



Role of CT in Identifying Air Leak Complications of Patients with COVID-19 Pulmonary Infection in Smokers as Frequent / Aggressive Complications

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ABSTRACT

To follow the characteristics of patients who were chronic smoker and hospitalized for COVID-19 pneumonia and developed air leak complications like pneumomediastinum (PM), pneumopericardium (PP), pneumothorax (PT), and subcutaneous emphysema (SE) and to observe which factors seem to influence the development and prognosis of these aggressive complications. This retrospective study done from 1st February until 31st May 2021 after obtaining institutional ethical clearance, we followed a total of 22 chronic smoker patients who were Covid 19 positive out of 150 sample study who developed the air leak complications and obtained their demographic data, clinical and laboratory parameters and followed their prognosis and outcome. 22 patients out of 150 total smoker patients showed these complications indicating the incidence of 14.67% which is high compared to other studies. Out of 22 patients 14 patients showed poor prognosis giving mortality of about 63.64% and 8 patients with good prognosis showed the survival rate of 36.36%. About 50% females (2 patients) showed good prognosis, while other 50% showed poor prognosis. On the other hand, 12 male patients (66.67%) showed poor outcome and only 6 male patients (33.33%) showed good prognosis. CT scan helps in early detection of air leak complications like PM, PP, SE and PT and these complications were diagnosed more frequently in chronic smoker patients (male > female) affected with severe COVID-19 pneumonia. Thus, these complications are being associated with prolonged hospitalization and poor prognosis on the outcome indicating the aggressive complications.

Keywords: COVID-19; chronic smoking, spontaneous pneumomediastinum (PM); pneumopericardium (PP); pneumothorax (PT); subcutaneous emphysema (SE); acute respiratory distress syndrome (ARDS).

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INTRODUCTION

COVID-19 has become one of the largest pandemic in recent times with high incidence of mortality and morbidity and associated with the large spectrum of complications. Multiple number of articles have been published in the literature [1,2,6,7], debate in the sporadic cases of spontaneous pneumomediastinum (PM), pneumopericardium (PP), pneumothorax (PT), and subcutaneous emphysema (SE) diagnosed in patients with SARS-CoV2 pneumonia, even without invasive mechanical ventilation thought to be associated as barotrauma. With the combination of damage to alveolus and weakening of wall of the trachea, severe pneumomediastinum can result during the intubation potentially in emergent scenarios, frequent proning and high ventilator pressures [12]. Furthermore, several retrospective studies [2,8], the largest one being the study analysis by Martinelli et al. [1], focused on this topic. The occurrence of these complications can be promoted due to rupture of alveolus by increase in the intrathoracic pressure [9]. The main pathophysiologic mechanism of pneumomediastinum (PM) principal is represented by the "Macklin phenomenon", indicating the development of increased pressure gradient between the marginal alveoli and the lung parenchyma, in the presence of the extensive injury to alveolus, implies that air leakage along the adjacent bronchovascular sheaths goes into the mediastinum [13]. Also inflammation can lead the alveolus more prone to rupture, which could be exacerbated by a chronic cough or any other factors that increase the intra-alveolar pressure gradient [14].

Some studies on these complications like PT (pneumothorax) and/or PM (pneumomediastinum), included both the patients who developed air leak spontaneously, and those occurring due to invasive positive pressure ventilation (PPV) [1], where barotrauma could be the main cause for air leakage. In our study,

we focused only on patients who had history of chronic smoking and developed these complications spontaneously during the course of COVID-19, with most of them having mild/moderate forms of the disease in the initial CT scan and later worsened gradually after hospitalization [10]. The aim of this study was to follow the characteristics of patients who smoke more than a pack of cigarettes a day for long period of time (chronic) and hospitalized for COVID-19 who developed air leak complications like spontaneous pneumomediastinum (PM), pneumothorax (PT), pneumopericardium (PP), and subcutaneous emphysema (SE) and to evaluate which factors seems to be influencing the development and prognosis of these aggressive complications.

To follow the characteristics of patients who were chronic smokers and hospitalized for COVID-19 pneumonia and developed air leak complications like PT (pneumothorax), PM (pneumomediastinum), PP (pneumopericardium), and SE (subcutaneous emphysema) and to observe which factors seem to influence the development and prognosis of these aggressive complications.

MATERIAL AND METHODS

This is a retrospective study. The patients who are smokers and hospitalized due to Covid-19 Pneumonia were followed up with their demographic data, history, clinical characteristics, laboratory parameters, and thorax computed tomography (CT) results and therapy and followed their evolution and outcome.

