Pulmonary Fibrosis: Post Covid-19 Complication and It's Risk Factors in a Tertiary Care Hospital in Vidarbha Region of Maharashtra

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Abstract

Background: Covid-19 was a catastrophe that had engulfed almost all the parts of the world.As we enter in a post covid era there has been concerns regarding the aftermath of this pandemic and the post recovery clinical and pathological changes in the recovered patients.This study is aimed to find the incidence of post covid pulmonary fibrosis in the survivors and analyze the spirometric pattern in these patients.It also helps us to predict the risk factors associated with post covid pulmonary fibrosis.

Results: We conducted a longitudinal study of 176 patients with a history of COVID-19 who presented to our hospital between May 2021 and December 2022. Patients with at least a one-time chest CT scan after discharge were enrolled. According to the presence of fibrosis on follow-up CT after discharge, patients were classified into two groups as the "non-fibrotic group" (without evident fibrosis) and "fibrotic group" (with evident fibrosis). Of these patients, 42.6% had residual pulmonary fibrosis during follow-up HRCT scan. The studied patients had an average age of 52 yrs,ranging from 18 to 75 yrs.Males were affected more than females Risk factors for pulmonary fibrosis included male sex,presence of comorbidities,use of NIV during hospital stay. The most common HRCT pattern seen in patients with pulmonary fibrosis was ground-glass opacities followed by reticulations and pleural thickening.Spirometry of these patients with post covid fibrosis showed varying degree of restriction.

Conclusion: These findings highlight the importance of long-term follow-up of COVID-19 survivors to identify and manage post-COVID-19 pulmonary fibrosis.

Keywords: COVID-19, High-Resolution Computer Tomography (HRCT), Longitudinal study, Pulmonary fibrosis, Risk factors

Introduction

COVID-19, caused by the novel coronavirus SARS-CoV-2, has resulted in a global pandemic that has affected millions of people worldwide.[1,2] Although most patients with COVID-19 experience mild to moderate symptoms, a significant proportion of patients develop severe respiratory illness that may require hospitalization and mechanical ventilation.Typical CT findings of covid-19 pneumonia are patchy ground-glass opacities with a peripheral and basal predominance pattern[3,4]. Pulmonary fibrosis, a progressive scarring of the lung tissue, is a known complication of several respiratory viral infections, including COVID-19. However, the risk factors and clinical characteristics of pulmonary fibrosis post-COVID-19 are not well understood. As the number of COVID-19 survivors increases, it is important to identify the risk factors and clinical characteristics of pulmonary fibrosis post-COVID-19 to help guide follow-up care and management of these patients. Therefore, the aim of this study is to identify the risk factors and clinical characteristics of

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pulmonary fibrosis in patients with a history of COVID-19.

Materials and Methods:

Study design: We conducted a longitudinal study of patients with a history of COVID-19 who presented to our hospital between May 2021 and December 2022.

Patient selection: We included all adult patients (aged 18 years or older) who were diagnosed with COVID-19 and had a positive SARS-CoV-2 polymerase chain reaction (PCR) test. We excluded patients who had pre-existing lung disease like interstitial lung disease and also pregnant women and patients who were on long term oxygen therapy at home.

Data collection:Demographic data, clinical characteristics, laboratory test results, chest radiograph and high-resolution computed tomography (HRCT) findings, and pulmonary function test (spirometry) results were collected and analysed.

Spirometry procedure:

All the enrolled patients were given prior pretest instructions about the procedure.

1. Do not smoke/drink coffee 1 hour prior to the test

2. Have light meal in the morning

3. Wear loose fitting clothes

4. Withhold inhaler therapy if any 12-24 hours prior to the test

Proper instructions were given about the procedure and the requirement of putting decent efforts for getting satisfactory results.Results were made as per the guidelines from the Ruppel's manual of Pulmonary Function Testing and were divided into mild, moderate and severe restrictive pattern.

HRCT procedure and patient positioning:

The patients were placed in the supine and headfirst position and received scanning with breath held technique.No contrast was administered. All images were transmitted to the post processing workstation and reconstructed using high resolution and conventional algorithms at a slice thickness of 1–1.25 mm .The images were viewed in both lung and mediastinal window settings. Initial and follow-up CT of all patients were reported by two experienced radiologists. Clinical details were not provided during reporting of follow-up CT to the radiologists. Consistency in reports of HRCT were accepted and compiled in master chart.

