rupture of an overdistended alveolus, allowing air to escape into the surrounding mediastinum and subcutaneous tissue via the cervical fascial planes. It can also cause pneumothorax [4]. This might be spontaneous or traumatic. It may also be a PPV complication, with a greater prevalence in COVID-19 patients than in ARDS.

In our study, the patients were more males than females with mean age of 58±2.51, and age range from 40–79. Hypertension was the most common associated comorbidity. Ten patients were smokers, five were diabetic and three had ischemic heart disease. All patients in our study were treated conservatively except for three that required chest tube insertion for pneumothorax.

Before COVID-19, SE was seldom documented in the literature, despite the fact that NIV is often used to treat acute respiratory failure from a variety of reasons [7]. According to **Lacroix et al.** [8], it is thus hypothesized that COVID-19 patients who have sustained significant lung damage may have elevated respiratory drive and persistently high spontaneous inspiratory attempts, which might result in self-inflicted lung harm.

In our study, we noticed that persistent dry cough may be a cause for alveolar rupture due to diffuse lung and alveolar injury in severe SARS-CoV-2 pneumonia. In patients with ARDS from various etiologies during MV, this lung and alveolar damage may have made the patient's lung more likely to rupture and cause complications including SE and pneumothorax, which are also mentioned by **Hsu et al.** [9]. Also, airway (larynx, trachea and bronchi) should be considered.

Radiological lung severity score averaged 3/ 6 on admission and 4.5/ 6 with the development of SE, signifying extensive involvement of lung parenchyma. This supports the theory that severe lung injury in COVID-19 ARDS, together with an increase in intra-alveolar pressure, may promote spontaneous rupture of these hyper-inflated alveoli, resulting in air dissection into the mediastinum, pleural cavity, and subcutaneous tissues (Macklin effect). Other viral pneumonias, as well as people with severe alveolar lung disorders as ARDS, COPD, influenza bronchiolitis, Pneumocystis carnii, necrotising parenchymal infection, and SARS, have been linked to the development of pulmonary interstitial emphysema (PIE) [8].

From the thirty- four patients included in our study, twenty-eight patients died (82.35%), and six patients survived (17.64%). All patients, both survivors and non-survivors had a prolonged ICU and hospital stay with an average of 21 days (range 9−30 days) ICU stay and average 26 days (range 13−35 days) hospital stay. In a case report by **Gahona et al.**[10], two out of three COVID-19 positive patients died during the two to three weeks of their hospital course, the third was discharged after 63 days of hospitalization. While in a case report by Manna et al,

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four out of eleven COVID patients with SE and pneumomediastinum died and the remaining survived but required long term hospital care, five of them received high-flow nasal cannula ventilation for long periods [11].

In a case study of three patients conducted by **Azzawi et al.** [2], spontaneous SE and pneumomediastinum occurred without MV, although all three patients eventually required MV to overcome dyspnea. Two of the three patients died, while the surviving required an extended stay in the intensive care unit.

Four case reports done by Wang, vazzana, Xiang, and Ucpinar had described spontaneous pneumomediastinum [3, 12, 13, 14] In COVID-19 patients. Additionally, a case report from Wuhan documented the appearance of numerous bullae in a COVID patient developing SE [15]. These bullae might represent an unusual COVID-19 appearance, prone to spontaneous rupture.

Due to the relatively recent occurrence of COVID 19 and still a lot is unknown about pathogenesis and proper treatment; literatures are still scarce about this disease and its complications. We searched the literatures thoroughly and most of what we found are case reports and small sized case series. Limitations of our study include small sample of patients included in the analysis, Furthermore, studies need to be done with a bigger number of patients.

CONCLUSION

Development of subcutaneous emphysema and/or pneumomediastinum can be considered a predictor of mortality in COVID-19 patients. We observed an increase in pneumomediastinum/subcutaneous emphysema in non-vaccinated COVID-19 positive patients. Persistent severe cough, high transpulmonary pressure and the fragility of the airways and the lungs could explain the cause.

LIMITATIONS OF THE STUDY

Due to the limited knowledge of the nature of this disease and ambiguity of its course and outcomes since its inception at the end of 2019, the outcome of this study may not be optimum regarding proper management of the conditions of our study, especially with the emergence of modalities and interventions that can impact the outcome of this disease which is announced as pandemic. These modalities and interventions like prone position, high frequency ventilation, vaccination and Extracorporeal membrane oxygenation (ECMO), they need to be implemented and studied thoroughly to solidify their impact on outcome.

Our study can help add to the growing COVID 19 literature and can give guidance and be a nucleus for further similar studies

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