Cases hospitalized in our institute under Infectious Diseases (Covid Ward) during the second outbreak of COVID-19 from 1st February until 31st may 2021. An “informed consent” will be taken from the patients before taking a detailed clinical history. And CT scan was done using 16 SLICE MULTIDETECTOR CT (GE Revolution ACTs). Routine lateral tomogram of the chest were taken, in all patients in supine position. Axial plain sections were taken using 5mm sections from the lung apices to the bottom of lungs to 2.5mm sections. Post processing reconstructions were done using 2.5mm reconstructions. Newer techniques such as maximum intensity projections and minimum intensity projections were done as and when required. Scans were reviewed in appropriate windows ie, pulmonary window, mediastinum window and bone window. The patients included under the study are smokers diagnosed with Covid-19 pneumonia by RTPCR and non-intubated patients.

SPSS (Statistical Software for the Social Sciences) software 19 version was used for statistical data analysis. Data obtained was shown in the form of charts and tables. Continuous variables as mean and standard deviation (SD) or median and interquartile range (IQR) and categorical variables as frequency and percentages were used. We considered the p-values below 0.05 as statistically significant. Level of significance was estimated with 95% confidence intervals.

RESULT

In this retrospective study, we followed 22 patients out of 150 patients over a period of 4months who had history of smoking diagnosed with COVID-19 pneumonia, eighteen men and four women, hospitalized between 5 to 9 days, since the onset of symptoms; the diagnosis is being confirmed by a Real Time Polymerase Chain Reaction (RTPCR). On arrival at casualty, six patients presented with a history of chronic hypertension (HTN), four patients with diabetes mellitus type 2, six of them with obesity and other six patients presented with HTN, DM and obesity. Among 22 patients, 15 patients with chronic habit of smoking and alcohol, while 7 patients were only chronic smoking, but no alcohol consumption. During the initial CT Chest there were no air leak complications seen in these patients, in the follow-up scan after 7 to 15 days of hospitalization, all patients have developed at least any one of the air leak complications like pneumothorax (PT), pneumomediastinum (PM), pneumopericardium(PP), and sub cutaneous emphysema(SE), some patients with more than one air leak complication. Ten patients presented with low Spo2 (oxygen saturation) on room air (range of 50% and 86%), which improved to 90–95% on a non-rebreather mask at 15 L/min, Table 1.

Table 1. Characteristics of patients group

No.	Age/sex	CT severity	Spo2	RR (per min)	SE	PM	PP	PT	Days of invasive ventilation	History of smoking	Outcome
1	37/M	Mild	88%	24	No	Yes	No	No	8 days	Yes	Good
2	60/M	Severe	56%	36	No	No	No	Yes	15 days	Yes	Poor
3	41/M	Severe	75%	25	No	Yes	No	No	10 days	Yes	Poor
4	43/M	Moderate	87%	32	Yes	Yes	Yes	No	9 days	Yes	Poor
5	46/F	Mild	90%	25	No	No	No	No	5 days	Yes	Good
6	65/M	Mild	92%	20	No	No	Yes	No	0 days	Yes	Good
7	35/M	Moderate	70%	35	No	Yes	No	Yes	11 days	Yes	Poor

8	45/M	Severe	87%	26	No	Yes	Yes	No	14 days	Yes	Poor
9	36/F	Moderate	60%	30	No	No	No	Yes	0 days	Yes	Poor
10	55/M	Severe	71%	28	Yes	No	No	Yes	16 days	Yes	Poor
11	51/M	Mild	88%	22	No	Yes	Yes	No	17 days	Yes	Good
12	57/F	Severe	59%	38	No	Yes	No	No	0 days	Yes	Poor
13	38/M	Mild	87%	22	No	No	Yes	No	0 days	Yes	Good
14	45/M	Mild	90%	27	No	Yes	No	No	10 days	Yes	Good
15	52/M	Moderate	89%	24	Yes	Yes	No	No	15 days	Yes	Poor
16	69/M	Severe	69%	26	No	Yes	Yes	No	7 days	Yes	Poor
17	40/F	Mild	91%	20	No	Yes	No	No	0 days	Yes	Good
18	72/M	Severe	75%	30	Yes	Yes	Yes	No	19 days	Yes	Poor
19	39/M	Moderate	89%	25	No	No	No	Yes	7 days	Yes	Poor
20	46/M	Moderate	78%	26	No	Yes	No	No	11 days	Yes	Poor
21	54/M	Severe	60%	32	Yes	No	Yes	No	24 days	Yes	Poor
22	38/M	Mild	92%	21	No	Yes	Yes	No	0 days	Yes	Good

