An Analysis of High Resolution Computed Tomography Chest Imaging Features of Covid-19 Pneumonia in Immunocompetent and Immunocompromised Patients

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Abstract

Background: The Coronavirus disease 2019 (COVID-19) is caused by the novel coronavirus severe acute respiratory syndrome (SARS) CoV-2. Immune system dysfunction increases susceptibility to infections. Due to the ongoing environmental exposure of the respiratory tract, pulmonary infections are highly frequent and relatively more severe in immunocompromised people. Also, immunocompromised people are susceptible to opportunistic infections in addition to the common diseases that can infect an immunocompetent person. The gold standard diagnostic test for corona virus pneumonia is the molecular detection of SARS-CoV-2 nucleic acid. On CT, patients with COVID-19 displayed typical characteristics, such as bilateral multilobar ground-glass opacities with a posterior or peripheral predominance. The current study is to help us look for the types and severity of the changes in the chest CT imaging brought by the disease and how it varies in immunocompromised patients of COVID-19. Subjects and Methods: This is a hospital based comparative study design with a sample size of 91 patients referred to the department of Radiodiagnosis. Narayana Medical College, Nellore. The study was conducted for a period of 12 months. Results: Of 91 patients who tested RTPCR positive for SARS-CoV-2, 74 (81.31%) patients showed features of COVID -19 pneumonia on HRCT and 17 (18.68%) patients had no chest CT features. Among these 91 patients, 40 were immunocompromised and 51 were immunocompetent. Of the 17 patients with no CT changes, 13 (76.4%) were immunocompetent, and 4 (23.6%) were immunocompromised. Of the 51 immunocompromised patients, 42 had uncontrolled diabetes, 12 patients had chronic kidney disease, 1 patient had acquired immunodeficiency syndrome due to human immunodeficiency virus. 5 patients had both diabetes mellitus and chronic kidney disease. Most of the patients with no immunocompromising co-morbidities showed mild changes (35.0%) followed by no changes (32.5%). 25.0% of these patients showed moderate changes and 7.5% showed severe changes. Majority of the patients with diabetes (45.23%) showed moderate changes, followed by severe and mild changes. Majority of the patients (66.66%) with chronic kidney disease showed moderate changes, followed by severe changes in 16.6%. Conclusion: Patients with immunosuppressing conditions such as diabetes mellitus and chronic kidney disease had significantly more severe CT scores as compared to patients with no such background. Immunosuppressed patients are at higher risk for more severe corona virus disease and complications such as pneumothorax and pneumomediastinum. High Resolution CT is an important imaging modality to determine the disease extent and severity. Prioritizing those patients who have COVID-19 and immunosuppression is crucial since the severity of HRCT results has been shown to be higher in these patients.

Keywords: SARS-CoV-2, COVID-19, HRCT Chest, Immunocompetent, Immunocompromised, Immunosuppressed, Ground glass opacities, Consolidation, Diabetes mellitus, Chronic kidney disease.

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Introduction

The Coronavirus disease 2019 (COVID-19) is caused by the novel coronavirus severe acute respiratory syndrome SARS-CoV-2. The pandemic has not only affected lives but also livelihoods pushing millions into prolonged periods of lockdown. There is a dire necessity for more knowledge and research regarding COVID-19 and various facets of the virus.^[1]

Immune system dysfunction increases susceptibility to infections. The state of immunocompromise can be acquired and it has become much more prevalent because of recent developments in cancer treatment, hematopoietic-stem cell & solid-organ transplantation, usage of immunomodulatory medications, and acquired immune deficiency syndrome (AIDS).^[2] The number of such patients is on the rise as a result of these recent

developments. Due to the ongoing environmental exposure of the respiratory tract, pulmonary infections are highly immunocompromised frequent in people. Also, immunocompromised people are susceptible to opportunistic infections in addition to the common diseases that can infect an immunocompetent person. Similar worries arise in relation to SARS-CoV-2 infected immunosuppressed patients.^[2]

The gold standard diagnostic test for corona virus pneumonia is the molecular detection of SARS-CoV-2 nucleic acid via a range of respiratory sources, including throat swabs, posterior oropharyngeal saliva, nasopharyngeal swabs, sputum, and bronchial fluid.^[3] When the molecular detection system in Wuhan reached capacity, patients were swiftly identified using chest CT scans. On initial CT, patients with COVID-19 displayed typical characteristics, such as bilateral multilobar groundglass opacities with predominant posterior or peripheral distribution. [3,4,5] Therefore, it has been recommended that CT scanning be performed in conjunction with swab testing for people who have a high clinical suspicion of having COVID-19.

