Journal of Chitwan Medical College 2022;12(39):106-110
Available online at: www.jcmc.com.np

ORIGINAL RESEARCH ARTICLE

HIGH RESOLUTION COMPUTED TOMOGRAPHY CHEST FINDINGS DURING ADMISSION AND FOLLOW-UP IN SEVERE COVID-19 INFECTION

Niraj Puri[1,*], Shital Adhikari[1], Madhur Dev Bhattarai[1], Basanta Gauli[1], Sailesh Gurung[1], Sunil Patel[1], Pratik Wagley[1], Deepak Adhikari[2], Bigyan Paudel[2]

[1]Department of Pulmonary and Critical Care Medicine, Chitwan Medical College Teaching Hospital, Bharatpur, Nepal
[2]Department of Radiology, Chitwan Medical College Teaching Hospital, Bharatpur, Nepal

Received: 01 Feb, 2022

Accepted: 08 Mar, 2022

Published: 15 Mar, 2022

Key words: Bronchiectasis; COVID-19; Fibrosis; HRCT.

***Correspondence to:** Niraj Puri, Department of Pulmonary and Critical Care Medicine, Chitwan Medical College Teaching Hospital, Bharatpur, Nepal.*
Email: dr.nirajpuri@gmail.com

*DOI:*https://doi.org/10.54530/jcmc.656

Citation

Puri N, Adhikari S, Bhattarai MD, Gauli B, Gurung S, Patel S, Wagley P, Adhikari D, Paudel P. High resolution computed tomography chest findings during admission and follow-up in severe COVID-19 infection. Journal of Chitwan Medical College. 2022;12(39):106-10.

Peer Reviewed

ABSTRACT

Background: The full extent of pulmonary damage and long-term prognosis due to severe COVID-19 pneumonia is still unclear. This study was aimed to characterize and compare changes in the radiological pattern of HRCT chest in severe COVID-19 pneumonia patients from admission to that of follow-up.

Methods: This was a one-year prospective study done at Chitwan Medical College from April 2020 to April 2021. Total 56 patients with severe COVID-19 pneumonia who had at least one HRCT chest during admission and another during follow-up within 5 weeks. Based on the total number of days on systemic steroids, patients were separated into three follow-up groups. Statistical Package for Social Science version 20 was used for data input and descriptive analysis. Point estimate at 95% Confidence interval was calculated along with frequency and descriptive statistics.

Results: The median CT severity index scores of follow-up HRCT chest improved from 14.5 to 10.0 in the 3rd week and from 16.0 to 11.5 in the 5th week. Ground Glass Opacity resolved early and steadily. The prevalence of bronchiectasis and fibrosis was considerable, with no meaningful improvement up to 5th week.

Conclusions: Significant radiological improvement can be seen as early as 3rd week from recovery phase of severe COVID-19 pneumonia where systemic steroids have a key contributory role. High frequency of bronchiectasis and fibrosis from in-patient HRCT chest may be due to acute COVID-19 pneumonia lesions on the preexisting undiagnosed lung diseases which may be falsely ascribed to the post-COVID.

INTRODUCTION

Coronavirus disease-19 (COVID-19) is still a global pandemic disease and the long-term pulmonary outcome from severe COVID-19 pneumonia survived patients is still unknown. Many previous studies have reported prolonged dyspnea and cough even after recovery from severe COVID-19 pneumonia.[1] There are also reports of decrease in total lung volume and diffusion capacity even at 3 months of follow up.[2] Although, the baseline chest x ray taken during admission can be valuable where the most common finding is peripheral basal ground glass opacities,[3] HRCT chest has proven to be more effective in radiologically diagnosing COVID-19 pneumonia.[4] It is also a primary screening tool for post-COVID pulmonary sequel and may predict early disease outcome.[5,6] It has been widely accepted for the prognostication of COVID-19 pneumonia with high sensitivity and high positive predictive value.[7]

Patients with COVID-19 are considered to have severe illness if they have SpO_2 <94% on room air, PaO_2/FiO_2 <300 mm Hg, a respiratory rate >30 breaths/min, or lung infiltrates >50%. These patients may experience rapid clinical deterioration.[10] Therefore, we included only severe COVID-19 infected patients in our study. There are numerous studies reporting about typical HRCT chest findings in severe COVID-19 patients,[8,9] however there are paucity of reports of HRCT chest findings comparing during severe COVID-19 pneumonia and during follow up after recovery from acute illness.

