Section: Radiodiagnosis

Research

STUDY OF COVID-19 DISEASE SEQUELAE ON HRCT THORAX

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Abstract

Background: To describe long term sequelae of mild, moderate and severe COVID 19 infection, on HRCT in patients who have recovered from the infection. Purpose- HRCT characterization of pulmonary sequelae in patients recovered from mild to severe Covid 19 infections - a six months follow-up study. **Materials and Methods:** A total of 59 patients, mean age 50 years were studied prospectively. Lung changes (opacification, consolidation, reticulation, and fibrotic-like changes etc) and CT extent scores (score per lobe, 0–5; maximum score, 25) were recorded. **Result:** With increase in CT severity score there were increased incidence of GGO, consolidation, reticulations, crazy paving (P <0.05 by comparative analysis) out of which GGO and consolidation showed significant resolution in follow up CT as seen with Wilcoxon Analysis. **Conclusion:** Follow-up CT showed resolution of lung findings predominantly GGO and consolidation. Fibrotic-like changes in the lung were seen in very few patients.

INTRODUCTION

The first report of a novel respiratory virus which was subsequently shown to be a coronavirus, severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2), emerged from Wuhan, China in December 2019.[1-5] Pathology studies have shown that COVID-19 causes injuries in multiple organs and tissues, with extensive pulmonary involvement similar to that found in other coronavirus infections (i.e., severe acute respiratory syndrome coronavirus and Middle East respiratory syndrome coronavirus infection).[5,6] Typical radiologic images of COVID-19 demonstrated bilateral, peripheral, and basal predominant ground-glass opacity, consolidation, or both.[7,8]

Predicting the likely respiratory consequences of COVID-19 is really challenging but there is an emerging need of a study which put insight on this important aspect. There may be important parallels from the severe acute respiratory syndrome (SARS) outbreak of 2002–2003 caused by SARS-CoV. We may have some insight from the severe acute respiratory syndrome (SARS) outbreak of 2002–2003 caused by SARS-CoV and Middle East respiratory syndrome (MERS) first identified in 2012.[9]

MATERIALS AND METHODS

Study Design and Participants

The study is an observational study performed over a period of six months using convenient sampling from the patients. The patients who fulfilled the following criterion were included for the purpose of the study:

(i) All the moderate to severe cases of COVID 19 patients who were discharged during the study periods;
(ii) Patients with HRCT Chest during acute infection and at 24 weeks;
(iii) Age >18 years.

A detailed radiological data was recorded along with the contact number at time of discharge from the hospital, of all the patients who fulfilled the above criterion. After 2 weeks of discharge enquiry about clinical symptoms and symptomatic treatment were advised on telephone; next follow-up was taken up after 6 weeks of discharge and also assessed for clinical symptoms, and PFT. Last follow-up at 24 weeks is also included in the study. HRCT is usually performed at 24 weeks in patients who showed abnormal HRCT at 6 weeks.

During follow-up, in clinical assessment- we looked for symptoms such as dyspnoea with severity

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(mMRC scale), cough, fever, chest pain, fatigue, weakness, loss of taste/smell, sleep disturbances or any other symptoms as complained by the patient along with physical examination. A six-minute walk test was conducted which measured the total distance walked, O2 desaturation among symptomatic patients. Spirometry and DLCO was also performed at every follow-up in all symptomatic patients.

CT Image Acquisition and Interpretation

Non-contrast CT chest with HRCT reformation are performed on 128 slice Philips Ingenuity CT scan system located in trauma center or Siemens Definition 256 slice CT scanner. Images obtained are evaluated using various MPRs (multiplanar reformations).

All CT images are reviewed in random order by a radiologist and a pulmonologist who are not aware of any clinical or laboratory findings or patient outcomes. For each patient predominant CT patterns according to the Fleischner Society glossary was enumerated as follows: ground-glass opacities (GGO), consolidation, reticulation, emphysema, thickening of the adjacent pleura, pleural effusion, presence of nodules or masses, honeycombing, bronchiectasis, and interlobar pleural traction (retraction of the interlobar pleura toward the lesions). The CT evidence of fibrotic-like changes was defined as the presence of traction bronchiectasis, parenchymal bands (and/or honeycombing). To quantify the extent of pulmonary abnormalities (total lesions, GGO, consolidation, reticulation, and fibrotic-like changes), a semiquantitative CT score was assigned on the basis of the area involved in each of the five lung lobes. Each lobe of the lung will be examined to get a CT severity score. The CT severity score will be assessed subjectively based on the percentage of opacification of each lobe:

0- no involvement
1- less than 5% involvement
2- 5%–25% involvement
3- 26%–49% involvement
4- 50%–75% involvement
5- Greater than 75% involvement

The total CT severity score will be calculated by summing the individual lobar scores, with possible scores ranging from 0 to 25.

(Grading of severity: Mild <8. 9-15 Moderate Severe >15)

Statistical Analysis

The analysis is divided into two parts. The first part talks about the comparative analysis on the basis of severity (CT Score) on the parameters of affected lung lobes. The table shows the number of cases of each symptom noticed in each lung lobe. The number of cases pertaining to each unit is mentioned in Appendix 1. The table further elaborates the cases based on the percentage of opacification of each lobe which enables one to see the difference by observation method.

To further fortify the results by observation, comparative analysis was done for each symptom noticed in the lung lobes with the help of Kruskal Wallis Test. The test was conducted to understand whether the differences noticed between the mild, moderate and severe cases were significantly different from each other or not. Appendix 2 shows the test statistic value along with the p-value and the adjusted p-value. The values of adjusted p-values less than 0.05 indicate significant difference.

The second part of the study further extended to analyze the difference in the symptoms of patients with the follow up reports. The follow ups were marked as old and new for identification of patients which had undergone follow up. To analyze whether there was any difference of symptoms as experienced by the patients, use of Wilcoxon test was made. This test is non-parametric in nature and compares medians of the groups which are formed as a result of before and after cases. The appendix 3 shows significant differences in case of GGO and right-lower and left-lower lung lobe of CONSOLIDATION only. The rest of the symptoms did not show a significant difference in medians.