No.- number; CT - thorax computer-tomography; Spo2 - oxygen saturation; RR - respiratory rate (per minute); SE - subcutaneous emphysema; PM - pneumomediastinum; PP - pneumopericardium; PT - pneumothorax

In this study 22 patients out of 150 total smoker patients showed these complications indicating the incidence of 14.67% which is high compared to other studies. Most common and frequent complication occurred was pneumomediastinum (14 cases) followed by pneumopericardium (9 cases). Out of 22 patients 14 patients showed poor prognosis giving mortality of about 63.64% and 8 patients with good prognosis showed the survival rate of 36.36%. Despite the ICU care measurements patients who developed Pneumothorax (5 cases) and Subcutaneous emphysema (5 cases) in about 10 cases respectively showed 100% mortality rate.

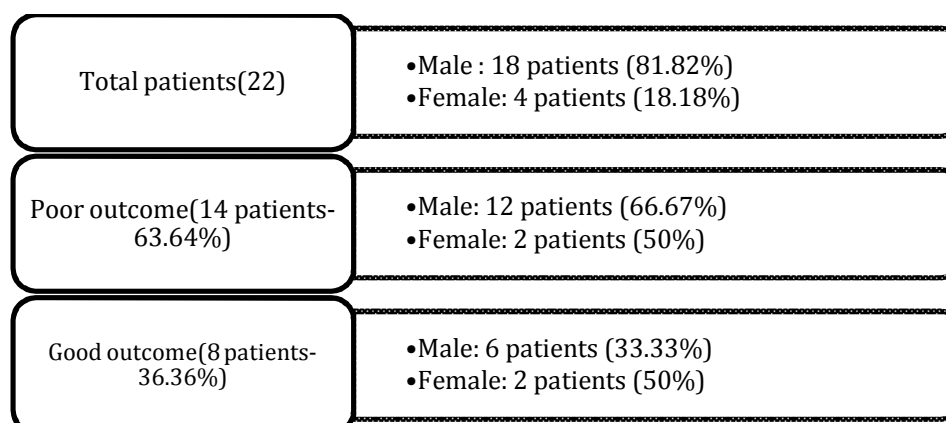


Fig 1. Final clinical outcome among cases

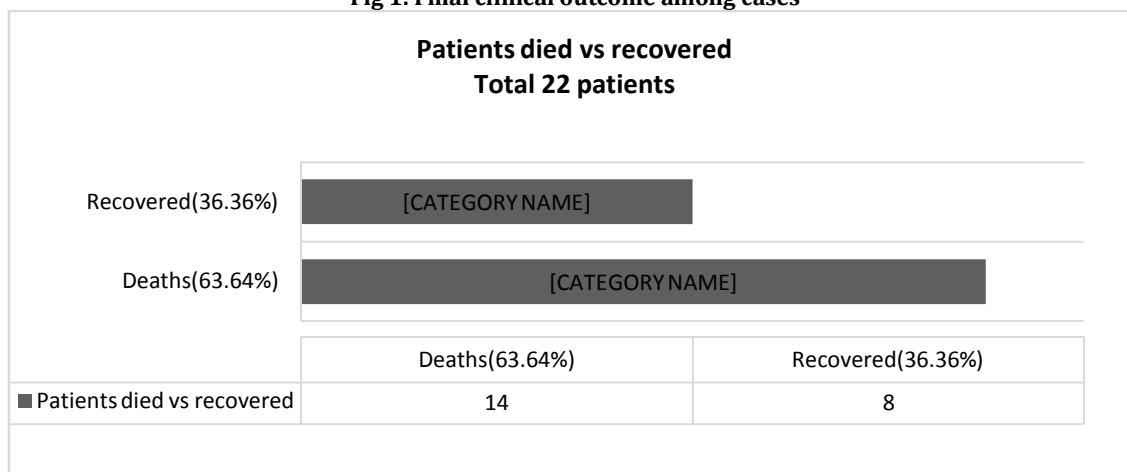


Fig 2. Deaths and recovered patients after occurrence of spontaneous air leak complications