This study was aimed at comparing the initial HRCT chest during severe COVID-19 pneumonia to that of follow-up after symptom resolution and therefore understanding the pattern of pulmonary lesion resolution.

METHODS

This was a one-year prospective study from April 13, 2020 to April 12, 2021 conducted at Chitwan Medical College Teaching Hospital (CMCTH), Bharatpur, Nepal. The study was approved by the Institutional Research Committee (IRC) of CMCTH, Ref: CMC-IRC/078/079-031. A written and an informed consent was provided to the patient and/or the closet relative prior to enrolling in the study. COVID-19 infection was diagnosed by reverse transcription polymerase chain reaction (RT-PCR) test

from the nasopharynx and/or throat swab. COVID-19 positive patients with one HRCT chest during admission and other during follow up within 5 weeks were included in the study. We recorded the baseline demographic and clinical characteristics of all patients during admission and the HRCT chest findings were recorded during admission and follow-up. All HRCT chest examinations were non-enhanced and no intravenous contrast medium was administered [11]. All patients were kept in supine position and it was performed in a single breath hold inspiratory view by using a multi-detector 128 slice, Simens Somatom definition AS. Axial, coronal and sagittal view were all reconstructed, where axial view provided the most in-depth view of COVID-19 pneumonia lesion. The interpretation was performed by two senior radiologists and final scores were determined by consensus. HRCT chest abnormalities noted for calculations were ground glass of opacities (GGO), consolidation, crazy paving, bronchiectasis and fibrosis. Although there are many HRCT chest scores for COVID-19 pneumonia including CO-RADS and CTSI, we choose the simple conventional, CT Severity Index (CTSI) for ease of calculation. Here, the three right and two left pulmonary lobes were given score ranging from 1 to 5 for each lobe.[12-13] The total CTSI score was the sum of the individual lobar scores and ranged from 0 (no involvement) to 25 (maximum involvement). Calculation for each lobe by the radiologist was done as follows: no involvement = 0 score, < 5% involvement = 1 score, 6–25% involvement = 2 score, 26–49% involvement = 3 score, 50–75% involvement = 4 score, 75% involvements = 5 score. The follow up schedule was based on the total number of days on systemic steroids. No patient was prescribed steroids for more than 3 weeks. The patients were divided into three follow up group schedules with intention to treat analysis. Group 1 within 3rd week for patients on ≤7 days of systemic steroids. group 2 within 4th week for patients on 8-14 days of systemic steroids and group 3 within 5th week for patients on 15-21 days of systemic steroids.

Statistical analysis was performed using IBM SPSS Statistics Software version 20. Quantitative data were presented as the mean/median value and the counting data are presented as the percentage of the total unless otherwise specified. The comparisons of counting data were evaluated using the Chi-square test. A p-value of less than 0.05 was defined as statistically significant. The association between COVID-19 severity indices and main outcomes were assessed by univariate logistic regression analyses. Z test for two proportions at 95% confidence interval was used to compare data of different follow up phases.

RESULTS

Out of total 1732 admitted COVID-19 patients in the CMCTH, 47.8% who were admitted in the COVID ICU had severe COVID-19 infection. Among them, 56 patients fulfilling the all inclusion criteria were enrolled in the study.

Table 1: Demographic and clinical characteristics of the patients

Characteristics	Baseline: All patients during admission n=56 (%)	Group 1 (3rd week follow up) n=14 (%)	Group 2 (4th week follow up) n=28 (%)	Group 3 (5th week follow up) n=14 (%)	p
Male	33 (58.92%)	10 (71.42%)	14 (49.99%)	9 (64.28%)	0.369
Female	23 (41.07%)	4 (28.57%)	14 (49.99%)	5 (35.71%)	
Mean Age (SD)	55.5± 15.74	55.0± 18.34	54.2±13.03	58.5±18.59	0.425
Active/occasional smokers	32 (57.14%)	8 (57.14%)	16 (57.14%)	8 (57.14%)	1
Diabetes	21 (37.49%)	7 (50 %)	11(39.28%)	3 (21.42%)	0.599
Symptoms					
Cough	50 (89.28%)	12 (85.71%)	24 (85.71%)	14 (100%)	1
Fever	47 (83.92%)	12 (85.71%)	22 (78.57%)	13 (92.85%)	0.979
Shortness of breath	40 (71.42%)	11 (78.57%)	19 (67.85%)	10 (71.42%)	0.1
Myalgia	24 (42.85%)	6 (42.85%)	12 (42.85%)	6 (42.85%)	0.813
Loss of taste/smell	17 (30.35%)	4 (28.57%)	10 (35.71%)	3 (21.42%)	0.686
Hemoptysis	9 (16.07%)	3 (21.42%)	5 (17.85%)	1 (7.14%)	1
GI symptom	17 (30.35%)	5 (35.71%)	8 (28.57%)	4 (28.57%)	1
Mean CRP (mg/L),	65.921	53.571	75.31	63.166	0.759
D-dimer (mcg/ml) ± SD	1113.5±1585.5	1054.2±1226.5	919.18±1609.9	1561.54±1856.6	0.467
Median days on steroids					
≤ 7 days	9 (16.07%)	10 (71.42%)	0	0	**0.018**
8-14 days	29 (51.78%)	4 (28.57%)	24 (85.71%)	0	
15-21 days	18 (32.14%)	0	4 (14.28%)	14 (100%)	

