

PULMONARY FIBROSIS IN COVID-19 SURVIVORS -A MYTH: PROSPECTIVE ONE YEAR FOLLOW UP STUDY TO PROVE IT

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Abstract

Pulmonary Fibrosis in covid-19 survivors -A myth: Prospective one year follow up study to prove it. Background: Many uncertainties are prevailing regarding the chronic lung manifestations of Covid-19 and long-term sequelae of covid-19. Data are relatively lacking. To address this problem, this study is undertaken. Purpose: To look for Pulmonary fibrosis and to assess the residual pulmonary abnormalities on HRCT Chest in Covid-19 survivors at one year follow up. Materials and Methods: After discharge from Regional Institute of Medical Sciences, Imphal, Manipur covid-19 survivors with CTSS (Computed Tomography Severity Score) of moderate and severe grade, discharged between May 2021 and August 2021 were prospectively evaluated at one year through systematic assessment of HRCT thorax. Results: 40 participants (mean age \pm SD, 56.83 years \pm 12.52) were assessed. Patients with co morbidities like hypertension in 7(17.5%), diabetes mellitus in 8(20%) and pulmonary hypertension in 2(5%) were assessed. Previously seen crazy paving pattern, broncho vascular thickening, consolidation was completely absorbed in follow up studies in respective patients. Honey-combing was not observed. 21 (52.5%) patients had complete resolution of lung abnormalities. No evidence of fibrosis was noted in them. 19 (47.5%) patients had residual pulmonary abnormalities in the form of traction bronchiectasis, reticulation and fibrous stripes. No statistically significant difference was found between mean age in years, comorbidities, CTSS and fibrotic like changes. Clinically the patients were feeling better with no complains of shortness of breath. Conclusion: This study has revealed that significant amount of HRCT lung parenchymal abnormalities gets absorbed. Very few of them persist up to 12 months. Reticulation is observed in 65% patients but it is not considered to be a specific feature of established pulmonary fibrosis. It has been observed that reticulation and other residual abnormalities also gets absorbed in subsequent longer follow ups. We conclude that HRCT features of established pulmonary fibrosis are not observed in post covid survivors.

Keywords: Post Covid-19, Pulmonary Fibrosis, HRCT Chest, One year follow-up.

MAIN TEXT

After passing of the acute stage of covid-19 pneumonia, it was feared that the patients who has recovered from their acute covid-19 pneumonia will be left with residual pulmonary fibrosis and lifelong oxygen dependence.

It was said that post covid-19 interstitial lung disease will be the most frequently encountered condition as this virus spreads its tentacles across the globe. This study tries to throw light on

post covid pulmonary fibrosis by doing a follow up in patients having moderate and severe covid, based on Computed tomography severity score (CTSS).

We were also concerned about the long-term pulmonary sequelae of covid -19. Data is lacking. Very few studies are done. Also, many uncertainties were there regarding the chronic lung manifestations of covid-19. Clinicians were doubtful about the long-term manifestations of post covid-19 infection.

We already had an experience of worldwide outbreak of SARS and Middle East Respiratory Syndrome, where pulmonary fibrosis was encountered. So, this was another concern regarding covid-19, if they would eventually lead to pulmonary fibrosis. To address this problem, this study was undertaken.

Objectives: To look for pulmonary fibrosis in covid-19 survivors at one year follow -up. To assess the residual pulmonary abnormalities on HRCT chest in covid-19 survivors at one year follow up.

METHODS

Study Design and Participants

This is an observational cohort study in Covid -19 survivors. This study was conducted in a tertiary care Hospital in Regional Institute of Medical Sciences, Imphal, and Manipur, India in the department of Radiodiagnosis. The study is carried out in covid-19 survivors with moderate to severe CT severity score, who were discharged from the hospital between May 2021 and August 2021. These patients were prospectively followed up at one year. These patients were identified through electronic case record review and the date on which HRCT chest study done in the department of radiodiagnosis is noted. They were approached by telephonic call.

The inclusion criteria were

- 1) Confirmed covid-19 positive cases confirmed by real time RT-PCR with a standard protocol recommended by the National Centre for Disease Control, Government of India.
- 2) Patients have been hospitalized and then after treatment being discharged.
- 3) All patients with CTSS of moderate to severe with or without co morbidities were included. Co morbidities were Diabetes, Hypertension, Asthma, Heart disease.
- 4) Patients underwent HRCT Chest scan once during admission with CTSS of moderate to severe.
- 5) Patients underwent follow up HRCT chest scan at one year.

