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Original Research Paper

Radio-Diagnosis

IMPACT OF POST COVID PULMONARY SEQUELAE IN DECIDING RADIOLOGICAL OUTCOME: AN OBSERVATIONAL STUDY

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ABSTRACT

Background: A number of patients with COVID-19 pneumonia were discharged from hospitals in central India.This study highlights the relevant affecting factors, and to describe the chest CT findings and sequelae during follow up.

Aims And Objectives: our aim was to determine the cumulative percentage of complete radiological resolution at the time of active disease and at follow up after discharge ,highlight the predominant findings in follow-up post covid CT and to correlate CTSS and the type of lung parenchymal opacity with chances of radiological resolution.

Methods: Patients with COVID-19 pneumonia confirmed by RT-PCR who were discharged consecutively from the hospital between September 2020 and November 2020 and who underwent serial chest CT scans on their visit to post COVID OPD were enrolled in a retrospective observational study. The radiological characteristics of all patients were collected, analyzed and the total CT score was calculated. Imaging features and distributions were analyzed across different time points.

Results: A total of 385 patients were evaluated; there were 286 (74.2%) men and 99 (28.7%) women, with a median age of 43 years old (IQR 36–56). Complete radiological resolution was seen in 74(19%) patients on follow up CT, while 49(12.7%) patients showed normal chest CT during active disease. Patients ≤40 years old showed a slightly higher cumulative percentage of complete radiological resolution than patients > 40 years old at the follow-up CT. The predominant patterns of abnormalities observed during the active disease were ground-glass opacity (GGO) (321 [83.3%]), consolidation (283 [73.5%]), and sub-pleural atelectatic fibrotic bands (235 [61%]). While on follow up scan, the positive count of GGO and consolidations gradually decreased, few fibrotic bands remained in almost all 235 patients who showed fibrotic changes earlier.

Conclusion: Most of the lung lesions in COVID-19 pneumonia patients can be absorbed completely during short-term follow-up with sequelae of subcentimetric pleural atelectatic fibrotic bands only. The optimal time point for early radiological estimation might be three to four weeks after discharge.

KEYWORDS : COVID-19, CT, Follow-up, Sequelae, GGO, sub- pleural atelectatic bands

INTRODUCTION:

Since the first report in December2019 in Wuhan, China ; COVID-19 has become a worldwide outbreak. At present, confirmation of COVID-19 infection mainly depends on detection through reverse transcription polymerase chain reaction (RTPCR) of throat swabs, sputum, lower respiratory tract secretions, and other specimens [1]. Chest high-resolution computed tomography (HRCT) is an important method for detecting lung abnormalities. It plays a significant role in the screening of suspected COVID 19 patients, the diagnosis and differential diagnosis of diseases, detection of disease progression and complications and follow-up after discharge [1].Several previous studies have revealed the radiological features at different stages of the disease [1-3]. In a previous study on severe acute respiratory syndrome (SARS) , Wu et al. reported that residual pulmonary lesions such as GGO and intralobular and interlobular septal thickening could be persistently observed years after recovery [4]. It is still unclear whether similar severe sequelae also exist for COVID-19. Our observational study aims to provide the radiographic manifestations of COVID-19 in discharged patients with chest CT follow-up.

Methods

This retrospective observational study was approved by the Ethics Review Committee of our institution. Written informed consent was waived.

Definition And Criteria

The diagnostic criterion was based on RT-PCR results. The discharge criteria were as follows:

1. Afebrile for more than 2 days;
2. Respiratory symptoms significantly improved;
3. Two consecutive negative COVID-19 nucleic acid tests detected at least 24 h apart [5].

Complete radiological resolution was defined as the absence of any abnormality on HRCT thorax potentially related to COVID 19 infection [6].

Based on the clinical presentation at admission, these patients were divided into four groups[7]:

1. Asymptomatic group: Individuals who test positive for SARS-CoV-2 using a virologic test (i.e., a nucleic acid amplification test [NAAT] or an antigen test) but who have no symptoms that are consistent with COVID-19.

2. Mild/ Grade I Individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do not have shortness of breath, dyspnoea, or abnormal chest imaging.

3. Moderate/ Grade II Individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have an oxygen saturation (SpO2) ≥94% on room air.

4. Severe and critical/grade IV group Individuals who have SpO2 <94% on room air, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO2/FiO2) <300 mm Hg, respiratory frequency >30 breaths/min, or lung infiltrates >50%,respiratory failure, septic shock, and/or multiple organ dysfunction.

Data Collection

We collected clinical and laboratory data for analysis ,derived from HMIS, an electronic medical record system, concerning a total of 385 patients who were admitted to our hospital between September 2020 and November 2020 and were confirmed as having COVID-19 infection using RT-PCR. Chest HRCT images of these patients during active disease and at follow up visit at 3-4 weeks post discharge were collected and evaluated using the Picture Archiving and Communication Systems (PACS). Patients were given treatment based on clinical severity and follow up scans adviced by clinicians based on patient symptomatology.