Appendix 1: CT score of parameters affecting lung lobes

		Mild (29)						Moderate (23)						Severe (7)					
		0	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
GGO	RU	19	9	1	0	0	0	1	4	12	6	0	0	0	0	2	2	2	1
	RM	19	10	0	0	0	0	1	8	10	4	0	0	0	0	0	3	3	1
	RL	14	10	3	2	0	0	0	0	7	15	1	0	0	0	0	1	4	2
	LU	13	13	3	0	0	0	0	1	11	11	0	0	0	0	0	4	1	2
	LL	12	14	2	0	1	0	0	0	7	12	2	2	0	0	0	0	4	3

		Mild (29)						Moderate (23)						Severe (7)					
		0	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
CON	RU	28	1	0	0	0	0	18	5	0	0	0	0	3	4	0	0	0	0
	RM	28	1	0	0	0	0	19	4	0	0	0	0	5	2	0	0	0	0
	RL	28	1	0	0	0	0	20	3	0	0	0	0	4	3	0	0	0	0
	LU	26	3	0	0	0	0	16	7	0	0	0	0	3	4	0	0	0	0
	LL	27	2	0	0	0	0	20	3	0	0	0	0	4	3	0	0	0	0

	Mild (29)						Moderate (23)						Severe (7)					
	0	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**

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NODULES	RU	25	4	0	0	0	0	19	4	0	0	0	0	6	1	0	0	0	0
	RM	28	1	0	0	0	0	22	1	0	0	0	0	7	0	0	0	0	0
	RL	28	1	0	0	0	0	22	1	0	0	0	0	7	0	0	0	0	0
	LU	24	5	0	0	0	0	16	7	0	0	0	0	7	0	0	0	0	0
	LL	26	3	0	0	0	0	20	3	0	0	0	0	7	0	0	0	0	0

		Mild (29)						**Moderate (23)**						**Severe (7)**					
		0	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
CP	RU	29	0	0	0	0	0	18	5	0	0	0	0	4	3	0	0	0	0
	RM	29	0	0	0	0	0	18	5	0	0	0	0	4	3	0	0	0	0
	RL	29	0	0	0	0	0	18	5	0	0	0	0	4	3	0	0	0	0
	LU	29	0	0	0	0	0	19	4	0	0	0	0	4	3	0	0	0	0
	LL	29	0	0	0	0	0	18	5	0	0	0	0	4	3	0	0	0	0

		Mild (29)						**Moderate (23)**						**Severe (7)**					
		0	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
RET	RU	21	8	0	0	0	0	5	18	0	0	0	0	1	6	0	0	0	0
	RM	18	11	0	0	0	0	5	18	0	0	0	0	1	6	0	0	0	0
	RL	19	10	0	0	0	0	2	21	0	0	0	0	1	6	0	0	0	0
	LU	18	11	0	0	0	0	4	19	0	0	0	0	1	6	0	0	0	0
	LL	16	13	0	0	0	0	1	22	0	0	0	0	0	7	0	0	0	0

		Mild (29)						**Moderate (23)**						**Severe (7)**					
		0	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
BRON	RU	22	7	0	0	0	0	12	11	0	0	0	0	2	5	0	0	0	0
	RM	23	6	0	0	0	0	12	11	0	0	0	0	2	5	0	0	0	0
	RL	22	7	0	0	0	0	10	13	0	0	0	0	1	6	0	0	0	0
	LU	23	6	0	0	0	0	12	11	0	0	0	0	2	5	0	0	0	0
	LL	22	7	0	0	0	0	10	13	0	0	0	0	1	6	0	0	0	0

		Mild (29)						**Moderate (23)**						**Severe (7)**					
		0	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**	**0**	**1**	**2**	**3**	**4**	**5**
FIBRO	RU	28	1	0	0	0	0	21	2	0	0	0	0	4	3	0	0	0	0
	RM	27	2	0	0	0	0	21	2	0	0	0	0	4	3	0	0	0	0
	RL	28	1	0	0	0	0	19	4	0	0	0	0	4	3	0	0	0	0
	LU	25	4	0	0	0	0	21	2	0	0	0	0	4	3	0	0	0	0
	LL	28	1	0	0	0	0	19	4	0	0	0	0	4	3	0	0	0	0

Appendix 2: Comparative Analysis of parameters noticed in lung lobes.

		Mild-Moderate			**Mild-Severe**			**Moderate-Severe**		
		Std. test stat	**p-value**	**Adj. p-value**	**Std. test stat**	**p-value**	**Adj. p-value**	**Std. test stat**	**p-value**	**Adj. p-value**
GGO	RU	-5.091	0.000	0.000	-4.999	0.000	0.000	-1.584	0.113	0.340
	RM	-4.685	0.000	0.000	-5.472	0.000	0.000	0.021	0.021	0.063
	RL	-4.999	0.000	0.000	-5.39	0.000	0.000	-2.025	0.043	0.129
	LU	-5.344	0.000	0.000	-5.253	0.000	0.000	-1.668	0.095	0.286
	LL	-5.198	0.000	0.000	-5.29	0.000	0.000	-1.798	0.072	0.216

		Mild-Moderate			**Mild-Severe**			**Moderate-Severe**		
		Std. test stat	**p-value**	**Adj. p-value**	**Std. test stat**	**p-value**	**Adj. p-value**	**Std. test stat**	**p-value**	**Adj. p-value**
CON	RU	-1.731	0.083	0.250	-3.370	0.001	0.002	-2.167	0.030	0.091
	RM	4.428	0.109	0.330	4.428	0.109	0.330	4.428	0.109	0.330
	RL	-1.054	0.292	0.876	-2.869	0.004	0.012	-2.118	0.034	0.103
	LU	-1.677	0.094	0.281	-2.590	0.010	0.029	-1.442	0.149	0.448
	LL	-0.638	0.524	1.000	-2.473	0.013	0.040	-2.000	0.045	0.136

		Mild-Moderate			**Mild-Severe**			**Moderate-Severe**		
		Std. test stat	**p-value**	**Adj. p-value**	**Std. test stat**	**p-value**	**Adj. p-value**	**Std. test stat**	**p-value**	**Adj. p-value**
NODULES	RU	0.132	0.936	-	0.132	0.936	-	0.132	0.936	-

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	RM	0.305	0.859	-	0.305	0.859	-	0.305	0.859	-
	RL	0.305	0.859	-	0.305	0.859	-	0.305	0.859	-
	LU	3.348	0.187	-	3.348	0.187	-	3.348	0.187	-
	LL	0.984	0.611	-	0.984	0.611	-	0.984	0.611	-

		Mild-Moderate			**Mild-Severe**			**Moderate-Severe**		
		Std. test stat	**p-value**	**Adj. p-value**	**Std. test stat**	**p-value**	**Adj. p-value**	**Std. test stat**	**p-value**	**Adj. p-value**
CRAZY PAVING	RU	-2.255	0.024	0.072	-2.947	0.003	0.010	-1.417	0.159	0.470
	RM	-2.255	0.024	0.072	-2.947	0.003	0.010	-1.417	0.159	0.470
	RL	-2.255	0.024	0.072	-2.947	0.003	0.010	-1.417	0.159	0.470
	LU	-1.91	0.056	0.168	-3.120	0.002	0.005	-1.809	0.070	0.211
	LL	-2.255	0.024	0.072	-2.947	0.003	0.010	-1.417	0.159	0.470