CTSS out of 25[1]

Score	Severity
<8	Mild
9-15	Moderate
>15	Severe

Exclusion Criteria were: Patients who could not come for one year follow up.

Written Informed Consent from the participants was waived by the Institutional Review Board.

The ethical committee of RIMS, Imphal has given their approval for this study.

Procedures

Patients were referred for HRCT Chest with RT-PCR test positive for Covid-19. Patients underwent non contrast enhanced chest CT examination in supine position and with breath holding following inspiration (CT-SIEMENS, Somatom go. All, 128 slice) 1 mm collimation at 5 mm intervals were taken. Images were obtained in both lung (width 1500 HU; level -700 HU) and mediastinal (width 350 HU; level 50 HU) window settings. For the follow up at 12 months, we called the patients telephonically according to their date of first HRCT chest study.

For assessment of images, two radiologists with 10 years and 20 years of thoracic radiology experience reviewed the images independently. In case of discrepancy final findings were reached by discussion and consensus.

Both the radiologists were unaware about the clinical progress of the patient. They only knew that these images were of patients with covid-19. The CT patterns in our study is described according to the terms defined by Fleischner Society and peer reviewed literature on viral pneumonia. The CT severity scores of patients during hospitalization were recorded with a method described previously and were labelled as CT-1 i.e., first CT study during acute stage of Covid-19.

For Follow up HRCT at 12 months, interstitial changes in lungs were assessed like traction bronchiectasis, reticulation, fibrous stripe and honey combing. These, if present were labelled as 'fibrotic like changes'[2]. Fibrosis on chest scan were defined as a combination of fibrous stripes, reticular pattern, traction bronchiectasis and honey combing[3,4,5]

HRCT scans at 12 months follow up were compared with HRCT scans performed at admission (n=20) or during treatment (n=20) depending on availability.

Statistical Analysis

Bivariate analysis was done using Fisher's exact test to compare proportions. T test was used to compare means between two groups.

P values less than 0.05 were considered statistically significant. All data analysis and graphs were done SPSS (version 22.0)

RESULTS

40 participants (mean age \pm SD, 56.83 years \pm 12.52), 32 male (80 %), 8 female (20%) were assessed. CTSS at baseline means CTSS during admission - was 20 in 11 patients (27.5%).

7 patients were having CTSS of 15 i.e., moderate grade and 7 patients (17.5%) were having CTSS of 22 (severe grade).

Patients with co-morbidities like hypertension in 7 (17.5%) patients, diabetes mellitus in 8 (20%) patients and pulmonary arterial hypertension in 2 (5%) patients were assessed.

CT Abnormalities in first HRCT Chest Study

Central Ground glass opacities	5 patients (12.5%)
Peripheral GGO	35 patients (87.5%).
Fibrous stripes	32 patients (80%)
Subpleural lines	23 patients (57.5%)
Reticulation	36(90%)
Crazy paving	13(32.5%)
Broncho-vascular thickening	20(50%)
Consolidation	22(55%)
Traction Bronchiectasis	5(12.5%)
Pleural Effusion	1(2.5%)

Maximum number of lung segments involved were 18 in 25 patients (62.5%).

CT abnormalities at one year follow up

Ground glass opacities were almost completely absorbed in most of the studies.

Subtle GGO	8 patients (20%).
Fibrous stripes	19(47.5%)
Subpleural lines	11 (27.5%)
Reticulation	26(65%)
Traction Bronchiectasis	9 (22.5%)
Honey combing	0(0%)

No pleural effusion or pleural thickening in follow up CT study.

Maximum number of lung segments involved were 18 segments in one patient.

3 lung segments were involved in 15 patients (37.5%)

In 6 patients, no lung segment was involved in follow up HRCT study.

Previously seen crazy paving pattern, broncho-vascular thickening, and consolidation was completely absorbed in follow up studies in respective patients.