HRCT inspection

All chest HRCT scans were performed using SIEMENS SOMATOM DEFINITION 128 slice CT and PHILIPS BRILLIANCE ICT 256.Patients underwent a non-contrast HRCT scan during the course of the disease and the next scan at the follow up visit after discharge. The mean time between the first symptom onset and the first CT scan was 3.2 ± 3.8 days (range, 0–15 days). Patients were placed in a supine position with head first with a single inspiratory phase. Scanning parameters were tube voltage (100 kV) with automatic tube current modulation, tube current (10−235 mA), slice thickness (5 mm), interval between slices(5 mm), consecutive 1.25mm slices for high-resolution reconstruction scan, and scanning time (4.85 s).

From the raw data, CT images were reconstructed with a matrix size of 512 × 512 as axial images (thickness of 1.5 mm and increment of 1.5 mm) with hybrid iterative reconstruction.

HRCT Image Analysis

Two senior radiologists evaluated the images separately to identify HRCT characteristics of each patient and final scores were reached on by consensus.

The conventional CT score was subjectively calculated to reflect the extent of parenchymal involvement. Each of the 5 lung lobes was visually scored from 0 to 5 as: 0, no involvement; 1, < 5% involvement; 2, 5–25% involvement; 3, 26–49% involvement; 4, 50–75% involvement; 5, > 75% involvement. The total CT score was the sum of the individual lobar scores and ranged from 0 (no involvement) to 25 (maximum involvement) [8]. In addition to this, radiological features including GGO, consolidations, sub-pleural fibrotic atelectatic bands, crazy pavement pattern and miscellaneous findings like small pleural effusions were also evaluated and estimated. When the number of lesions per lobe was>5, only 5 obvious lesions were analyzed. The glossary of findings used were in accordance with Fleischner's society. [9-12].

Statistical Analysis

Continuous variables were presented as mean ± standard deviation, categorical variables were expressed as frequency and percentages. Mean CTSS was compared at diagnosis and at follow up imaging by performing independent t-test. Categorical variables were compared by performing chi-square test; P-value was <0.05 was considered as statistically significant. Statistical software STATA version 14.0 was used for data analysis.

RESULTS

Baseline Information

In this retrospective observational study, a total of 385 patients with a male to female ratio of 289:99 ranging in age from 5 to 82 years (average age, 43.0 ± 17.2 years) were included in our study. Based on the clinical presentation at admission, these patients were divided into four groups(7): 1. Asymptomatic group (8 cases, 2.07%), 2. Mild/ Grade I (230 cases, 59.7%),3. Moderate/ Grade II (48 cases, 12.4%), 4. Severe and critical/grade IV group (99 cases, 25.7%) .

At first presentation, the most common symptoms were fever (85.9%) and non productive cough (83.2%).

Co-morbidities of hypertension, diabetes, obstructive lung disease and hyperthyroidism were reported in 41.3, 34.5, 8.6, and 4.1% of the patients, respectively. The details are summarized in Table 1-4.

Table No.1 Age Distribution Of Study Population.

Age in years	No. of Cases	Percentage
≤20	7	1.82
21 – 30	31	8.05
31 – 40	60	15.58
41 – 50	70	18.18
51 – 60	110	28.57
61 – 70	65	16.88
71 – 80	42	10.91

Table No.2 Gender Wise Distribution Of Study Population.

Gender	No. of Cases	Percentage
Male	286	74.29
Female	99	28.71

Table No.3 Symptomatology

Symptoms	No. of Cases	Percentage
Fever	331	85.97
Cough	331	85.97
Dyspnoea	254	65.97
Myalgia	135	35.06
Others	63	

Table No 4. Clinical Severity Grade

Grade	No. of Cases	Percentage
Asymptomatic	08	2.07
1	230	59.74
2	48	12.46
3	99	25.71

Complete Radiological Resolution

During active disease, 49 (12.7%) patients showed no lung parenchymal changes while 87.3% showed lung parenchymal abnormalities .On follow up scan 3-4 weeks after discharge, the cumulative percentage of complete radiological resolution was 19% (74 patients)and 81% (311 patients) showing residual changes with maximum residual changes being sub-pleural fibrotic atelectatic bands(Figure 1) in 59%(230 patients) and second most prevalent residual change being GGOs which were seen in 47% (183 patients).177 out of the total 385 patients (45%) during active disease had a CTSS in the moderate category(CTSS 8-15) with slightly lower results in the follow up scan where 38% patients fell in the moderate category.(8) (Table 5,6)

