Residual Lung Parenchymal CT Changes in COVID-19 Patients and its Association with Common Predictors

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ABSTRACT

Introduction: Chest computed tomography (CT) is used for the screening and diagnosis of COVID-19 pneumonia. The aim of the study is to study the prevalence of residual lung parenchymal CT changes in COVID-19 patients and its association with common predictors.

Methods: Longitudinal study conducted at Shree Birendra Hospital in which diagnosed COVID-19 patients with initial CT scan showing COVID-19 related changes were retrospectively enrolled after ethics approval. The study period was from 15 February 2020 to 15 November 2021. Chest CT changes were evaluated and CT scan severity score (CT SS) assigned. Data was entered in Microsoft Excel and analysed in SPSS (Statistical Package for Social Sciences) version 16.

Results: Males were more common (72.6%) among the 62 enrolled participants with the mean age 53.63 ± 15.05 years. Median interval between two scans was 137 days. Residual lung parenchymal CT changes were seen in 43 (69.4%) participants. Hypertension (25, 40.3%) and GGO (55, 88.7%) were the most common comorbidity and CT features respectively. The mean initial and final CT SS was 10.84 ± 5.87 and 3.55 ± 4.58 respectively (Total score 25, p = 0.001). Age was significantly associated with severity of CT score (p = 0.04).

Conclusions: A large percentage of COVID-19 patients have chest CT changes after three months of initial chest CT scan. CT SS reduced significantly in the second scan. Similar studies with long term serial CT follow up of patients is recommended to be carried out in future.

Key Words: Chest CT; COVID-19; Predictors; Severity Score

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) became a pandemic after the outbreak of pneumonia in Hubei Province of Wuhan, China in December 2019.[1] Chest computed tomography (CT) is an imaging modality used for the screening and diagnosis of COVID-19 pneumonia widely used after the initial findings of COVID-19 had certain consistency and specificity.[2,3]

Most studies have found small subpleural ground glass opacities (GGO) in lung on chest CT that grew larger with a crazy-paving pattern and consolidation up to two weeks. After two weeks, the lesions were gradually absorbed leaving extensive GGO, interlobular septal thickening, irregular lines and subpleural parenchymal bands representing fibrosis which is also seen in Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) infection.[4-7] With these observations the burden of pulmonary fibrosis could be substantial after COVID-19 recovery. Common predictors of pulmonary fibrosis in COVID-19 infection are advanced age, smoking, chronic alcoholism, length of Intensive Care Unit (ICU) stay, illness severity and mechanical ventilation.[8]

There are many studies on temporary changes of the radiological findings but very little study is available for long term changes of the findings in COVID-19 patients in our context. Hence, this study aims to study the prevalence of the residual lung parenchymal CT changes in COVID-19 patients and its association with common predictors.

METHODS

A longitudinal study was conducted at Shree Birendra Hospital, Chhauni, Kathmandu, Nepal. It is a tertiary care hospital of Nepali Army and one of the designated COVID-19 centers of the Government, in which participants were enrolled by purposive sampling. Study participants were taken retrospectively from 15 November 2020 to 15 February 2021. All patients who were over 18 years, real-time reverse transcription-polymerase chain reaction (RT-PCR) positive patients for COVID-19 and COVID-19 related chest CT changes were enrolled in the study. Patients not giving consent, past or pre-existing diagnosed lung or systemic illness associated with lung fibrosis, chronic obstructive pulmonary disease (COPD), carcinoma lung, idiopathic pulmonary fibrosis, past or active pulmonary tuberculosis, past documented atypical, viral or lobar pneumonia, interstitial lung disease, chronic inflammatory and autoimmune conditions like sarcoidosis, Wegener's granulomatosis, rheumatoid arthritis, systemic lupus erythematosus (SLE), ionising radiation to chest for intrathoracic or extrathoracic tumours, pregnant females, patients not being able to be contacted for a period of one year from initial CT scan, time interval between diagnostic RT-PCR test and initial Chest CT scan exceeding one month and death during follow-up periods were excluded from the study. Demographic and clinical information were noted in a proforma which included information on the common predictors for lung fibrosis like age, illness severity, length of ICU stay, mechanical ventilation, smoking and alcohol intake. Data was collected from the patients as well as hospital charts. The initial CT scan of participants from the hospital database were re-read by a team of radiologists consisting of the primary researcher with over 15 years of experience in the Radiology Department, and two radiologists who were trained by the primary researcher for the research. Final CT scan was taken after the patient completed at least three months from the initial CT scan. Chest CT changes were evaluated and CT scan severity score (CT SS) assigned in a score of one to 25 with scores having one to eight being classified as mild severity score (SS), nine to 15 as moderate SS and 16 to 25 as severe SS.[9] Both chest CT scans were performed in Hitachi Scenario 128 slice multidetector CT machine made by HITACHI medical corporation, Japan with a reconstructive resolution of 0.6 mm. To mitigate the radiation risk, high resolution CT (HRCT) were performed instead of conventional CT scan which has a lower dose of radiation as compared to conventional CT scan.[10] Additionally, on final scan, instead of regular dose, low dose radiation i.e. (½) half dose of the scan was done.[11] Ethics approval was taken from Institutional Review Committee (IRC) of Nepalese Army Institute of Health Sciences (NAIHS) in February 2021 with Ref no 393. Data was entered in Microsoft Excel and analysis was done using SPSS (Statistical Package for Social Sciences) version 16. Descriptive data were given as frequency and percentages. Paired t test was used to see the difference in mean severity scores of initial and final chest CT scan. Chi square test was used to see association between categorical variables (Predictors of lung fibrosis) and residual chest CT scan changes in final CT scan. Statistical significance was set at a p-value of < 0.05.