		Mild-Moderate			**Mild-Severe**			**Moderate-Severe**		
		Std. test stat	**p-value**	**Adj. p-value**	**Std. test stat**	**p-value**	**Adj. p-value**	**Std. test stat**	**p-value**	**Adj. p-value**
Reticulations	RU	-3.612	0.000	0.001	-2.747	0.006	0.018	-0.344	0.731	1.000
	RM	-2.915	0.004	0.011	-2.290	0.022	0.066	-0.349	0.727	1.000
	RL	-2.494	0.013	0.038	-4.173	0.000	0.000	0.266	0.791	1.000
	LU	-3.253	0.001	0.003	-2.307	0.021	0.063	-0.146	0.884	1.000
	LL	-3.985	0.000	0.000	-2.868	0.004	0.012	-0.221	0.825	1.000

		Mild-Moderate			**Mild-Severe**			**Moderate-Severe**		
		Std. test stat	**p-value**	**Adj. p-value**	**Std. test stat**	**p-value**	**Adj. p-value**	**Std. test stat**	**p-value**	**Adj. p-value**
Bronchiectasis	RU	-1.725	0.085	0.256	-2.283	0.022	0.067	-1.112	0.266	0.799
	RM	-1.993	0.046	0.139	-2.470	0.013	0.040	-1.121	0.262	0.787
	RL	-2.316	0.021	0.062	-2.920	0.003	0.010	-1.351	0.177	0.530
	LU	-1.993	0.046	0.139	-2.470	0.013	0.040	-1.121	0.262	0.787
	LL	-2.316	0.021	0.062	-2.920	0.003	0.010	-1.351	0.177	0.530

		Mild-Moderate			**Mild-Severe**			**Moderate-Severe**		
		Std. test stat	**p-value**	**Adj. p-value**	**Std. test stat**	**p-value**	**Adj. p-value**	**Std. test stat**	**p-value**	**Adj. p-value**
FIBROSIS	RU	4.513	0.105	-	4.513	0.105	-	4.513	0.105	-
	RM	2.939	0.230	-	2.939	0.230	-	2.939	0.230	-
	RL	4.428	0.109	-	4.428	0.109	-	4.428	0.109	-
	LU	1.781	0.410	-	1.781	0.410	-	1.781	0.410	-
	LL	4.428	0.109	-	4.428	0.109	-	4.428	0.109	-

	Mild-Moderate			**Mild-Severe**			**Moderate-Severe**		
	Std. test stat	**p-value**	**Adj. p-value**	**Std. test stat**	**p-value**	**Adj. p-value**	**Std. test stat**	**p-value**	**Adj. p-value**
Subpleural bands	-2.543	0.011	0.033	-3.306	0.001	0.003	-1.580	0.114	0.343
Bronchial wall thickening	-703.000	0.482	1.000	-3.062	0.002	0.007	-2.533	0.011	0.034
Pulmonary vessel prominence	4.036	0.133	-	4.036	0.133	-	4.036	0.133	-
Emphysema	0.278	0.781	1.000	1.806	0.071	0.213	2.295	0.022	0.065
Hyper-expansion	0.000	1.000	-	0.000	1.000	-	0.000	1.000	-
Air-trapping	3.179	0.204	-	3.179	0.204	-	3.179	0.204	-
Pleural effusion	0.000	1.000	-	0.000	1.000	-	0.000	1.000	-
Pericardial Effusion	0.588	0.745	-	0.588	0.745	-	0.588	0.745	-
Pericardial Thickening	0.000	1.000	-	0.000	1.000	-	0.000	1.000	-

Appendix 3: Wilcoxon test to analyze difference of parameters in the follow up reports [Old-New]

		Old-New	
		Std. test stat	**p-value**
GGO	RU	-1.633	0.102
	RM	-2.041	0.041
	RL	-2.232	0.026
	LU	-2.121	0.034
	LL	-2.588	0.010

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		Old-New	
		Std. test stat	**p-value**
CON	RU	-1.732	0.083
	RM	-1.414	0.157
	RL	-2.000	0.046
	LU	-1.414	0.157
	LL	-2.000	0.046
		Old-New	
		Std. test stat	**p-value**
NODULES	RU	-1.000	0.317
	RM	-	1.000
	RL	-	1.000
	LU	-	1.000
	LL	-	1.000
		Old-New	
		Std. test stat	**p-value**
CRAZY PAVING	RU	-1.000	0.317
	RM	-1.732	0.083
	RL	-1.732	0.083
	LU	-1.414	0.157
	LL	-1.732	0.083
		Old-New	
		Std. test stat	**p-value**
RETICULATIONS	RU	-	1.000
	RM	-1.000	0.317
	RL	-	1.000
	LU	-	1.000
	LL	-	1.000
		Old-New	
		Std. test stat	**p-value**
BRONCHIECTASIS	RU	-1.414	0.157
	RM	-1.732	0.083
	RL	-1.414	0.157
	LU	-1.732	0.083
	LL	-1.414	0.157
		Old-New	
		Std. test stat	**p-value**
FIBROSIS	RU	-	1.000
	RM	-	1.000
	RL	-	1.000
	LU	-	1.000
	LL	-1.000	0.317
		Old-New	
		Std. test stat	**p-value**
Subpleural bands		-1.000	0.317
Bronchial wall thickening		-	1.000
Pulmonary vessel prominence		-1.000	0.317
Emphysema		-	1.000
Hyper-expansion		-	1.000
Air-trapping		-	1.000
Pleural effusion		-	1.000
Pericardial Effusion		-	1.000
Pericardial Thickening		-	1.000

RESULTS

Demographic and Participant Characteristics

A total of 59 participants (47 men, 12 women; mean age, 50 years +/- 13; age range, 27– 73 years) were included (Table). The initial and follow-up scans were obtained a mean of 6 months after initial scan.

CT Findings and scores

Minimum CT score observed in participants was 0 and maximum 25. Nine out of 59 participants (~15 %) had 0 score, 29 out of 59 participants (~ 49 %) had mild disease with CT score <8, and 23 out of 59 participants (~ 39 %) had moderate disease with CT score between 8 to 15 and 7 participants out of 59 (~12%) had severe disease with CT score >15.

Appendix 4: Table showing severity of covid-19 infection on the basis of CT score in 59 participants.