Laboratory studies showed elevated white blood cell (WBC) count with neutrophil count, median 88 (87.5–88.5), and decreased lymphocytes, with a median 5.7 (3.4–8.0). C-reactive protein (CRP) values showed above 100 mg/L in fourteen patients, with a median of 113.75 (53.04–247). Elevated ferritin levels with median 2089.66 (802–2581.1), fibrinogen levels with median 8.1 (5.1–9.6), and interleukin-6 (IL-6) levels with a median 85.01 (27–1153) were observed in all patients. Ph values were varied during the follow-up, from a median of 7.4 (7.34–7.46) initially to 7.33(7.2–7.40, $p < 0.001$) finally, and lactate had an ascendant tendency from a median of 32.5 (21.5–43.49) initially to 34.2 (20.5–47.67, $p < 0.001$) finally. In followup, twelve patients were associated with elevated procalcitonin levels with a median of 1.21 (0.18–5.37), which is more likely towards sepsis.

An initial CT chest was done to assess the presence of percentage of lung involvement and severity of lung injury caused by Covid-19 infection. The most characteristic radiologic findings were peripheral ground glass opacities, consolidation changes, and septal thickening. At the time of admission into the hospital, 8 patients had mild pulmonary injury (10–35%), 6 patients had moderate pulmonary injury (50%), while 8 patients had severe form of lung injury (over 70%). None of these 22 patients showed pneumothorax(PT), pneumomediastinum(PM), pneumopericardium(PP), and sub cutaneous emphysema(SE) in the initial chest CT scan at the time of presentation during admission, but they occurred after 7 to 15 days of hospitalization seen in the follow-up CT scan, representing the aggravation of the lung injury severity. Patients were monitored, in terms of vital signs, electrocardiogram (ECG), oximetry (Spo2), and other biological parameters to adjust therapy. Thorax CT images of 4 patients with such complications are presented in Figures 1–4.