On chest radiographs, the lateral lung fields display scattered high-density shadows and some patients had diffuse distribution of ground glass opacities.^[6] Progression of illness was rather quick in some patients, and the consolidation was mostly concentrated in the bilateral lower lobes. "White lung" was observed in a few patients.^[6]

In the early period, ground-glass opacification is the predominant finding on the CT scan.^[6] There may be thickening of the interlobular septum and dilated blood vessels across the lesion. Epithelial shedding, inflammatory damage to the alveolar septal vessels, serous fibrinous exudation, and lymphocyte infiltration in the alveolar cavity are all responsible for these changes.

This is followed by the progressive period in which ground-glass opacities with consolidation and pulmonary interstitial changes such as interlobular, intralobular septal thickening, and subpleural line, are the prominent signs. Additionally, the "crazy-paving sign" is observed. These changes are due to diffuse intra-alveolar haemorrhage, fibrinous exudation, and interstitial inflammatory cell infiltration.

In the severe period, diffuse multiple patchy consolidation is the most prevalent manifestation, and in some cases, "white lung" may be present. These changes are attributed to diffuse alveolar damage, intra-alveolar edema, and hyaline membrane formation. The lesions clear in most of the patients, however, fibrosis may remain in some.^[6]

Bilateral lungs have multiple lesions, particularly in the lower lobes. The lesions were mostly found in the peripheral regions of the lung. The growth pattern of the lesions was often from the lung periphery to the centre. The lungs lesions "grow and disappear" throughout the course of the disease, demonstrating the co-existence of multiple manifestations.^[6]

The current study is to help us look for the types and severity of the changes in the chest CT imaging brought by the disease and how it varies in immunocompromised patients of COVID-19.

Aims and objectives

To study the HRCT chest features of patients with COVID-19 pneumonia.

To compare HRCT findings of immunocompromised and immunocompetent COVID-19 patients

Subjects and Methods

The main source of data was patients referred to the department of Radiodiagnosis, Narayana Medical College and Hospital, Nellore. This is a hospital-based comparative study consists of 91 patients. The study is conducted for a period of 12 months from March 2021 to February 2022. **Inclusion Criteria**

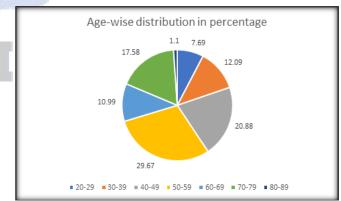
All patients who are COVID-19 positive and willing to participate in the study

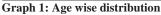
Exclusion Criteria

Claustrophobic patients, Pregnant females, Individuals younger than 14 years.

Results

Of the 91 patients included in the study, the mean age of the patients was 52.94 years; majority of the patients (29.67%) belonged to 50-59 years age group followed by 40-49 years (20.88%). Median age of the patients was 54 years. Among them 35 were female (38%) and 56 were male patients (62%).





All the patients were tested RT PCR positive for SARS-CoV-2 virus (CORADS - 6).

Of 91 patients who tested RTPCR positive for SARS-CoV-2, 74 (81.31%) patients showed features of COVID -19 pneumonia on HRCT and 17 (18.68%) patients had no chest CT features.

HRCT appearances of COVID-19 in the study

Ground glass opacity was the most common CT finding seen in 81.3% of the total patient sample. This was followed by subpleural fibrotic lines which were seen in 48.35% of the patients. Consolidation was seen in 39.5% of the patients with crazy paving pattern in 31.8% of the patients. Traction bronchiectasis was seen in 7% of the

patients. Reverse halo sign was seen only in 2 patients both of whom were diabetic.