Table 1: Bivariate Analysis of Characteristics with CT Changes at Follow up for Fibrotic like Changes

Variable	Present N (%)	Absent N (%)	P value
Age in years, mean (SD)	58.00(12.47)	50.17(11.57)	0.160
Male	28(87.5)	4(12.5)	0.580
Female	6(75.0)	2(25.0)	
Hypertension			0.567
Present	7(100.0)	0(0.0)	
Absent	27(81.8)	6(18.2)	
Diabetes			0.318
Present	8(100.0)	0(0.0)	
Absent	26(81.3)	6(18.8)	
CTSS at baseline, mean (SD)	19.41(2.79)	17.50(3.51)	0.144

Honey combing was not observed in any of the follow up CT study. ‘Fibrotic like changes’ at follow up were seen in 19(47.5%) patients. Fibrosis is considered to be present if any of the following were present; fibrous stripes, traction bronchiectasis, reticulation and honey combing. 21(52.5%) patients had complete resolution of lung abnormalities. No evidence of fibrosis was noted in them. 19(47.5%) patients had residual pulmonary abnormalities in the form of traction bronchiectasis, reticulation and fibrous stripes.

There were no complains of breathlessness in any of the patients except one. He was complaining of minimal breathlessness while walking for longer time. This patient was of age 82 years with diabetes, hypertension and CTSS on follow up was 15.

We found no statistically significant difference between mean age in years and fibrotic like changes at follow up. No significant association was found between male and female and fibrotic like changes at follow-up.

No association was found between hypertension and fibrotic like changes at follow up.

Similarly, no association was found between diabetes and fibrotic like changes at follow up.

No significant difference between mean of CTSS during first CT study and CTSS at follow up.

As in all these the p value was more than 0.05.

Bias

As we do not have pre-Covid CT imaging studies of these patients available with us possibility is there that certain fibrotic like changes may be present before Covid in these patients, due to some other cause. We cannot rule out this possibility and bias is possible.

Strength

We have included patients with moderate to severe CTSS, where more probability will be there of residual pulmonary abnormalities and pulmonary fibrosis.

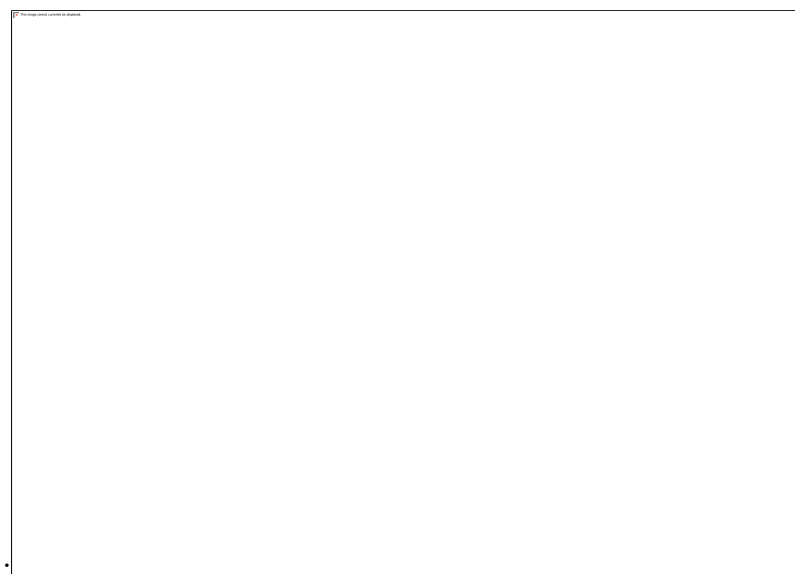


Figure 1: Axial HRCT at Admission

Image reveals consolidation in bilateral lobes

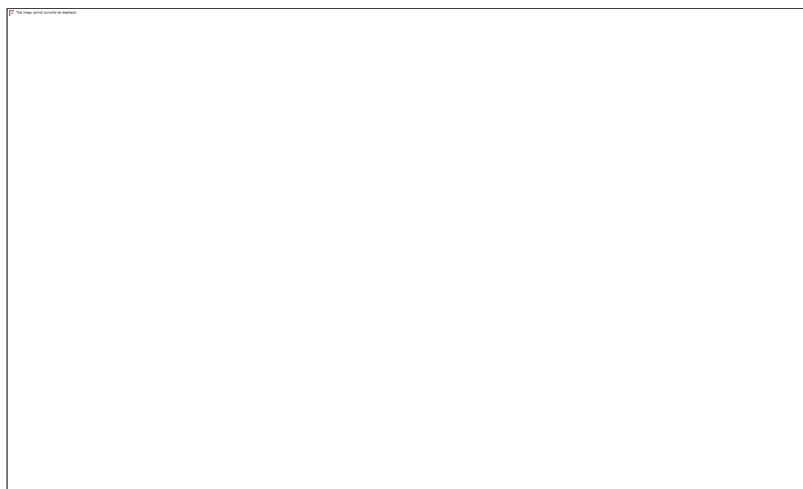


Figure 2: HRCT at One year follow up of the same Patient

Reveals clearing of all consolidation at the same level.