Severity on the basis of CT severity score	No. of participants	% of participants
None	59	15
Mild (< 8)	29	49
Moderate (8 to 15)	23	39
Severe (>15)	7	12

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According to the data shown in appendix 2, For GGO it can be seen that a significant difference in mild and moderate (p value = 0.00), as well as mild and severe (p value = 0.00) is noticed for all the lung lobes. P value <0.05 makes it significant. No significant difference is seen between moderate and severe disease for GGO (p value > 0.05). Further significant differences can be noticed in mild and severe in case of CONSOLIDATION (p value < 0.040) in all lung lobes except RM lobe. No significant difference is noticed between mild-moderate and moderate-severe disease for consolidation. For RETICULATIONS, Significant difference can also be noticed in mild-moderate (p value < 0.038) in all lung lobes, and also in mild and severe (p value < 0.018) in RU, RL and LL lobe. For CRAZY PAVING significant difference is noticed between mild-severe (p value < 0.010) in all lung lobes, and for BRONCHIECTASIS significant difference is noticed between mild-severe(p value < 0.040) in all lung lobes except RU lobe. No significant difference is noticed for mild-moderate and moderate-severe for BRONCHIECTASIS and CRAZY PAVING.

For NODULES no significant difference is noticed between disease severity. Nodules occurence in HRCT of patients with covid-19 pneumonia is rarely observed. Similarly, for FIBROSIS, no significant difference is noticed between disease severity.

On the other hand, symptoms which were not differentiated according to the different lobes of lungs were also compared. The results obtained indicated a significant difference between mild and moderate (p value < 0.033) and also between mild and severe (p value < 0.007) in case of subpleural bands. In case of bronchial wall thickening, a significant difference is noticed between mild and severe and also between moderate and severe cases. In case of pulmonary vessel prominence, emphysema, hyperexpansion, air trapping, pleural effusion, pericardial effusion and pericardial thickening no significant difference is obtained between mild and moderate, mild and severe and moderate and severe cases.

Appendix 5: Frequency of occurrence of changes in lung parameters in CT of participants suffering from Covid-19 pneumonia.

Lung parameters	No. of participants with changes	(in %)
GGO	50	84.7
Reticulations	46	77.97
Bronchiectasis	26	44.07
Pulmonary vessel prominence	24	40.7
Subpleural bands	23	38.98
Consolidation	16	27.11
Nodules	15	25.4
Fibrosis	12	20.3
Emphysema	9	15.25
Crazy paving	9	15.25
Air-trapping	6	10.1
Bronchial wall thickening	2	3.4
Pericardial Effusion	2	3.4
Pleural effusion	0	0
Pericardial Thickening	0	0

Appendix 6: Frequency of occurrence of changes in lung parameters in CT of participants suffering from Covid-19 pneumonia on the basis of disease severity.

Lung parameters	No. of participants with changes in mild disease (n = 29)	No. of participants with changes in moderate disease (n = 23)	No. of participants with changes in severe disease (n = 7)
GGO	17, 58.6%	23, 100%	7, 100%
Consolidation	3, 10.3%	7, 30.4%	4, 57.1%
Nodules	5, 17.2%	7, 30.4%	1, 14.3%
CP	0	5, 21.7%	3, 42.9%
Reticulations	13, 44.8%	22, 95.6%	7, 100%
Bronchiectasis	7, 24.1%	13, 56.5%	6, 85.7%
Fibrosis	4, 13.8%	4, 17.4%	3, 42.9%

From Appendix 5, predominant findings in cases of Covid patients were GGO followed by reticulations, bronchiectasis, pulmonary vessel prominence, subpleural bands, consolidation, nodules, fibrosis, emphysema and crazy pavings. These findings are more frequent in patients who had higher CT scores. Bronchial wall thickening and pericardial effusion were seen in very few patients. None of the participants showed lung hyper-expansion, pleural effusion and pericardial thickening.

50 participants out of 59 showed GGO (84.7%). Reticulations were seen in 46 participants (~78%), Bronchiectasis were seen in 26 participants (~44%), Pulmonary vessel prominence were seen in 24 participants (~40%), Subpleural bands were seen in 23 participants (~39%), Consolidation were seen in

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16 participants (~27%), Nodules were seen in 15 participants (~25.4%), Fibrosis wevre seen in 12 participants (~20.3%), Emphysema were seen in 9 participants (~15.25%), CP were seen in 9 participants (~15.25%), Air-trapping were seen in 6 participants (~10%), Bronchial wall thickening and pericardial effusion were seen in 2 participants out of 59 (~3.4%).

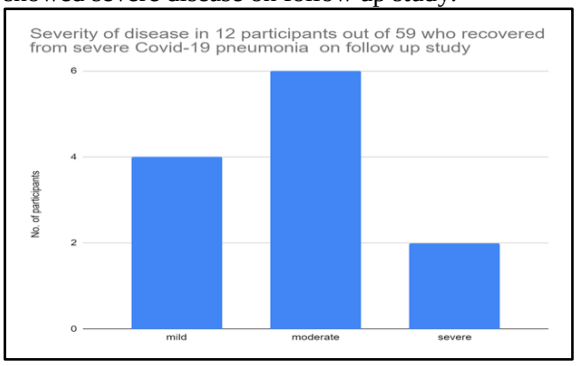
On the basis of Total CT severity score, In participants with mild severity up to 25% of lung parenchyma of each lung lobe showed findings suggestive of GGO. Similarly, in moderate cases, up to 49% of lung parenchyma of each lung lobe was involved and in severe cases, up to 100% of lung parenchyma of each lung lobe was involved. Consolidation involved up to 50% of lung parenchyma of each lung lobe in participants having severe disease. All other findings like Nodules, CP, Reticulations, Bronchiectasis, Fibrosis involved < 5% of lung parenchyma of each lung lobe in all participants irrespective of disease severity. These conclusions were drawn by observing the occurence of lung findings in different lobes of lungs on the basis of CT severity score from appendix 1. Also, occurrences of all findings were predominantly found in LL, RL lobe except Consolidation which was predominantly found in LU and RU lobe irrespective of the disease severity and Nodules which was predominantly found in LU, RU lobe in moderate and severe disease.

On further analysis, appendix 6 was constructed surmounting to the number of participants showing maximum changes rather than average in lung parameters in CT for convenience and further interpretation. Out of 29 participants who had mild disease severity, 17 (~59.6%) had GGO, 3 (~10.3%) had Consolidation, 5 (~17.2%) had Nodules, None had CP, 13 (~44.8%) had Reticulations, 7 (~24.1%) had Bronchiectasis and 4 (13.8%) had Fibrosis. Similarly, Out of 23 participants who had moderate disease severity, 23 (~100%) had GGO, 7 (~30.4%) had Consolidation, 7 (~30.4%) had Nodules, 5 (~21.7%) had CP, 22 (~95.6%) had Reticulations, 13 (~56.5%) had Bronchiectasis and 4 (17.4%) had Fibrosis. Out of 7 participants who had severe disease severity, 7 (~100%) had GGO, 4 (~57.1%) had Consolidation, 1 (~14.3%) had Nodules, 3 (~42.9%) had CP, 7 (~100%) had Reticulations, 6 (~85.7%) had Bronchiectasis and 3 (~42.9%) had Fibrosis.