Among these 91 patients, 40 were immunocompromised and 51 were immunocompetent.

Of the 17 patients with no CT changes, 13 (76.4%) were immunocompetent, and 4 (23.6%) were immunocompromised.

Table 1: Cl	Severity	of COVID	- 19	pneumonia	among		
immunocompetent Patients							

Count of	СТ				
Severity	Changes				
IMMUNOCO				Sever	Grand
MPETENT	Nil	Mild	Moderate	e	Total
Frequency	13	14	10	3	40
Percentage	32.5	35.0	25.0	7.5	100

Table 2: CT Severity of COVID – 19 pneumonia among immunocompromised Patients

Count of Severity	CT Changes					
IMMUNOCOMPROMI		Mil	Modera	Sever	Grand	
SED	Nil	d	te	e	Total	
Frequency	8	10	20	13	51	
	15.6	19.6				
Percentage	8	0	39.21	25.49	51	

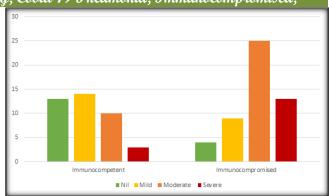
Of the 51 immunocompromised patients, 42 had uncontrolled diabetes, 12 patients had chronic kidney disease, 1 patient had acquired immunodeficiency syndrome due to human immunodeficiency virus. 5 patients had both diabetes mellitus and chronic kidney disease.

Most of the patients with no immunocompromising comorbidities showed mild changes (35.0%) followed by no changes (32.5%). 25.0% of these patients showed moderate changes and 7.5% showed severe changes.

Majority of the patients with diabetes (45.23%) showed moderate changes, followed by severe and mild changes. Majority of the patients (66.66%) with chronic kidney disease showed moderate changes, followed by severe changes in 16.6%.

Majority of the patients in the study showed moderate changes (38.5%) followed by mild changes (25.3%). 18.7% of the patients showed no changes whereas 17.6% had severe changes.

Table 3: Cross tabulation of immune status with CT severity						
Immune Status	Severit	Total				
	Nil	Mild	Moder	Sever		
			ate	e		
IMMUNOCOMPETE	13(32.	14(35.	10(25.0)	3(7.50	40(100	
NT	5)	0))	.0)	
IMMUNOCOMPRO	4(7.80	9(17.6	25(49.0)	13(25.	51(100	
MISED))		5)	.0)	
Total	17(18.	23(25.	35(38.5)	16(17.	91(100	
	7)	3)		6)	.0)	
STATISTICAL	X ² =17.456, P VALUE < .001, SIGNIFICANT					
SIGNIFICANCE						



Graph 1: Immune status and CT severity of the study

The probability of getting a Chi squared value of 17.456 or greater at 3 degrees of freedom is 0.001 (p value less than 0.05). This means we reject the null hypothesis and accept the alternative hypothesis that the CT severity among immunocompromised patients is significantly higher than that among immunocompetent patients.

Involvement of lobes

The median score for right upper lobe was 2. Less than 75% of the upper lobe was involved in all the cases. No changes (i.e., 0 involvement) were seen in right upper lobe in majority (47.5%) of the immunocompetent patients.

54.9% of the right upper lobes of immunocompromised patients showed a lobar severity score of 2 (5 - 25%) or 3 (26 - 49%). 3.9% of the patients showed more than 75% involvement of the lobe.

A score of 1 i.e., less than 5% involvement was seen in 25%. Less than 75% of the upper lobe was involved in all the immunocompetent cases. No changes (i.e., 0 involvement) were seen in right middle lobe in majority (55%) of the immunocompetent patients.

33.33% of the right middle lobes in immunocompromised patients showed a lobar severity score of 1 (<5%) followed by a score of 2 (5 – 25%) in 29.4% of the patients. 3.92% of the patients showed more than 75% involvement of the right middle lobe.