Follow-up: All patients were followed up for at least 6 months after their initial COVID-19 diagnosis. Patients underwent chest radiograph and HRCT at regular intervals during follow-up. Pulmonary function tests (Spirometry) were performed at 3-6 month follow-up.

Data analysis: We used descriptive statistics to summarize the demographic data and clinical characteristics of the patients. We used logistic regression analysis to identify the risk factors for pulmonary fibrosis post-COVID-19 infection. All statistical analyses were performed using SPSS software. A p- value of <0.05 was considered statistically significant.

Results and Discussion:

Table 1. General characteristics of study participants

Characteristics		
1) Age (Years)	Mean ± SD	
Mean ± SD	52.35 ± 12.37	
2) Gender	Frequency	Percentages
Male	95	53.9%
Female	81	46.1%

3) Duration of hospital stay (in days)	Mean ± SD	
Patients with comorbidities	10.2 ± 2.14	
Patients without comorbidities	5.9 ± 1.52	
4) Duration of O2 support (in days) Patients with comorbidities	8.5 ± 1.64	
Patients without comorbidities	4.5 + 1.61	Percentages
5) Fibrosis on F/u HRCT	Frequency	
Yes	75	42.6%
No	101	57.4%

The mean age of the population is 52.35 years with a standard deviation of 12.37. Among the participants, 53.9% are male and 46.1% are female.The duration of hospital stay is 10.2 ± 2.14 days for patients with comorbidities and 5.9 ± 1.52 days for patients without comorbidities.The duration o f oxygen support is 8.5 ± 1.64 days for patients with comorbidities and 4.5 ± 1.61 days for patients without comorbidities. Among the sample, 42.6% have fibrosis on follow-up HRCT, while 57.4% do not have fibrosis.

Table 2. HRCT pattern seen at the time of admission

HRCT pattern	Frequency	Percentage
1)GGO's with crazy paving	125	71%
2)Consolidation	105	59.7%
3)Reticulations thickening	70	39.8%

The most common HRCT pattern observed during admission with Covid-19 infection is ground-glass opacity (GGO) with crazy paving pattern, with a frequency of 125 and a percentage of 71. Consolidation with air bronchogram is the second most frequent HRCT pattern, observed in 105 cases (59.7%). The pattern of reticulation and thickening was observed in 70 cases (39.8%).

Table 3. HRCT pattern seen during follow up scan in fibrotic group patients (n=75)*

HRCT pattern	Frequency	Percentages

1)GGO's	62	82.7%
2)Reticulations	55	73.3%
3)Pleural thickening	34	45.3%
4)Tractional bronchiectasis	12	16%

*multiple possible option

Among these patients, the most frequently observed HRCT pattern is GGO, with a frequency of 62 and a percentage of 82.7%. Reticulations are the second most frequently observed HRCT pattern, found in 55 cases (73.3%). Pleural thickening is the third most frequent pattern observed in 34 cases (45.3%). Tractional bronchiectasis is the least commonly observed HRCT pattern, found in 12 cases (16%) during follow up scan.

Figure 1:HRCT axial images of a 55 yr old female covid patient showing b/l GGO's during admission and at 3 month f/u post recovery showing b/l GGO's with reticulations and subpleural bronchiectasis.
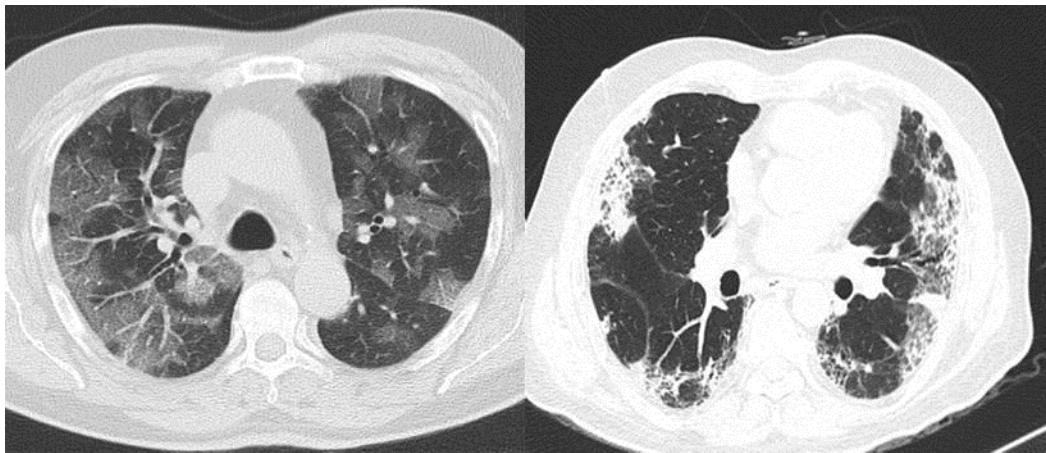