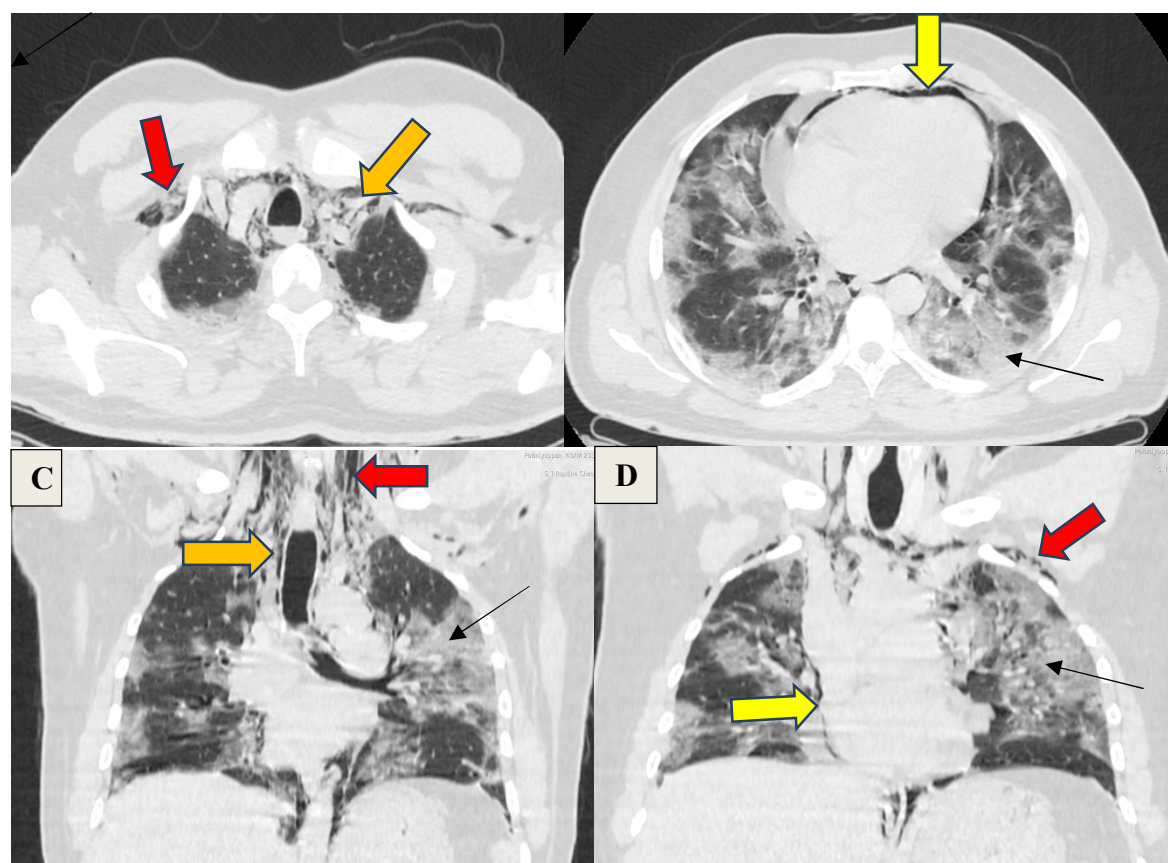


Figure 3. A,B,C&D) a 43 year old male patient, axial and coronal sections of CT Chest showing diffuse ground glass opacities(arrow) and upper neck free air extending to bilateral axilla- subcutaneous emphysema(red arrow), pneumopericardium(yellow arrow) and pneumomediastinum(orange arrow). CORADS-6 Category with CT Severity score of 15/25(moderate)

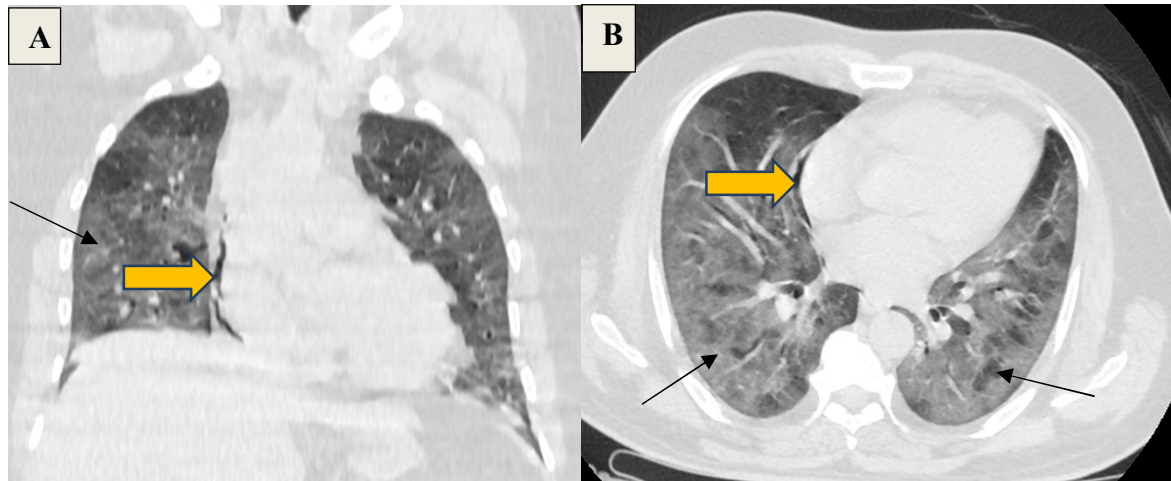


Figure 4. A&B) a 41 year old male CT Chest shows diffuse ground glassing(black arrow) in bilateral lung fields and thin rim of pneumomediastinum(orange arrow) seen in the lower right mediastinum adjacent to the right heart border and diffuse ground glass opacities in bilateral lung fields categorized as CORADS-6 with CT severity score of 21/25(severe)