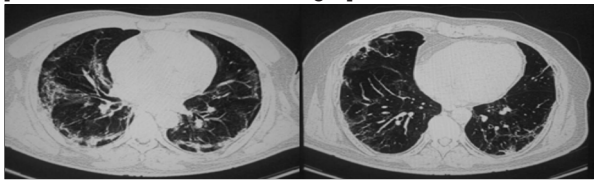
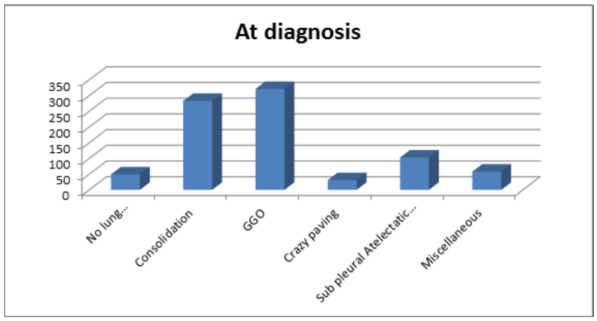


Figure 1: Dynamic Temporal Changes In Subpleural Fibrotic Bands During Active Disease And At Follow Up Study.

Table No.5 CT Findings At Diagnosis And At Follow-up

	At diagnosis	follow-up	p-value
No lung changes/ Complete Resolution	49	74	0.025,S
Consolidation	283	147	0.002,HS
GGO	321	183	0.001,HS
Crazy paving	31	31	1.000,NS
Sub pleural Atelectatic Bands	103	230	0.001,HS
Miscellaneous	58	75	0.105,NS



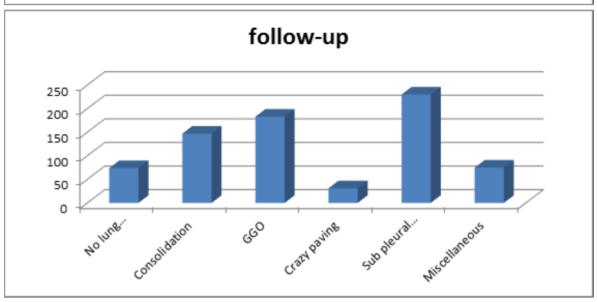


Table No.6 CTSS At Diagnosis And At Follow Up

CTSS category	CT severity Score		p-value
	At diagnosis	follow-up	
Normal(0)	49	74	Chi2=12.81
Mild (1 – 7)	110	131	P=0.005,HS
Moderate 8 – 17	177	150	
Severe (≥18)	49	30	
Mean ± SD	10.00 ± 7.10	8.55 ± 6.98	<0.0001, HS

Factors Favoring Complete Radiological Resolution

There was significant difference in complete radiological resolution at the follow-up between groups with different ages and sex; with a far greater number of younger patients and females showing complete radiological resolution . the patients falling into mild and moderate category of disease according to CTSS more commonly showed complete radiological resolution on follow up imaging while not a single patient in severe category had a normal chest film on follow up imaging.(Table 7).

Table No.7 Correlation Of Different Factors With Complete Resolution

	Factor	Complete resolution		p-value
		YES	NO	
Age in years	<40	16	230	<0.001,HS
	>40	9	81	
Gender	Male	17	271	<0.001,HS
	Female	8	40	
CTSS	Mild	16	92	<0.001,HS
	Moderate	9	118	
	Severe	0	101	

Dynamic Chest CT Features

The most common parenchymal abnormalities observed during active disease included ground-glass opacity (GGO) (321 [83.3%]), consolidation (283 [73.5%]), and sub- pleural atelectatic fibrotic bands (103 [26%]). While on follow up scan, the positive count of GGO and consolidations gradually decreased, the positive count of sub-pleural fibrotic bands increased substantially(59%).

DISCUSSION:

In this study, we found complete resorption of pulmonary changes in only 19% of patients on follow up at 3-4 weeks of discharge. However, more than 80% of patients demonstrated residual abnormalities, including sub-pleural fibrotic atelectatic bands , GGOs and consolidatory patches as the major CT manifestations at the radiological follow-up study. The CT score of non-GGO lesions was used to evaluate residual pulmonary involvement because decreased density GGO area over an extended surface may occur in some patients after discharge or during convalescence, which could have led to over-estimation of the CT scores.

The residual abnormality in patients who visited the post COVD OPD earlier i.e. at 3 weeks showed predominantly extensive GGOs and consolidatory patches compared to the ones who did follow up at 4 weeks or later where the most prevalent changes were subpleural bands.

Wang et al. [3] described the CT changes in COVID 19 patients according to 5 illness periods (0–5 days, 6–11 days,12–17 days, 18–23 days, _24 days) and assigned a CT score dividing the lungs into six zones. CT scores and the number of involved lung zones increased rapidly, with a peak on stage "days 6–11". The most common finding was GGO, which increased in the late stages, whereas consolidation was the second most observed finding in the first 11 days. Our findings are consistent with those numbers.