In our study, and from Appendix 7, 12 of 59 participants (20 %) who recovered from coronavirus disease 2019 pneumonia developed fibrotic-like changes in the lung. We found that 4 patients had mild disease, 6 had moderate disease (CT score between 8 to 15), 2 had severe disease with CT score of 23 and 25. Five out of these patients were in their 4th decade of life, only one was less than 40 years of age and the rest 6, above 50 years of age.

On further evaluation, 29 participants out of 59 (~49%) showed no involvement of lung lobes with bronchiectasis and fibrosis. 17 participants (~29%) showed bronchiectasis involving <5% of lung parenchyma without any fibrotic changes. 9 participants (~15%) showed both bronchiectasis and fibrosis involving <5% of lung parenchyma. 4 participants (~7%) showed no bronchiectasis but fibrosis involving <5% of lung parenchyma. Refer to Appendix 8.

Appendix 7: Severity of disease on the basis of CT score value in 12 participants out of 59 who recovered from severe Covid-19 pneumonia on follow up study. 4 out of 12 showed mild disease, 6 out of 12 showed moderate disease and 2 out of 12 showed severe disease on follow up study.



Appendix 8: Comparing occurrence of bronchiectasis and fibrosis in CT of patients suffering from Covid 19 pneumonia.

Relation between bronchiectasis and fibrosis	No. Of participants	In %
No bronchiectasis and fibrosis	29	49
Fibrosis without bronchiectasis	4	29
Bronchiectasis without fibrosis	17	15
Both	9	7

Comparison of CT Findings and Scores between Initial and Follow-up Scans

In follow up of participants there was reduction in CT findings with declining CT score as shown in Appendix 9. Out of 59 participants, only 9 came for follow up. Among these 9 participants, 4 had severe disease (CT score > 15), 2 had moderate disease (CT score 8 - 15) and 3 had mild disease (CT score < 8) in the initial CT scan, represented in Appendix 10. From Appendix 11, 4 out of 7 participants (~57.1%) who had severe disease underwent follow up CT scan and the rest were lost to follow up. Consequently, 2 out of 23 participants (~8.7%) who had moderate disease underwent follow up CT scan and the rest were lost to follow up. Also, 3 out of 29 participants (~10.3%) underwent follow up CT scan and the rest were lost to follow up. Thus, increased severity of initial CT scan leads to more participants presenting for follow up CT scan. In the follow up CT scan, we found 5 participants out of 9 to have moderate disease and 4 out of 9 to have mild disease. No participants had severe disease in the follow up CT scan.

Appendix 9: Comparison of initial CT score and score in follow up in 9 participants showing decrease in follow up CT score in follow up in all of them.

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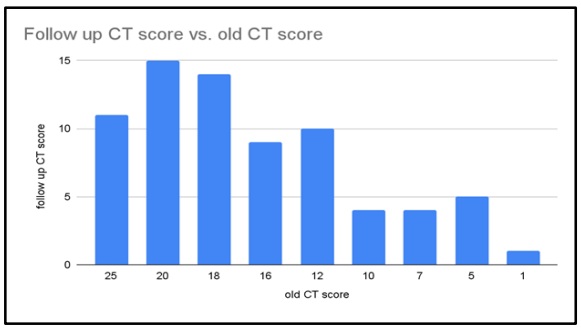

There was reduction in GGO, crazy paving, bronchiectasis, and consolidation on follow up. Appendix 12 represents the changes in lung parameters in follow up of 9 participants. There was significant resolution of GGO upon follow up. Upon follow up, parameters like reticulations, emphysema, bronchial wall thickening, fibrosis, sub pleural bands and pulmonary vessel prominence persisted. 1 participant out of 9 developed new fibrotic-like lesions upon follow up who initially showed no such lesions. Similarly, 1 participant out of 9 developed new pulmonary vessel prominence upon follow up who initially had no such findings.

Out of 9 participants, 8 (~88.9%) showed GGO in the initial scan. On follow up, all of them showed significant resolution of GGO. Similarly, 9 participants (100%) had reticulations in the initial scan, which persisted in all of them upon follow up. 5 participants (~55.6%) out of 9 had CP in the initial scan, which showed resolution in 3 participants (~60%) and persisted in 2 participants (~40%). 7 participants (~77.8%) showed bronchiectasis in the initial scan, which showed resolution in 3 participants (~43%) and persisted in 4 participants (~57%) upon follow up. 4 participants (~44.4%) showed consolidation in the initial scan, which showed resolution in all of them upon follow up. 3 participants (~33.33%) showed Nodules in the initial scan, which showed resolution in 1 participant (~33.3%) and persisted in 2 participants (~66.67%) upon follow up. 1 participant (~11.11%) showed fibrosis in the initial scan and persisted upon follow up. 6 participants (~67.67%) showed sub pleural bands in the initial scan, which persisted in 5 participants (~83.3%) and showed resolution in 1 participant (~16.7%) upon follow up. 1 participant (~11.11%) showed Bronchial wall thickening in the initial scan, which persisted upon follow up. 5 participants (~55.6%) showed Pulmonary vessel prominence in the initial scan, which persisted in all of them upon follow up. 2 participants (~22.22%) showed Emphysema in the initial scan, which persisted in both upon follow up. 1 participant (~11.11%) showed Air trapping in the initial scan, which persisted upon follow up.

Appendix 10: Disease severity on the basis of CT severity score among 9 participants who underwent follow up CT scan.

Disease severity on the basis of CT score	No. of participants in initial CT scan	No. of participants in follow up CT scan
Mild (<8)	3	4
Moderate (8 - 15)	2	5
Severe (>15)	4	-

Appendix 11: Table showing the tendency to follow up in participants on the basis of severity in initial CT scan.

Disease severity on the basis of CT severity score	No. of participants (n = 59)	No. of participants who underwent follow up (n = 9)	% of participants
Mild (<8)	29	3	10.3
Moderate (8 - 15)	23	2	8.7
Severe (>15)	7	4	57.1

Appendix 12: Comparison of changes in lung parameters in follow up of 9 patients suffering from Covid 19 pneumonia.