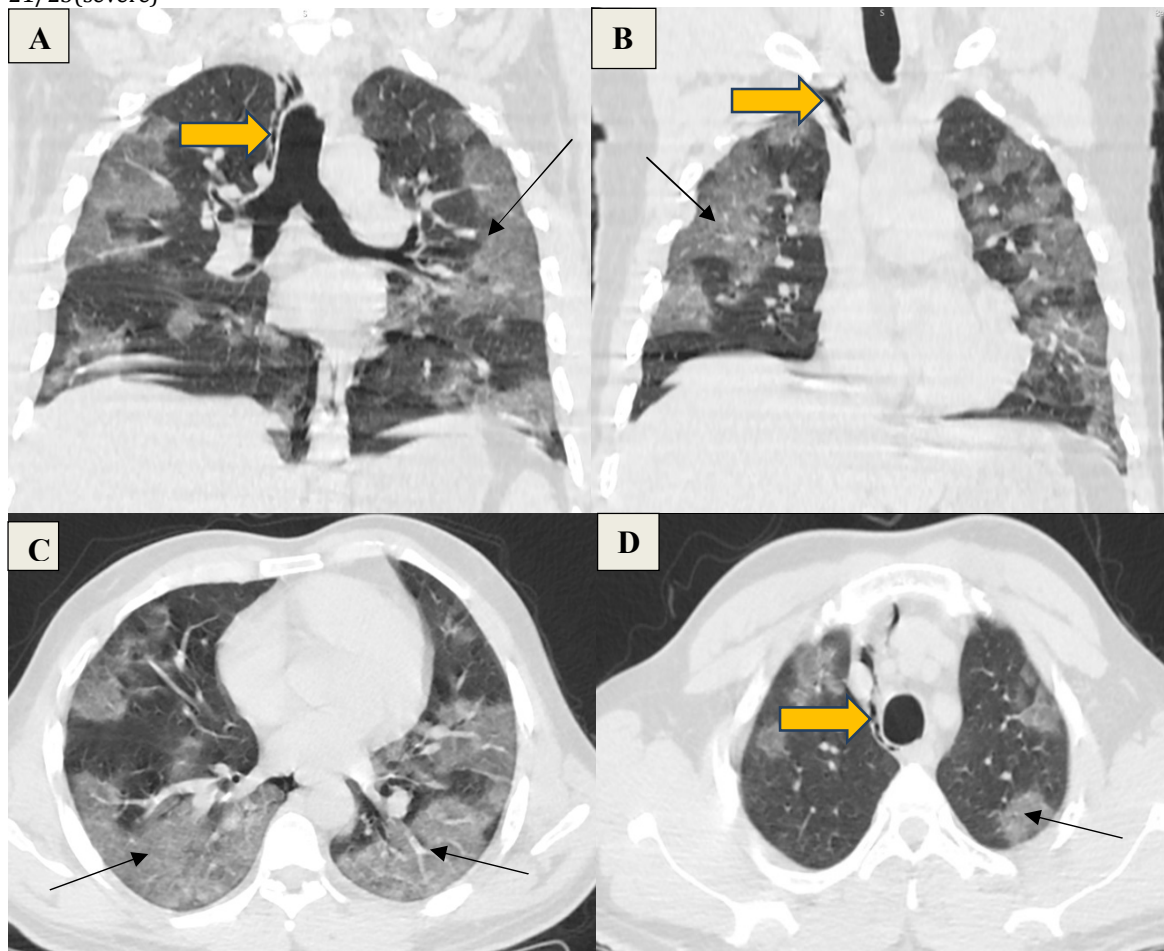


Figure 5. A,B,C&D) a 37 year old male smoker, coronal and axial sections of CT chest showing and right upper pneumomediastinum(orange arrow) with patchy ground glass opacities(black arrow) in bilateral lung fields categorized as CORADS-6, CT Severity score – 17/25(severe)