Table 1 showed the baseline characteristics of total patients and sub follow-up groups. Mean age of all the patients was 55.5 years and about 60% were smokers. The frequency of male, mean age, smokers, diabetes, symptoms, CRP and D-dimer was similar in all the three groups. More than 1/3rd had diabetes, which is believed to be an independent risk factor for COVID-19 complication.14 Shortness of breath was present in 71.42%, gastrointestinal symptoms in 30.35%, and loss of taste/smell in 30.35%. Higher level of CRP and D-Dimer was not statistically significant in co-relation with severe COVID-19

pneumonia. Few numbers of patients were prescribed steroids for longer duration than planned with intention to treat as per the decision of the treating physician. In sub group analysis, in group-1, 4 patients (28.57%) and in group-2, 4 patients (14.28%) were prescribed systemic steroids for longer duration. Group-3 included all 14 patients (100%) who took systemic steroids as planned duration. This distribution had a significant statistical p value of 0.018.

Table 2 compared the initial and follow up HRCT chest. The median CTSI scores was similar in all three groups. However, there was statistically significant improvement in the median CTSI score between group-1 (p=0.031) and group-3 (p=0.009) patients which implied there was rapid improvement in early resolution phase and progressive improvement at 5th week. Ground Glass Opacity (GGO) and crazy paving significantly decreased in the follow-up HRCT chest in all the three groups. The total initial frequency of bronchiectasis and fibrosis was high with no significant improvement during follow-up at any group even after prolonged systemic steroids prescription.

Table 2: Comparison of HRCT chest findings during admission and at follow-up

HRCT chest findings	Group 1 (3rd week follow up) n=14 (%)			Group 2 (4th week follow up) n=28 (%)			Group 3 (5th week follow up) n=14 (%)		
	Baseline	Follow-up	P *	Baseline	Follow-up	P *	Baseline	Follow-up	P *
GGO	13 (92.9%)	4 (28.6%)	**0.0002**	25 (89.3%)	6 (21.4%)	**0.0001**	14 (100%)	0 (0%)	**0.0001**
Consolidation	13 (92.9%)	12 (85.7%)	0.270	23 (82.1%)	24 (85.7%)	0.642	9 (64.3%)	9 (64.3%)	0.500
Crazy paving	8 (57.1%)	2 (14.3%)	**0.009**	12 (42.9%)	4 (14.3%)	**0.009**	7 (50%)	2 (14.3%)	**0.021**
Bronchiectasis	7 (50%)	7 (50%)	0.500	6 (21.4%)	10 (35.7%)	0.881	4 (28.6%)	6 (42.9%)	0.784
Fibrosis	9 (64.3%)	11 (78.6%)	0.798	16 (57.1%)	20 (71.4%)	0.867	7 (50%)	7 (50%)	0.500
Median CTSI score	14.5	10.0	**0.031**	16.5	9.5	0.074	16.0	11.5	**0.009**