Lung parameters	No. of participants with changes (in %)	No. of participants with no changes (in %)	No. of participants with persistent changes in long term follow up (in %)	No. of participants with resolution of changes in long term follow up (in %)
GGO	8 (88.9%)	1	0 (0%)	8 (100%)
Reticulations	9 (100%)	0	9 (100%)	0 (0%)
Crazy paving	5 (55.6%)	3	2 (40%)	3 (60%)
Bronchiectasis	7 (77.8%)	2	4(57.1%)	3 (43%)
Consolidation	4 (44.4%)	3	0 (0%)	4 (100%)
Nodules	3 (33.33%)	6	2 (66.67%)	1(33.3%)
Fibrosis	1(11.11%)	8	1(100%)	0 (0%)
Subpleural bands	6(67.67%)	3	5 (83.3%)	1 (16.7%)
Bronchial wall thickening	1(11.11%)	8	1(100%)	0
Pulmonary vessel prominence	5 (55.6%)	4	5 (100%)	0
Emphysema	2 (22.22%)	7	2 (100%)	0
Hyper-expansion	0	9	0	0
Air-trapping	1(11.11%)	8	1(100%)	0
Pleural effusion	0	9	0	0
Pericardial Effusion	0	9	0	0

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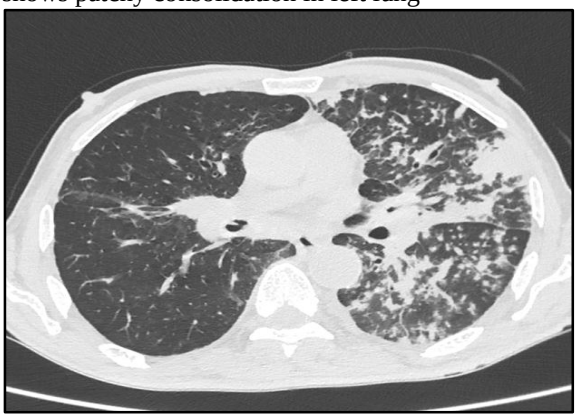
Pericardial Thickening	0	9	0	0

To compare chest CT parameters in follow-up patients with that of their old findings, Wilcoxon analysis was done and represented in Appendix 3. Results showed Significant p value in GGO (p value < 0.041) in all lung lobes except RU lobe and consolidation (p value <0.046) in RL and LL lobe. At follow-up, Significant decrease in CT scores for total lesions, GGO, and consolidation were observed compared with the initial CT. Although the predominant CT pattern at follow-up CT was still GGO, the densities had visually decreased. No significant p value in Nodules, CP, reticulations, bronchiectasis, fibrosis, sub pleural bands, bronchial wall thickening, pulmonary vessel prominence, emphysema, hyper expansion, air trapping, pleural effusion, pericardial effusion and pericardial thickening.

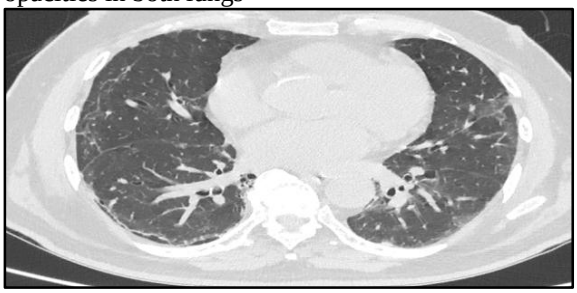
In follow up of patients with CT scan, there was resolution of prominent CT findings like GGO and consolidation. Fibrosis was observed in 12 participants out of 59. In long term follow up of 9 participants, among which 1 participant initially had fibrotic like lesions in CT showed persistence of fibrotic like lesions upon follow up, and 1 participant showed slight development of new fibrotic like lesions in lung lobe upon follow up. Bronchiectasis was observed in 26 participants out of 59. 7 participants out of 9 who showed bronchiectatic lung changes in initial scans, 4 participants showed persistence and 3 participants showed resolution of bronchiectasis on follow up CT scan.

The resolution of bronchiectatic lung changes observed among most of the participants in follow up raises suspicion of occurence of bronchiectasis in the first place. As bronchiectasis represents permanent lung changes, its resolution in follow up scans represents the likelihood of temporary changes in CT following Covid 19 pneumonia like bronchial dilatation. The participants who showed no resolution in bronchiectatic changes in follow up might have underlying fibrotic lesions involving lung.

Appendix 13: Axial CT of thorax in lung window shows patchy consolidation in left lung



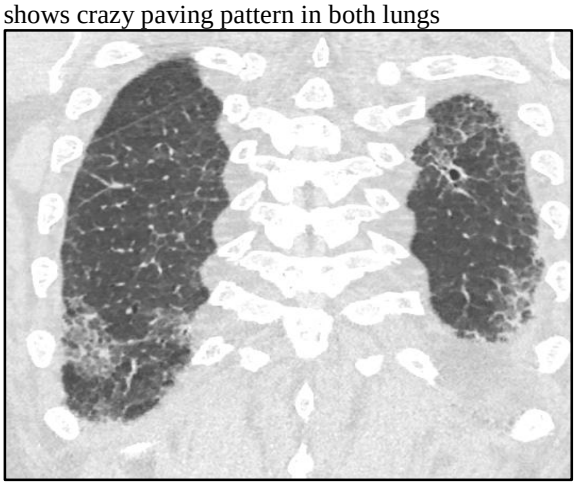
Appendix 14: Axial CT of thorax in lung window shows subpleural bands and few ground glass opacities in both lungs



Appendix 15: Axial CT of thorax in lung window shows fibrotic bands in left lung

Appendix 16: Axial CT of thorax in lung window shows fibrotic bands and bronchial dilatations in both lungs

Appendix 17: Coronal CT of thorax in lung window shows crazy paving pattern in both lungs



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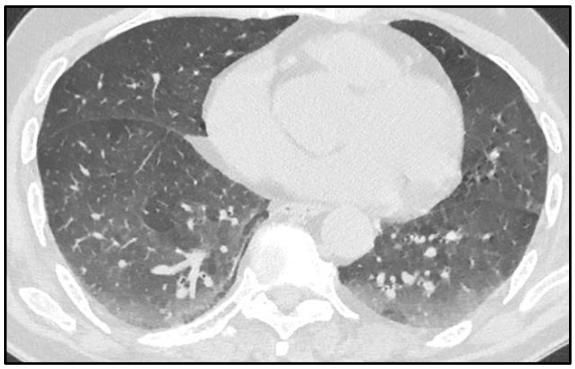
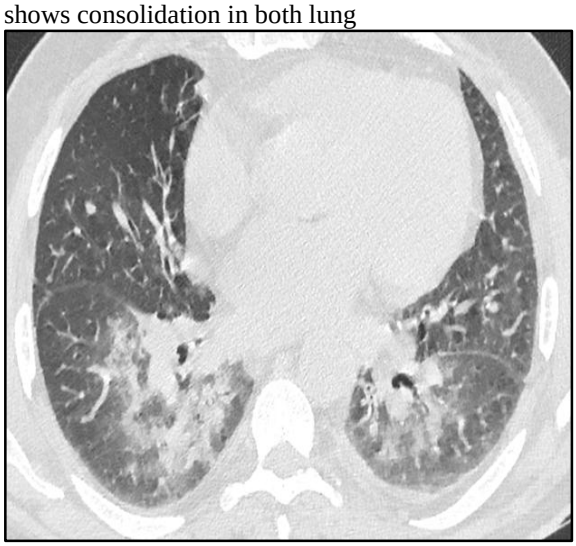
Appendix 18: Axial CT of thorax in lung window shows ground glass opacities in both lung