RESULTS

A total of 62 patients were included in the study with mean age range of 53.63 ± 15.05 years. Males were more common (72.6%). Nearly half were ever smokers (48.4%) and among those with history of smoking, one third were current smokers. Hypertension (40.3%) was the most common comorbidity. Almost half of the patients had mild symptoms (51.6%). Three quarters were admitted in hospital (74.2%) with a quarter of them needing ICU admission (19.4%). The mean hospital stay and ICU stay was 9.94 and 2.34 days. No cases of pulmonary embolism or myocarditis were recorded in the study. Table 1 shows the demographic characteristics of the study population.

All patients enrolled in the study underwent a second scan. The median interval between the two scans was 137 days. Prevalence of abnormal findings in the second scan was seen in 43 (69.4%) participants. Peripheral lung involvement was seen to be more common in both initial and final scan. Right lower lobe (RLL) and left lower lobe (LLL) were the most common lobes involved in both scans. GGO was the most common feature in the chest CT scan. The initial and final chest CT findings are shown in Table 2.

Table 1. Demographic profile of study population (n = 62)

Variable	Frequency n (%)
Gender	
Male	45 (72.6)
Female	17 (27.4)
History of smoking	30 (48.4)
Alcohol consumption	20 (32.3)
Comorbidities	
Hypertension	25 (40.3)
Diabetes mellitus	19 (30.6)
Asthma	7 (11.3)
Cardiovascular disease	5 (8.1)
Symptoms	
Mild	32 (51.6)
Moderate	24 (38.7)
Severe	6 (9.7)
Hospitalisation	46 (74.2)
ICU Admission	12 (19.4)
Oxygen therapy	28 (45.2)
Steroid therapy	15 (24.2)

Table 2. Initial and final Chest CT scan findings (n = 62)

Characteristics	Initial CT scan (N %)	Final CT scan (N %)
Peripheral involvement	62 (100)	33 (53.2)
Subpleural involvement	2 (3.2)	14 (22.6)
Diffuse involvement	4 (6.5)	0
Right Upper Lobe	50 (80.6)	31 (50)
Right Middle Lobe	48 (77.4)	26 (41.9)
Right Lower Lobe	56 (90.3)	39 (62.9)
Left Upper Lobe	46 (74.2)	32 (51.6)
Left Lower Lobe	56 (90.3)	35 (56.5)
Ground Glass Opacities	55 (88.7)	31 (50)
Consolidation	37 (59.7)	1 (1.6)
Interlobular septal thickening	11 (17.7)	33 (53.2)
Atelectatic bands	3 (4.8)	7 (11.3)
Pleural Effusion (Bilateral)	2 (3.2)	0
Traction bronchiectasis	0	3 (4.8)
Honeycombing	0	1 (1.6)

Almost half the patients (45.2%) had moderate SS scores on initial CT scan. On the final CT scan, 19 patients (30.6%) had a normal CT scan. The initial and final chest CT SS is given in Table 3. Mean initial CT SS was 10.84 ± 5.87 and final CT SS was 3.55 ± 4.58. The p value on application of paired t test for mean initial and final CT SS was 0.001 which was statistically significant.

Association of the common predictors for residual lung changes like age, gender, smoking, alcohol, use of oxygen, use of mechanical ventilation and steroid with final chest CT SS was seen by the application of Chi Square test.

Table 3. Initial and final chest CT scan Severity Score (n = 62)

Category	Initial CT scan findings N%	Final CT scan findings N%
Normal CT scan	0	19 (30.6)
Mild SS	20 (32.3)	35 (56.5)
Moderate SS	28 (45.2)	6 (9.7)
Severe SS	14 (22.6)	2 (3.2)

Table 4. Association of final SS score with common predictors (n = 62)

Study variables		SS2 score		p- value
		Normal N (%)	Abnormal N (%)	
Age	< 60	17 (37.8)	28 (62.2)	0.04
	>= 60	2 (11.8)	15 (88.2)	
Gender	Female	3 (17.6)	14 (82.4)	0.172
	Male	16 (35.6)	29 (64.4)	
Smoking	No	8 (25)	24 (75)	0.319
	Yes	11 (36.7)	19 (63.3)	
Oxygen Therapy	No	12 (35.3)	22 (64.7)	0.382
	Yes	7 (25.0)	21 (75.0)	
Mechanical Ventilation	No	18 (32.1)	38 (67.9)	0.435
	Yes	1 (16.7)	5 (83.3)	
Steroid therapy	No	14 (29.8)	33 (70.2)	0.795
	Yes	5 (33.3)	10 (66.7)	
Alcohol intake	No	13 (31.0)	29 (69.0)	0.939
	Yes	6 (30.0)	14 (70.0)	

The results are given in table 4. Age was found to be statistically significant to the final CT scan score (p = 0.04). No statistically significant association was seen for comorbidities and other common predictors like heart disease, asthma, hypertension, diabetes mellitus and variables like hospital and ICU stay (p > 0.05).