DISCUSSION

In our study, there was statistical improvement in the median CTSI score between the in-patient and follow-up HRCT chest at 3rd week and 5th week. More than half of the patients needed steroids for 2 weeks. Therefore, there were larger population at 4th week follow up, which may have created data dilution. After the clearance of the reversible element, the extent of the affected area significantly improves as early as 1 month after pulmonary symptom resolution.[1] GGO is the most common and early finding in COVID-19 infections. Bilateral, multi-lobar GGO with a peripheral or posterior distribution, mainly in the lower lobes and less frequently in the middle lobe are the initial findings in COVID-19 pneumonia.[15] GGO has a hazy increase in lung opacity without obscuring underlying vessels unlike in consolidation where the vessels are obscured by the lung opacity. In the early phase of the disease, GGO may present as a unifocal lesion and atypical initial imaging presentation of consolidative opacities superimposed on GGO may also be found in a smaller number of cases.[13,15] There was significant reduction in GGO between the in-patient and follow-up HRCT chest scans in all the three groups in our study because GGO is considered a reversible disease process.[13] This may be possible due to the aid of systemic steroids. The decrease in GGO is due to the transformation from GGO with or without crazy-paving pattern to increased consolidation, indicating progressive alveolar epithelial damage and more severe proteinaceous exudates in both alveolar and interstitial tissue.[16] Crazy Paving is a combination of ground glass opacity with superimposed septal thickening.[13,17] The frequency of crazy paving decreased significantly in the follow-up scan in all the three groups in our study. The frequency of GGO and crazy paving findings in the in-patient HRCT chest and their significant decrease later in the follow-up HRCT chest are consistent with the sequence of changes reported in the literature.[13,15] The improvement of crazy paving could be due to decrease in interstitial edema and cellular infiltration in collapsed alveoli.[16] Septal thickening and bronchiectasis are some of the less common findings, mainly in the later stages of the disease.[13,15] Finally, pleural effusion, pericardial effusion, lymphadenopathy, cavitation, CT halo sign, and pneumothorax are some of the uncommon but possible findings seen with disease progression.[13,15] Such findings were not found in our study. The high frequency of bronchiectasis and fibrosis in the in-patient HRCT chest without any significant resolution even at 5th week follow up may have several possible reasons. First, the bronchiectasis and fibrosis observed in the in-patient HRCT chest in our study may be the findings observed due to the combination of various reversible or irreversible acute lesions due to COVID-19 infection. If so, the reversible pulmonary elements may require up-to 3 months for improvement after discharge.[1] Second, even with the initial judicious prescription of systemic steroids, the non-significant resolution of bronchiectasis may be due to higher frequency of already existing asymptomatic bronchiectasis and fibrosis

secondary to the past tuberculosis and other pulmonary infections. Up to 50% of TB patients may develop bronchiectasis involving more than one lobe.[18,19] Bronchiectasis may, thus, be quite prevalent in our community as an undiagnosed lung disease (ULD). Bronchiectasis was earlier considered as an 'orphan lung disease' but has a prevalence of u- to 1.2% in those aged 40 years or older.[14,20] Hence, the bronchiectasis and fibrosis findings observed during the follow-up stage may falsely be ascribed solely to be due to post-COVID-19 pneumonia sequel. Lastly, infection may provoke further inflammation and fibrin deposition in the pre-existing bronchiectasis and fibrosis. Since, apart from as a primary, genetically influenced, and age-related fibro-proliferative process, pulmonary fibrosis can develop following acute or chronic inflammation.[21] Although the characteristics and evolution of pulmonary lesions in COVID-19 patients are increasingly available, at present the full extent of the long-term pulmonary consequences of COVID-19 remains speculative.[12,13,15,21,22]

This was a single institution study with relatively a smaller number of patients as we only included severe COVID-19 pneumonia patients. HRCT chest might also have been selectively done due to many technical and financial restrain. Also, some of the patients who did not or could not follow-up in schedule even up to 5 weeks from initial HRCT chest were excluded. The non-significant reduction in bronchiectasis and fibrosis may probably be due to the small sample size and single follow-up. Longer follow-ups up to 3 months' duration might give a different picture in resolution of these so called non resolving patterns.

CONCLUSION

There was significance improvement in the median CTSI score between the in-patient and follow-up scan done in the single follow-up period of 3rd week and 5th week. The frequency of GGO and crazy paving findings in the in-patient HRCT chest and their significant decrease later in the follow-up HRCT chest in our study are consistent with the sequence of changes reported in the literature especially with the aid of systemic steroids. The higher frequency of crazy paving and consolidation in the in-patient HRCT chest could be due to the admission criteria of severe clinical severity only. The non-resolving bronchiectasis and fibrosis observed even with clinically adequate prescription of systemic steroids for up to 3 weeks could have been due to the combination of various reversible or irreversible acute lesions or due to the higher frequency of asymptomatic bronchiectasis and fibrosis, prevalent as undiagnosed lung diseases (ULD) in the community, caused by past tuberculosis and other infections. Hence this might be falsely ascribed as post COVID pneumonia effect.

CONFLICT OF INTEREST: None

FINANCIAL DISCLOSURE: None

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