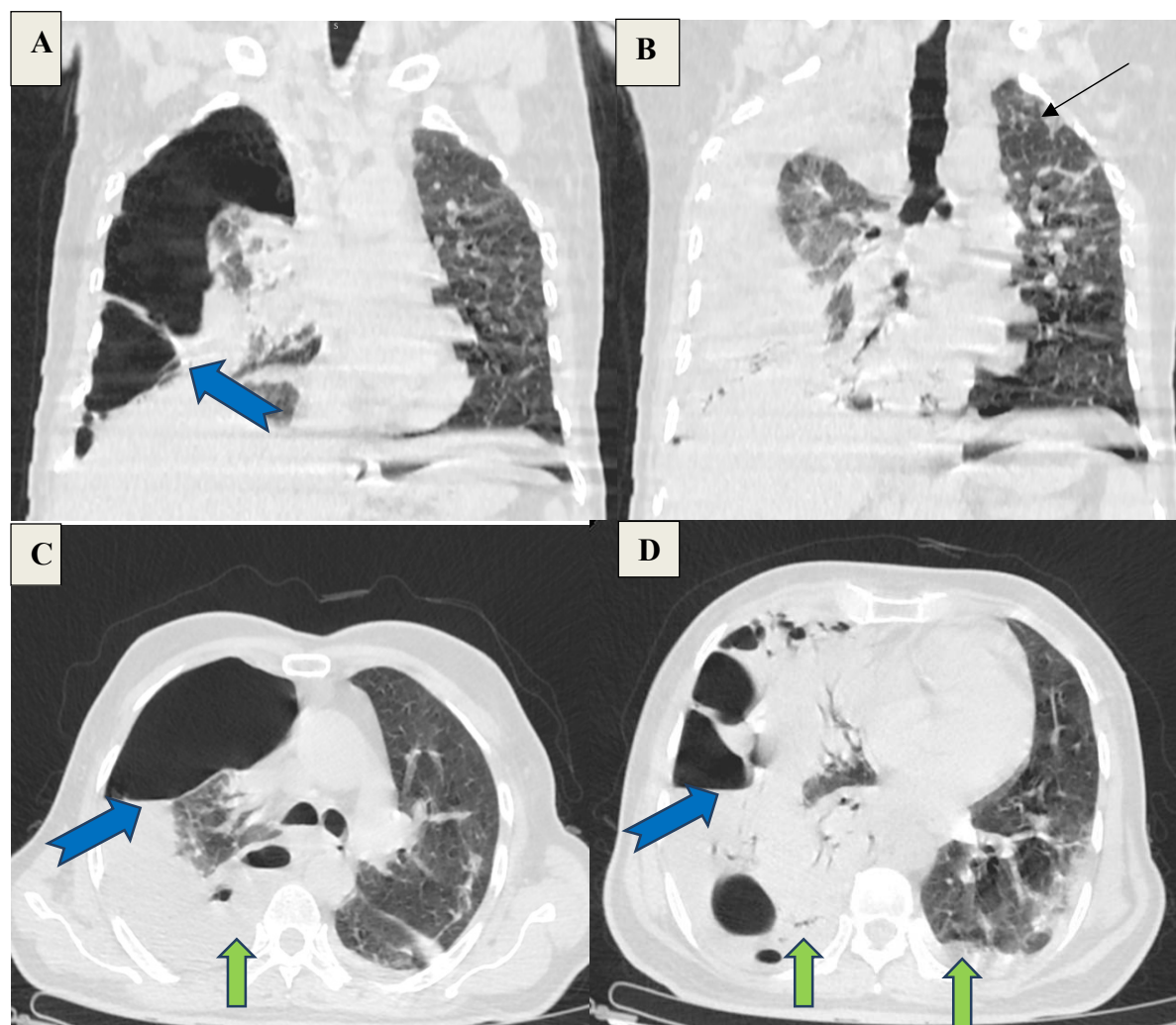


Figure 6. A,B,C&D) a 60 year old male with chronic history of smoking, coronal and axial sections of CT Chest shows hydropneumothorax(blue notched arrow) with complete collapse of right lower lobe and partial collapse of right upper lobe and consolidation changes(green arrow) in bilateral lung fields. And few patchy ground glass opacities(black arrow) in left lung. RTPCR positive - CORADS-6 Category.

All patients admitted finished a general overall course of ceftriaxone with levofloxacin and dexamethasone. Remdesivir and tocilizumab injections were given to twelve patients (with severe lung involvement and high IL-6 levels). During the entire stay in hospital, 20 patients needed additional oxygen supply and also underwent self proning position during sleeping to increase the ventilation of air. Sixteen patients who didn't improve with supplemental oxygen had been transferred to intensive care unit (ICU), and mechanical invasive ventilation was given. Sixteen patients died after 12 to 40 days, median 23.5 (14–32) days of hospitalization in the hospital, with a median interval of 19.5 (9.25–25.5) days after the occurrence of the air leak in the followup CT Scan. The remaining six, with significantly less pulmonary injury at the time of admission, were discharged from the hospital with satisfactory clinical condition of patient after a median hospital stay of 4.5 (2–7) days.

DISCUSSION

As coronavirus 2019 pandemic, several reports of aggressive and unusual frequent complications in covid-19 patients have been published. Acute respiratory distress syndrome (ARDS) is major and aggressive complication leading to mortality, observed in about 41% of hospitalized patients with COVID-19 [5]. PT, PM, SE or even PP, in the absence of invasive mechanical ventilation, these conditions were initially considered rare complications of the SARS-Cov2 pulmonary infection. A large study on these complications was published by Martinelli *et al.*[1], who analyzed the complete results of patients with COVID-19 getting treatment in hospitals in the UK, and concluded that the characteristics of 71 patients with SE, PT, and PM occurring as both spontaneously and also after invasive mechanical ventilation. A