DISCUSSION

Chest CT is a key component in the diagnostic workup for COVID-19 patients, and our study has shown important imaging findings encountered in the patients at short term and at follow-up of at least three months. In our study, the most common initial findings were GGO, located at peripheral and subpleural sites with few of the cases showing a diffuse pattern of distribution involving central areas as well. Second most common finding was consolidation with the same pattern of involvement. Interlobular septal thickening and atelectatic band formation were other changes in initial CT scan. These findings are in concordance with study conducted by Plesner et al which reported findings that are frequently peripheral and bilateral, involving multiple lobes and GGO with vascular enlargements along with consolidations and reticulations that often appear during progression.[12]

Interlobular septal thickening, atelectatic bands and traction bronchiectasis were seen more frequently in follow-up scans in our study with one case showing subpleural honeycombing appearance. Our findings are again in concurrence with many of the studies that followed-up chest CT after COVID-19 pneumonia. In their prospective longitudinal study, Han X et al found that approximately one-third of participants showed chest CT findings with pulmonary fibrosis-like changes (Like traction bronchiectasis, parenchymal bands, and / or honeycombing) within six months after recovery from severe COVID-19 pneumonia.[13] In another study, GGO with reticular pattern was observed in 31% of the lung zones in severe patients at six months.[14] This value declined to 13% by 12 months after discharge, showing a gradual radiological recovery.[14] Solomon et al reported that at three months after acute infection, a group of patients had CT abnormalities like GGO and subpleural bands.[15] At six months after acute infection, some patients in the early recovery phase had resolution of GGOs and had persistence or development of changes suggestive of fibrosis like reticulation with or without parenchymal distortion.[15]

In our study, about one third of the patients had a normal follow-up chest CT scan while in a study of follow up scan at three months by van Gassel et al, 4.3% showed normal scan.[16] Mean CT involvement score for initial and final CT scan was lower in our study compared to the study done by van Gassel et al who reported a median CT SS of 11.[16] This difference could be because of difference in enrollment as van Gassel et al enrolled and followed up mechanically ventilated survivors. Results of a one year follow up study indicated substantial recovery on chest CT at one year after discharge which is in line with our findings where significant decrease in final CT was seen (p < 0.001).[14]

The mean age of the patients enrolled was 53.63 ± 15.05 years. Regarding the relationship between age and CT severity of COVID-19, we found a statistically significant association (p = 0.04). So, age is a predictor to the severity according to the findings. These findings support the findings of other studies where elderly are at higher risk of developing severity.[14,17] Despite our participants being the majority of males and with comorbidities, we found no statistical difference between gender, smoking, comorbidities like hypertension and total CT-SS, which are seen in some other studies.[14,17] In the study by Gassel et al, in mechanically ventilated patients, fibrosis, evident from reticular pattern of opacities, was seen in majority

of participants (91.3%) along with GGO (89.1%) at three months after hospital discharge.[16] They also noted fibrosis in their study cohort was diffusely distributed, while fibrosis in severe ARDS is usually in the anterior parts of the lungs.[16] However, no statistical significance was observed between mechanical ventilation and total CT SS ($p = 0.41$) in our study. This may be due to the small number ($n = 6$) of the mechanically ventilated patients.

The strength of our study was that we conducted a longitudinal follow up of the patients who had COVID-19 related changes in the lung. Most of our study participants were army personnel or their dependents so there was no loss to follow up. Our study does have some limitations. The major limitation is that it was conducted in a single centre and being the army hospital, most of the participants were army personnel or dependents, so it may not be generalised to the entire population. We enrolled participants with COVID-19 related findings in early initial chest CT. So participants who did not have initial severe symptoms may have been missed as they would not be recommended CT scan by clinicians as chest CT is not mandatory for all patients.[18] The sample size is limited to 62 patients and hence a larger sample size would be more ideal for studying association with the predictors of changes in chest CT scan. Single follow up scan was done and final disease progression was not studied which requires longer follow up duration and serial scans. Our study did not take into account the laboratory investigations and predictors such as CRP, D-dimer, lymphocytosis, LDH and plasma ferritin in assessing the disease progression and severity.

CONCLUSIONS

Our study found that a significant percentage of COVID-19 patients have chest CT changes after three months of initial chest CT scan. We found that the overall severity score in chest CT reduced significantly in the follow up final scan. As COVID-19 has caused a huge burden to the health care system, our study also aids in identification of early predictors and risk factors for chronic lung changes in COVID-19 patients and envisages long-term changes in patients' lungs.

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