Jin et al. [9] divided the most frequent imaging findings according to a classification in 5 stages: ultra-early, early (1–3 days from onset of symptoms),rapid progression (3-7days) consolidation (7–14 days),and the dissipation stage (2–3 weeks). The characteristic finding seen in first two phases were GGOs, in phases three and four were consolidations, whereas the last stage showed a progressive increase of thickening of the interlobular septa, bronchial walls and subpleural fibrotic bands. We found similar results in our study.

Few previous studies have reported that worse outcomes were seen in male patients with COVID-19 who were older in age with comorbidities[10, 12,13].In our study, we observed similar pattern with females and younger patients less than 40 years of age without any co morbid condition showing a faster resolution rate.

Radiological abnormalities in a patient who has recovered from SARS are usually transient interlobular septal thickening and reticulation over a course of several weeks to months.

The reticulation appears after the 2nd week and peaks around the 4th week [14]. About one-third of patients showing incessant persistent respiratory symptoms will have imaging findings of fibrosis, including inter-lobular and intralobular reticulation, traction bronchiectasis, and, rarely, honeycombing [15]. Damage to ciliated respiratory epithelium resulting in areas of air-trapping have been reported in 92% of patients who have recovered from pneumonia and are less likely to resolve completely [16].

Similarly, in patients with MERS; the majority recover completely, however 33% patients show changes of lung fibrosis on follow-up imaging. These changes were more common in older patients who had history of prolonged ICU admission or extensive lung involvement in the acute phase of the disease [17].

In our cohort, consolidations (figure 2) and subpleural fibrous bands were the main imaging findings during the follow up study ofCOVID-19 pneumonia, which could be gradually absorbed fully if followed up regularly at longer durations, whereas a crazy-paving pattern was demonstrated in a few patients[3].

The extent of GGOs increased in the patients who presented earlier for follow up , however there was a significant decrease in the density of the residual GGOs. This has been described as tinted sign in few of the previous studies[18] or the "melting sugar" sign[19].

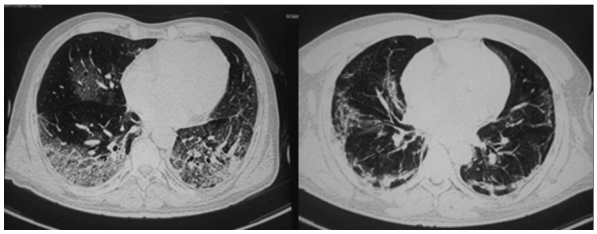


Figure 2: Dynamic Temporal Changes Consolidations During Active Disease And At Follow Up Study

in this study, few(4) of the patients showed areas of parenchymal breakdown with cavitatory changes in previous consolidatory patches on follow up imaging(figure 3). In two of the patients, there was a soft tissue component in the cavitatory areas.These changes could represent superimposed fungal infection like aspergillosis over resolving COVID 19 changes.

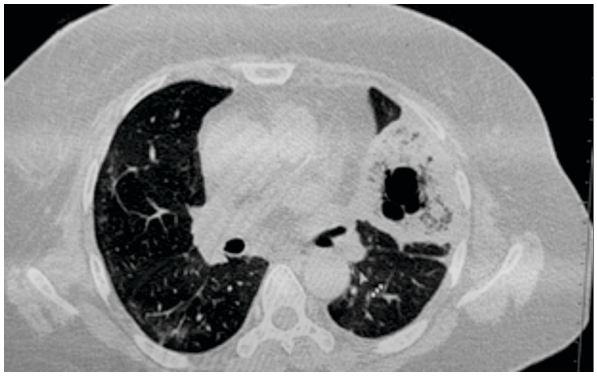


Figure 3: Cystic Cavitatory Changes In A Consolidatory Patch

The chest X ray is an important diagnostic tool in the detection and management of Covid 19 pnuemonia. Chest X ray is useful tool to detect changes to suggest the diagnosis, CT chest however has a higher sensitivity. The common CT findings of bilateral involvement, peripheral distribution, and predominantly in lower zones were also appreciated on CXR which was commensurate with other studies.

Among laboratory confirmed cases of COVID-19, patients with any comorbidity yielded poorer clinical outcomes than those without. A greater number of comorbidities also correlated with poorer clinical outcomes.

A main limitation of the current study is that only a single follow up study was done instead of multiple follow up scans at regular intervals. Second only the patients who were clinically stable enough to be discharged were included in this study.

In conclusion, this study showed the temporal resolution process of pulmonary lesions in patients who got discharged and were recovering from COVID-19 pneumonia.

This study may help to understand the late modifications of image findings, residual changes, complications and course of recovery of this disease and to reach an optimized point of time for follow up HRCT chest in discharged patients.

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