review of literature by Elkahim *et al.*[2] the study has identified 15 cases of SPM developing in patients with COVID-19 and showed complete recovery in most of the case and only 26% mortality rate seen. As per the literature review by Cut TG *et al.*[3] air leak complications are seen in 11 patients in second wave showed findings more frequently in male patients and are non-smokers with severe COVID-19 pneumonia that prolonged hospitalization and poor prognosis in the outcome. Study by Quincho Lopez *et al.*[4], of all the pneumomediastinum cases male gender predominance is seen (66.6%; 4/6) and in 50% of the cases the risk factors were not reported. Review of literature by Wu C *et al.* [5] 46% patients presented with pneumothorax as complication and 38% needed intubation and ultimately 31% patients expired. However all the studies conducted on general patients who diagnosed as covid-19 positive, very few studies have conducted on chronic smokers who got Covid 19 pneumonia. In our study period of 4 months from February 2021 to May 2021, out of 150 patients (both male and female) who were smokers selected during admission into our hospital. We got a total of 22 patients who developed air leak complications after 7 to 15 days of hospitalization without any invasive procedures, indicating the incidence of 14.67% which is high compared to other studies. Our results are similar to that of study conducted by Cut TG *et al.*[3] and Quincho Lopez *et al.*[4] in the aspect of male predominance, but our study is solely based on history given by patients who had history of chronic smoking. May be due to small sample size of female smoker patients we got 50% mortality rate. Among all the smoker patients (18 males and 4 females) who got severe pulmonary injury after hospitalization due to air leak, 50% females(2 patients) showed good prognosis and recovered completely, while other 50% showed severe lung injury and died. On the other hand, 12 male patients (66.67%) showed poor outcome and only 6 male patients (33.33%) showed good clinical improvement and discharged. So our study showed the significant relation between smoking and the associated increased mortality. As seen in the many other studies, the male gender predominance and the supposed theory of mechanisms were air leakage through the alveolar damage by inflammation and cytokine storm during the progression of the disease.[6,7,8]. In a retrospective study done by McGuinness *et al.* found that incidence of pneumothorax, pneumomediastinum, pneumopericardium, subcutaneous emphysema in 15% of the patients with COVID-19 requiring invasive mechanical ventilation, excluding barotrauma due to line or any surgical procedure [11]. In our study the theory behind these complications was spontaneous after few days of hospitalization with aggravation of lung involvement without invasive ventilation and associated smoking as risk factor developing these increased incidence of air leak complications. Out of 22 patients 14 patients showed poor prognosis giving mortality of about 63.64% and 8 patients with good prognosis showed the survival rate of 36.36%. Most common and frequent complication occurred was pneumomediastinum (14 cases) followed by pneumopericardium (9 cases). Despite the ICU care measurements patients who developed Pneumothorax (5 cases) and Subcutaneous emphysema (5 cases) in about 10 cases respectively showed 100% mortality rate. which were considered as serious or aggressive complications leading to increased mortality. In all the cases with poor outcome, clinical status worsening was coincided with the raise in inflammation markers such as C-reactive protein, ferritin, fibrinogen, procalcitonin and interleukin 6, as well as with deterioration of lactate, arterial blood gases and PH values were seen. In our study, the patients who recovered completely (8 patients) had a mild to moderate pulmonary involvement and were hospitalized immediately after the onset of early signs and symptoms and earlier start of specific medical therapy to avoid the aggression of the existing pulmonary involvement and reducing the infectious rate, which expressed as decreased levels of procalcitonin in the serum.

This study has limited number of patients, due to difficulty in patients revealing their smoking history and small number of cases presented to our institute that matched the inclusion & exclusion criteria of the study. We didn't compare our results with control group which is inclusion of non-smokers as it was discussed in many studies previously. Also we didn't include the vaccinated patients who got infected with covid19 pneumonia in our inclusion criteria. No availability of ECMO (Extracorporeal Membrane Oxygenation) machine at our institute might have increased the mortality in our study, as it can be used in seriously ill patients as advanced life support. As there are limited numbers of studies available on smokers with these complications for comparison, we couldn't have more references to be compare the results. Further studies with big sample size other inclusion criteria also required.

CONCLUSION

CT scan helps in early detection of air leak complications like Pneumomediastinum (PM), Pneumopericardium(PP), Subcutaneous emphysema(SE) and Pneumothorax(PT) and thus helps in prompt management. These complications were diagnosed more frequently in chronic smoker patients (male>female) affected with severe COVID-19 pneumonia. Thus, these complications are being associated

with prolonged hospitalization and poor prognosis on the outcome indicating the aggressive complications and increased mortality.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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