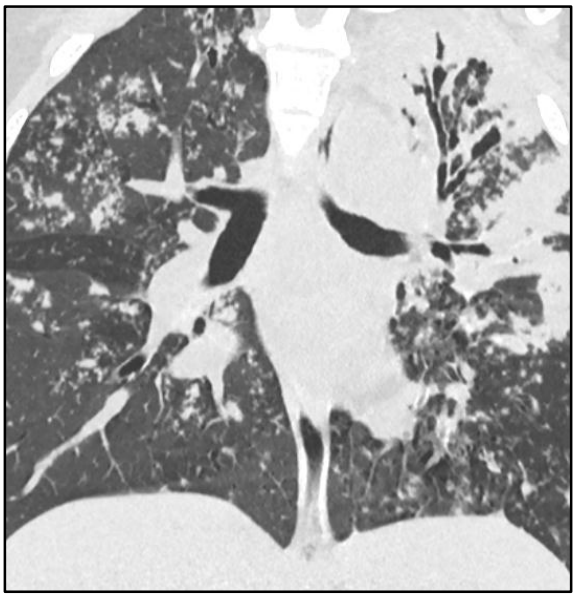


Appendix 19: Coronal CT of thorax in lung window shows ground glass opacities in both lung

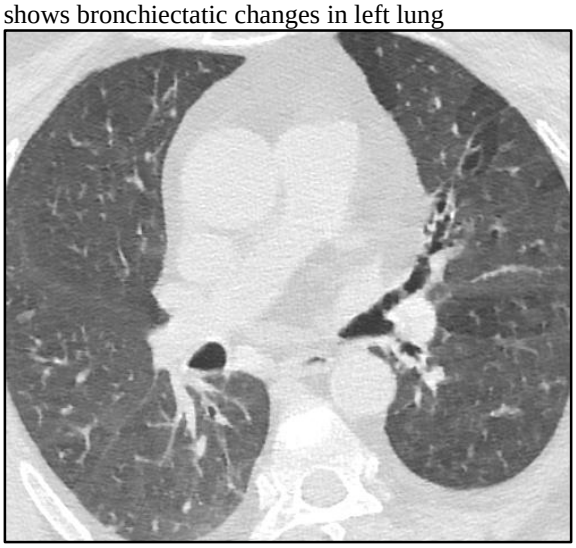
Appendix 20: Axial CT of thorax in lung window shows consolidation in both lung



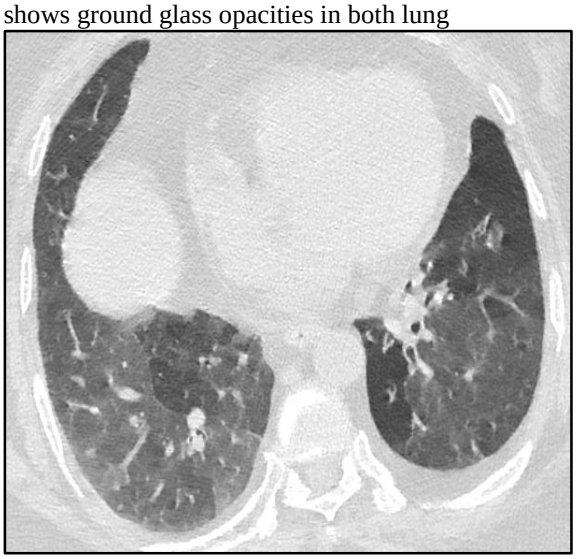
Appendix 21: Coronal CT of thorax in lung window shows consolidation with bronchiectatic changes and random soft tissue nodules



Appendix 22: Axial CT of thorax in lung window shows bronchiectatic changes in left lung



Appendix 23: Axial CT of thorax in lung window shows ground glass opacities in both lung



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DISCUSSION

The typical CT findings of COVID-19 consist of ground-glass opacity, consolidation, and crazy-paving patterns, which were similar to those described by several groups of investigators.[10,11,13]. According to the study done by Pan et al, the typical mild COVID-19 mainly starts as small subpleural unilateral or bilateral GGOs in the lower lobes, which then develops into the crazy-paving pattern and subsequent consolidation.[12] In our study, we found GGO (50 out of 59 participants, 84.7%) predominantly followed by reticulations (46 out of 59 participants, 77.97%) and bronchiectasis (26 out of 59 participants, 44.07%) which confirms prior reports in relation to CT findings of participants with covid 19 pneumonia. These findings are more frequent in patients who had higher CT scores. Furthermore, the occurrence of pulmonary vessel prominence (24 out of 59 participants, 40.7%) and subpleural bands (23 out of 59 participants, 38.98%) were found to be more frequent in our study. Unlike previous reports, findings like consolidation (16 out of 59 participants, 27.11%), CP (9 out of 59 participants, 15.25%) occur less frequently than above-described findings in our study. Findings like nodules (15 out of 59 participants, 25.4%), emphysema (9 out of 59 participants, 15.25%) and fibrosis (12 out of 59 participants, 20.3%) were also found in a large number of participants in our study. Very few participants showed changes like bronchial wall thickening and pericardial effusion. No participants showed pleural effusion or pericardial thickening in CT.

The evolution of chest CT scans from the onset of symptoms were described in 4 stages in a study done by Pan et al. The four stages were early stage (0-4 days), progressive stage (5-8 days), peak stage (9-13 days) and absorption stage (>14 days). Lung abnormalities on chest CT scans of patients recovering from covid 19 showed greatest severity 10 days after initial onset of symptoms.[12]

A study done by Dai et al, divided participants in severe and non-severe groups based on the treatment options. In the non-severe group, median total CT score was 9.5 and in severe group, median total CT score was 20. In week 1, GGO patterns were dominant in 72% of severe and 65% of non-severe group. In week 2, consolidation patterns were seen in 73% of the severe and 32% of the non-severe group. In both groups peak CT changes were seen in the 2nd week of presentation. In the non-severe group, disease progressed slower than in the severe group. By week 4, both groups showed a decrease in total CT scores but the reticular pattern became dominant in both group involving more than 40% participants. In the severe group, the dominant residual lung lesions were reticulations and consolidations whereas in the non-severe group, the dominant residual lung lesions were GGO and reticulations.[17]

In our study, we observed mild disease (CT score < 8) being the most common among participants which is approximately 49% of the total participants, followed by moderate severity (CT score 9 - 15) which approximately accounts to 39% of the total participants. 15% of the total participants had no CT changes. 12 % of the total participants had severe disease with CT score > 15. In participants with mild disease severity, GGO was seen predominantly (58.6%), followed by Reticulations (44.8%), Bronchiectasis (24.1%), Nodules (17.2%), Fibrosis (13.8%) and Consolidation (10.3%). In participants with moderate disease severity, GGO was seen predominantly (100%), followed by Reticulations (95.6%), Bronchiectasis (56.5%), Nodules (30.4%), Consolidation (30.4%), CP (21.7%) and Fibrosis (17.4%). In participants with severe disease severity, GGO was seen predominantly (100%), followed by Reticulations (100%), Bronchiectasis (85.7%), Consolidation (57.1%), Fibrosis (42.9%), CP (42.9%), and Nodules (14.3%).