DISCUSSION

This prospective observational study of covid-19 survivors discharged from the hospital was undertaken to know the long-term pulmonary sequelae of covid-19 at one year follow up. In a study by P Barria et al [6], HRCT abnormalities were detected in 43% at one year follow up. This is closely consistent with our study where HRCT abnormalities were detected in 47.5%.

In P Barria study [6], the most prevalent HRCT pattern at one year follow up were ground glass opacities (71%), subpleural reticulation and atelectasis (35%) and bronchiectasis (10%). In current study, the most prevalent HRCT pattern were reticulation 26(65%), fibrous stripes 19(47.5%), subpleural lines 11 (27.5%) and traction bronchiectasis (22.5%).

A study at 15 month follow up [7], concluded that less than 10 % patients are likely to develop radiological features of post covid-interstitial lung disease (PC-ILD).

In one study, (21/296) 7% presented with pulmonary sequelae (fibrotic like changes) at one year follow up with preserved lung function. These patients were smokers, received higher level of medical care during hospitalization and a prolonged hospital stay.[8]

In a study by Wu X et al [9], 20 patients (24%), had abnormal HRCT at 12 months. None of the HRCT showed evidence of established fibrosis. This study did not include patients with history of hypertension, diabetes, cardiovascular diseases, cancer, asthma, COPD, patients who has received corticosteroids or patients who required intubation and mechanical ventilation. This may be the reason for small percentage of patients with abnormal HRCT.

In the current study, patients with co-morbidities i.e., hypertension, diabetes, heart disease, asthma, COPD and who has received corticosteroids were included. Also, the included patient's CTSS was moderate to severe. This may be the reason that 'fibrotic like changes' are observed in larger percentage of patients (47.5%) in our study. Although in our study, patient with intubation and mechanical ventilation were excluded.

The significant risk factors for the development of post covid-19 lung abnormalities were proved to be increased age, severity of covid-19 and degree of pulmonary involvement during acute infection, according to our study. Similar risk factors were put forward by A sanna et al [7]. None of the covid survivors showed progression of CT findings at 1 year follow up. This is in align with a recent study by Vijaykumar et al. [10]

It is assumed that fibrous stripes, subpleural lines represent established fibrosis. However, in our study, fibrous stripes (from 80% to 47.5%) and subpleural lines (from 57.5% to 27.5%) significantly disappeared at subsequent one year follow up study. Hence, we propose that the terms like 'covid related fibrosis' and 'Post covid- interstitial lung disease' just on the basis of HRCT findings alone need not be used as the current study and other studies [7,8,9,10] did not reveal presence of established fibrosis.

In our study, patients did not have shortness of breath at one year follow up. Shortness of breath is an important clinical symptom in case of established fibrosis. [11]

LIMITATIONS

Considering the relatively small sample size, generalizability of this study is not possible. Studies with large sample size is needed. Breathlessness was assessed using participant reported symptoms.

RECOMMENDATIONS

It has been observed that there is rapid absorption of crazy paving pattern, broncho-vascular thickening, and consolidation in follow up studies. We expect that the residual lung abnormalities will resolve with time. We would recommend for further long term follow up to look for complete resolution of HRCT abnormalities or persistence of them.

In summary, this study has revealed that significant amount of HRCT lung parenchymal abnormalities gets absorbed (52.5%) and few of them persist up to 12 months follow up (47.5%). Reticulation is observed in 26/40 (65%) patients but it is not considered to be a specific feature of pulmonary fibrosis. It has been observed that reticulation gets absorbed in subsequent longer follow ups. [12] We conclude that HRCT features of established fibrosis are not observed. We propose that patients being clinically free of any symptoms of shortness of breath, it's not worth to get one HRCT done for longer follow up.

We recommend that follow-up HRCT study need to be done only in those who are complaining of shortness of breath.

Acknowledgement

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