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Prevalence of lung fibrosis amongst COVID-19 patients admitted in ICU and their clinical profile: An observational study

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Abstract
Background: We are observing a very tough time once again fighting an invisible enemy, the novel coronavirus. A novel coronavirus spill over event, with its epicenter in Wuhan, China, has emerged as a public health emergency as an international concern today. Chest computed topography and investigating the role of inflammatory mediators plays an important role in evaluation of covid-19 and effective therapy for this infection.
Materials and Methods: An observational study in patients of covid-19 admitted in Geetanjali medical college, Udaipur. After taking all necessary consent, patients were enrolled. In each patient: symptom onset, blood and radiological investigations were compared during and after covid-19 treatment.
Result: In our study, 68 patients were enrolled, out of which 36 were males and 32 were females. 52 patients were aged above 60 years out of which 50 patients were having co-morbid conditions (DM, HTN, Hypothyroidism, obesity and CAD). Out of the total 68 patients included in our study, 60 patients showed deranged inflammatory markers (CRP, D-Dimer, and Lymphocytes) for more than 45 days amongst these patients. In 39 patients fibrotic changes were observed after three months in chest radiography.
Conclusion: From our study we conclude that the positive predictor of pulmonary fibrosis in covid19 infection are old age, co-morbid conditions, high severity index and inflammatory markers.

Keywords: Fibrosis, Covid-19

Introduction
Fibrotic lung disease is one of the possible consequences of COVID-19 pneumonia, and it is one of the most worrying long-term complications. Lung fibrosis is associated with non-reversible lung damage. The long-term lung changes of previous COVID-19 infection still not completely understood [1]. We evaluate the evidence in support of the risk factors for the development of lung fibrosis in COVID-19. We conclude that, from the available literature, the predictors of pulmonary fibrosis in COVID-19 infection are advanced age, illness severity, length of ICU stay and mechanical ventilation, smoking and chronic alcoholism [2].
Coronavirus cause respiratory system infections in humans, which can range from a minor symptoms to severe diseases. Which often leads to severe clinical symptoms and high mortality rates [3, 4], clinical epidemiological studies on COVID-19 have demonstrated that the majority of infected patients display mild symptoms, and many of them have recovered after appropriate medical treatments [5]. Of the confirmed COVID-19 pneumonia patients 5.0% were admitted to the ICU, 2.3% of them underwent invasive mechanical ventilation, and 1.4% of patients died [5]. Here we took patients of COVID-19 who were admitted in ICU with severe pneumonia, and kept on Antifibrotics to prevent fibrosis in patients with ARDS.

Material and Methods
In this study, 68 patients who had been hospitalized for COVID-19 at Geetanjali Medical college and hospital between June, 2020 and march, 2021 were tracked after discharge. The inclusion criteria included: 1) COVID-19 positive cases confirmed by pharyngeal swab nucleic acid testing; 2) patients have been hospitalized and then discharged after treatment;

3) patients underwent thin-section chest CT scans at least one during the hospitalization and had at least one follow-up CT scan after 3 months. Discharge criteria were in line with the Indian guideline for COVID-19 pneumonia. Clinical data for comparative analysis performed between the two groups included age, sex, comorbidities, signs and symptoms, laboratory test results, steroid therapy, antiviral therapy, length of hospital stay, days from illness onset to initial and worst-state CT scans, and days after discharge to latest follow-up CT scans. Laboratory test results were obtained when patients were in their most critical condition. CT imaging features were also collected from these 68 patients.

Results

Among 68 patients 36 were males and 32 were females. 52 patients were aged above 60 years out of which 50 patients were having co-morbid conditions (DM, HTN, Hypothyroidism, obesity and CAD). Out of the total 68 patients included in our study, 60 patients showed deranged inflammatory markers (CRP, D-Dimer, and Lymphocytes) for more than 45 days amongst these patients. In 39 patients fibrotic changes were observed after six months in chest radiography. All patients who developed lung fibrosis were having longer hospital stay and almost all patients were having comorbid condition.