After stratifying the participants on the basis of the CT severity score under mild, moderate and severe disease severity, comparative analysis was done for each symptom noticed in the lung lobes with the help of Kruskal Wallis test. Statistically significant differences were noticed in mild and moderate disease, as well as mild and severe disease for GGO in all lung lobes. Statistically significant differences were also noticed in mild and severe disease in Consolidation, Reticulations, Bronchiectasis, CP, Subpleural bands and Bronchial wall thickening. No significant difference was noticed for Nodules, Fibrosis and other findings.

According to a study done by Wang et al, Sixty-six of the 70 discharged patients (94%) had residual disease on final CT scans, with ground-glass opacity being the most common pattern.[13]

According to a study done by Han et al, the CT scores of all lesions, ground-glass opacification, reticular pattern and ILAs declined on 1-year follow up CT scans. Total of 62 participants were included in the study. 35 of 62 (56%) participants showed fibrotic ILAs and the remaining 27 of 62 (44%) participants showed no fibrotic ILAs on 6-month follow-up CT scans. All participants who initially developed fibrotic ILAs (35 of 35, 100%) demonstrated persistent fibrotic ILAs on 1-year follow-up CT scans. Specifically, 27 of 35 (77%) participants had stable lung fibrotic ILAs, whereas the extent of fibrotic ILAs was slightly reduced in 8 of 35 (23%) cases. 17 of 27 (63%) participants who showed no fibrotic ILAs showed complete resolution at 1-year CT, whereas the remaining 10 of 27 (37%) participants showed either partial resorption of the abnormalities (6 of 27, 22%), or static radiologic changes (4 of 27, 15%) However, CT scores of the fibrotic ILAs and traction bronchiectasis showed no differences between the two CT scans. Fibrotic ILAs were persisting at 1-year follow-up, which indicate that fibrotic diseases in late stage might be irreversible, although whether the findings represent

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actual pathologic fibrosis remain to be confirmed with other measures like lung biopsy.[16]

According to our data, there was a significant decline in CT score and CT severity score in follow up of patients when compared to that of their initial findings in CT. Our study shows resolution of GGO in 100% participants, Consolidation in 100% participants, CP in 60% participants, Bronchiectasis in 43% participants, Nodules in 33.33% participants, and subpleural bands in 16.7% participants in long term follow-up.

Wilcoxon analysis was done to compare chest CT parameters in follow-up patients with that of their old findings. Results showed Significant p value in GGO (p value < 0.041) in all lung lobes except RU lobe and consolidation (p value <0.046) in RL and LL lobe. At follow-up, Significant decrease in CT scores for total lesions, GGO, and consolidation were observed compared with the initial CT. Although the predominant CT pattern at follow-up CT was still GGO, the densities had visually decreased. No significant p value in Nodules, CP, reticulations, bronchiectasis, fibrosis, sub pleural bands, bronchial wall thickening, pulmonary vessel prominence, emphysema, hyper expansion, air trapping, pleural effusion, pericardial effusion and pericardial thickening. Our study concluded persistence of Reticulations (9 of 9, 100%), fibrosis (1 of 1, 100%), Pulmonary vessel prominence (5 of 5, 100%), Emphysema (2 of 2, 100%) and Bronchial wall thickening (1 of 1, 100%).

Initially, out of 9 participants, 4 had severe disease, 2 had moderate disease and 3 had mild disease. On follow up CT scan, no participants continued to have severe disease, 5 participants had moderate disease and 4 had mild disease.

According to a study conducted by Han et al, Six-month follow-up CT showed fibrotic-like changes in more than one-third of patients (40/114, 35%) who survived severe COVID-19 pneumonia. These changes were associated with an older age, acute respiratory distress syndrome, longer in-hospital stays, tachycardia, non-invasive mechanical ventilation and higher initial chest CT score (≥18 out of a possible score of 25).[14] An article published by Li et al concluded that fibrosis developed in Covid 19 patients could be reversed in about a third of the patients after 120 days from onset.[15] Earlier studies done to evaluate the consequences of SARS-CoV in long term among the patients who survived showed reversible CT evidence of lung fibrosis,[18] lung fibrotic changes on CT images persisted in survivors of SARS-CoV until 1 year after discharge.[19] Furthermore, a long-term follow-up SARS-CoV study found that the proportion of lung fibrosis could remain stable from 1-year to 15-year follow-up.[20]

In our view occurence of fibrosis followed by its resolution is implausible. In our study, 12 of 59, 20% of patients who recovered from severe Covid-19 pneumonia showed fibrotic lung changes. Out of 12, 4 had mild disease, 6 had moderate and 2 had severe disease. Only one participant was found to have persistent fibrotic-like changes upon follow up. Resolution of such changes found in our study makes the occurrence of collapse or bronchial dilation a more likely finding in initial CT, which was interpreted as fibrosis and bronchiectasis per se. These findings need to be confirmed by further investigations on a larger population.

11 out of the 12 participants who developed fibrotic lung changes were more than 40 years of age. This clearly represents the increased risk of fibrotic lung changes with increased age. According to the study done by Gaba et al, the most severe disease and the highest mortality rates were found in the 50-59 years age group.[21] A number of other risk factors can be associated with increased disease severity like that of male gender (possibly due to reduced estrogen, which plays a protective role), presence of patients comorbidities particularly hypertension, diabetes, lung, and coronary artery diseases. Presence of multiple risk factors lead to worse outcomes.[22-24]

Limitation

Our study has several limitations. First, of all being small in sample size. Second, lost follow up that could affect the results of the study. Third, the inability to verify CT findings of patients with lung histopathology. Fourth, there is a lack of quantitative analysis of lung parenchyma. Also, random follow-up patterns lead to inadequate information about sequence of occurrence of lung changes in affected patients. Thus, a larger sample and longer even follow up are needed to better describe the long-term sequelae of mild, moderate and severe COVID 19 infection.

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We would like to thank all colleagues for helping us during the study, all volunteers who participated in the study. We are also very grateful to the members of the frontline medical staff for their audacious dedication during the outbreak, despite the potential threat to their own lives and the lives of their families.

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