Figure 2:HRCT axial images of a 49 yr old male covid patient showing b/l GGO's with consolidation and air bronchogram during admission and at 4 month f/u post recovery showing b/l GGO's with reticulations
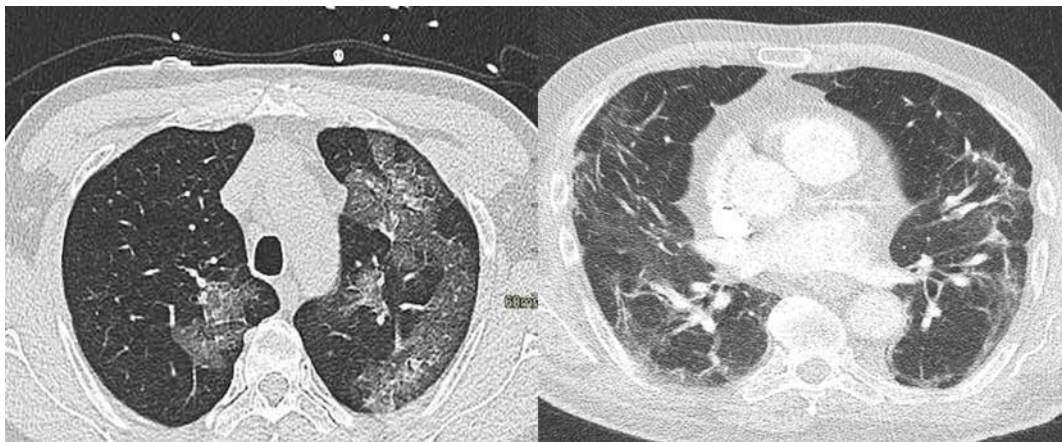

Table 4. Features of patients with fibrosis on follow up HRCT scan (n=75)

1) Comorbidities	Frequency	Percentage
Yes	46	61.3%

No	29	38.7%
2) Type of comorbidities		
DM	12	16%
HTN	5	6.6%
IHD	4	5.3%
COPD	8	10.6%
Obesity	8	10.6%
Multiple comorbidities	9	12%
3) Use of NIV		
Yes	19	25.3%
No	56	74.7%

Among those with comorbidities, the most frequently observed comorbidity was diabetes mellitus (DM), observed in 16% of the patients. Hypertension (HTN) was observed in 6.6% of the patients, ischemic heart disease (IHD) in 5.3%, chronic obstructive pulmonary disease (COPD) in 10.6%, and obesity in 10.6%. Multiple comorbidities were observed in 12% of the patients. Among the patients with fibrosis on follow-up HRCT, 25.3% required the use of non-invasive ventilation (NIV) during their stay at hospital, while 74.7% did not require NIV.

Table 5. Spirometry findings in patients with fibrosis (n=75)

1) Spirometry abnormality	Frequency	Percentages
Yes	63	84%
No	12	16%
2) Pattern on spirometry		
Mild restriction	30	47.6%
Moderate restriction	18	28.5%
Sever restriction	7	11.1%
Mixed airway disease	8	12.6%

Among the patients with post covid fibrosis on follow up HRCT, 84% had spirometry abnormalities, while 16% had normal spirometry. Among those with spirometry abnormalities, the most frequently observed pattern was mild restriction, observed in 30 cases (47.6%). Moderate restriction was the second most frequent pattern, observed in 18 cases (28.5%). Severe restriction was observed in 7 cases (11.1%), while mixed airway disease was observed in 8 cases (12.6%).

Discussion:

The clinical presentation of COVID-19 infection can range from mild symptoms to severe illness that leads to severe lung damage or even mortality.[5]

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Pulmonary fibrosis in post covid patients has been considered as a worrisome sequalae. It results in permanent architectural distortion and may cause irreversible pulmonary dysfunction. HRCT thorax had been pivotal in the diagnosis of COVID-19 and assessment of disease severity. The major imaging features of COVID-19 pneumonia have been discussed in detail in many publications.[6] However, the post-recovery outcome of the disease and its long- term effects on lung parenchyma remain unanswered questions.