Table 1: Showing Inflammatory Markers after discharge:

Parameter at the time of discharge	Derranged in no of patients	Normal in no. of patients
Lymphocyte %	56	12
D-Dimer	11	57
CRP	68	0

Table 2: Showing Inflammatory Markers after discharge:

Parameter After 3 months	Derrangedi n no of patients	Normal in no. of patients
Lymphocyte %	6	62
D-Dimer	0	68
CRP	9	59

Table 3: Showing CT scan finding

CT Scan thorax after 3 month	No. Of Pts.
Fibrosis present	39
Fibrosis absent	29
Total	68

Table 4: Showing Comorbidities

Comorbidities	No. of Patients
DM	48
HTN	46
Hypothyroidism	12
Obesity	18
CAD	16

Discussion

In our study, we took 68 patients Out of the total 68 patients included in our study, 60 patients showed deranged inflammatory markers (CRP, D-Dimer, and Lymphocytes) for more than 45 days amongst these patients. Clinically, patients with fibrosis after discharge were older than those without fibrosis, which implied that fibrosis was likely to be more common in elderly or immunocompromised patients, similar to SARS [6]. Patients with evidence of fibrosis after discharge had worse lung function at the time of illness onset.

Reduced lymphocyte count may be significant for the diagnosis of COVID-19 pneumonia. The increase in the inflammatory indicators CRP and cytokine factor leukomyin-6 indicated inflammatory damage caused by COVID-19 virus, and generated a series of immune responses, similar to the immunopathogenesis observed in SARS [7]. Furthermore, considering the higher level of CRP in patients with fibrosis, an increased inflammatory reaction might lead to the formation of pulmonary fibrosis during recovery. Therefore, these clinical parameters might contribute to predicting which patients with COVID-19 pneumonia are at a higher risk of developing pulmonary fibrosis after discharge. Patients with fibrosis had a longer period of hospital stay than those without fibrosis.

Pulmonary fibrosis is an important prognostic manifestation of a series of lung diseases [8, 9]. In our study, follow-up thin-section CT scans from all discharged patients showed that evidence of fibrosis, such as irregular interface and parenchymal band, was found in almost half of patients. The most common CT features in COVID-19 pneumonia were pure GGO, GGO with consolidation, interstitial thickening, crazy paving, irregular interface, and parenchymal band located mainly in bilateral lower lobes with peripheral distribution. As the disease progressed, there were more segments involved and a larger lesion diameter manifested on worst-state CT imaging. More patients on worst-state CT exhibited irregular interface and parenchymal band than on initial CT. For the latest follow-up CT after discharge, typical features such as interstitial thickening and crazy paving were almost absorbed, but evidence of fibrosis, such as irregular interface and parenchymal band were still obvious. These results indicate that irregular interface and parenchymal band may manifest during the whole course of COVID-19 pneumonia, although part of them was resolved eventually. However, most of the other lesions were gradually absorbed, with the exception of residual GGO, which is partly consistent with a previous study [10].

This study has some limitations. Firstly, the sample size of 68 patients was relatively small. However, as more COVID-19 patients are being discharged, further studies will consider increasing the sample size of discharged patients. Secondly, only patients who were discharged from hospitals after being cured were included in this study. Thus, this may introduce a selection bias for the distribution and extent of pulmonary lesions. Finally, the follow-up time for these patients is relatively short, and it is unknown whether irregular interface and parenchymal band features will permanently remain.

Conclusion

We found that fibrosis was more likely to develop in patients with severe clinical conditions, especially patients with high inflammatory indicators. Interstitial thickening, irregular interface, coarse reticular pattern, and parenchymal band, manifested in the process of the disease, may be predictors of pulmonary fibrosis. Irregular interface and parenchymal band could predict the formation of pulmonary fibrosis early.

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