Male participants (53.9%) outnumbered female participants (46.1%) in the present study. **Amin BJ et al** [7] reported that their study comprised of nearly equal number of male (51.9%) and female (48.1%).Most commonly affected sex by COVID-19 were male (88.0%) in a study be **Saluja M et al**[8].

At the current study, of the 176 patients with HRCT thorax report during admission 42.6% patients showed fibrotic changes on follow-up HRCT while 57.4% patients showed no fibrotic changes. Similar to the present study, 48.1% patients showed fibrotic changes on follow-up HRCT in a study conducted by **Yasin R et al**.[9] In other study by **Alkhayat KF et al**, pulmonary fibrosis was noted among 21 (33.9%) paricipants[10]. **Rai DK et al** in their study observed 20 % prevalence of pulmonary fibrosis in post covid-19 patients.[11]

In our study we found that patients with comorbidities were at significant high risk (61.33%) than those without comorbidities (38.66%) to develop fibrosis in post covid phase. Similar findings were seen by **Zhou F et al** who found that DM, HTN, IHD, obesity were significant in causation of post covid fibrosis in the survivors.[12]

Similarly, our results showed that, of the 75 patients with post recovery fibrosis the most common HRCT pattern seen in patients on follow-up was ground glass opacities in 82.7% patients followed by reticulations and pleural thickening in 73.3% and 45.3% patients. This results are in line with the study conducted **by Manolescu D et al,**[13] where ground glass opacities were seen in 86.6% patients and reticulation seen in 78.80%.

Additionally in the present study, of the 63 patients with restrictive pattern on spirometry, mild restrictive patterns (47.6%) were most predominently observed among the patients with residual changes followed by moderate restrictive pattern (28.6%) followed by severe restrictive pattern (11.1%). In a study conducted by **Modi P et al,**[14] among those with restriction 47.8% had mild, 43.5% had moderate and 8.7% had severe abnormality. **R. Torres-Castro et al,**[15] done systematic review and meta-analysis of Respiratory function in post-COVID-19 cases and observed altered diffusion capacity, restrictive pattern and obstructive pattern were found in 39%, 15% and 7% of patients, respectively.

These variations in the prevalence of restrictive lung defect among COVID-19 pneumonia survivors could be explained by the differences in the time of assessment which range from close to discharge to three months after discharge. These studies suggest that patients affected by COVID-19 pneumonia are at increased risk of developing restrictive pulmonary diseases after recovery from the acute illness.

Limitations and future prospectives:

1. The study was carried out on post covid patients at 3 to 6 month interval. All the symptoms and clinical evaluation along with radiological and spirometry was done and assessed. However further follow ups required to check for resolution or progression of symptoms was not carried out in all study subjects due to poor compliance to follow up , as most of the study population were of elder age group.

2. Spirometry is a subjective test, the results of which depends on patients performance and efforts. As most of the patients were elderly, performance affected the results.

3. The current study was carried out at a tertiary care health center. Its replicability in the programmatic conditions at the primary health care level in the field must be assessed.

4. The current study raises future perspectives in understanding the pulmonary involvement of long COVID syndrome. It promotes a further follow-up analysis of patients with persistent radiologic findings to observe whether a slow but significant remission is likely to occur, or irreversible fibrosis happens.

5. Another key question is to determine which particular risk factors are predictors for fibrotic lung damage.

Conclusions:

HRCT imaging studies should be utilized more often in the setting of the COVID-19 pandemic, since they prove to have an important role in assessing disease severity at hospital admission and following prognosis. HRCT chest exams performed throughout the course of illness help in patient treatment and provide a stronger association of the patient clinical presentation with their radiological features that might benefit in further decreasing the SARS-CoV-2 infection-related complications and deaths.

Ethics approval and consent to participate

Approval from Institutional Ethics Committee were sought before start of the study and informed consent were taken from the participants.

List of abbreviations

HRCT: High-resolution computed tomography; SARS-CoV: Severe acute respiratory syndrome coronavirus; ARDS: Acute respiratory distress syndrome; RT-PCR: Reverse transcriptase polymerase chain reaction; GGO: Ground glass opacity; CT: Computerized tomography; CPAP: Continuous positive airway pressure; ILD:Interstitial lung disease; LTOT: Long term oxygen therapy; NIV: Non invasive ventilation.

Authors' Contributions

DJ Bhanushali conduct literature search, analysis and interpretation of data and manuscript writing. RK Rathod reviewed the manuscript. All authors read and approved the final manuscript.

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