A score of 2 i.e., 5-25% involvement was seen in 17.5% followed by 3 (25-50%) in 15%. 5% of the patients showed a score of 5 (>75% involvement). No changes (i.e., 0 involvement) were seen in right lower lobe in majority (40%) of the immunocompetent patients.

Majority (35.29%) of the right lower lobes in immunocompromised patients showed a lobar severity score of 3 (<5%) followed by a score of 4 and 5 in 19.6% of the patients. There was no involvement of the right lower lobe in 9.8% of the cases.

A score of 1 i.e., <5% involvement was seen in 22.5% followed by 2 (25-50%) in 17.5%. All patients had less than 75% of involvement. No changes (i.e., 0 involvement) were seen in left upper lobe in majority (47.5%) of the immunocompetent patients.

Majority (25.5%) of the left upper lobes in immunocompromised patients showed a lobar severity score of 1 and 2 (<5% and 5-25% respectively) followed by a score of 3 and 4 in 17.6% of the patients. There was

no involvement of the left upper lobe in 11.7% of the cases.

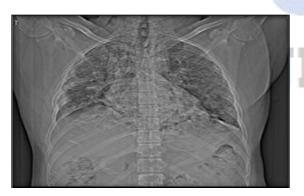
In left lower lobes of immunocompetent patients, a score of '2' i.e., 5-25% involvement was seen in 25% followed by '4' (50-75%) in 12.5%. 2 patients (5%) showed a score of '5', i.e., more than 75% involvement. No changes (i.e., 0 involvement) were seen in left lower lobe in 50% of the immunocompetent patients.

Majority (27.5%) of the left lower lobes in immunocompromised patients showed a lobar severity score of '4' (50-75% involvement) followed by a score of '3' and '5' in 15.6% of the patients each. There was no involvement of the left upper lobe in 13.7% of the cases.

Repeat CTs were done in 14 out of 91 patients, of which 7 patients (50%) showed progression of disease from milder to more severe forms. Decrease in CT severity was seen in 2(14.2%) of the patients. No significant change in CT severity was seen in 5 (35.7%) of these 14 patients. Of them 8 were immunocompromised and 6 were immunocompetent. 6 out of 8 (75%) immunocompromised patients showed progression of disease from milder to more severe forms in an average interval of 8.1 days. Whereas, in the 6 immunocompetent patients, 3 (50%) showed no significant change in severity, 2(33.33%) of them showed improvement in lung parenchyma and only 1 (16.66%) of them progressed to more severe form.

Representative cases.

Case 1 Patient history: 43-year-old diabetic male with complaints of SOB. RT-PCR for SARS-CoV-2 positive







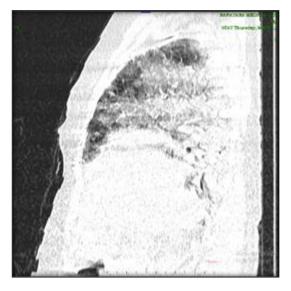
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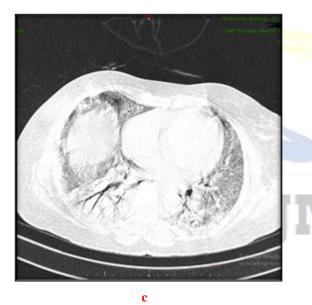
a. Topogram b,c,d. MPR of HRCT chest showing diffuse consolidatory changes and fibrosis in bilateral lung parenchyma with pneumomediastinum

Case 2. Patient history: 58-year-old female with chronic kidney disease with complaints of SOB. RT-PCR for SARS-CoV-2 positive





b





a. Topogram b. Sagittal section of HRCT chest showing extensively diffuse consolidatory changes with surrounding ground glass opacities in bilateral lung parenchyma c and d. Axial and coronal sections of HRCT chest showing consolidatory changes with air bronchogram in bilateral lungs. CT severity score -24 indicating severe disease

Discussion

In order to determine whether there is any correlation between haemoglobin A1c (HbA1c) levels and highresolution chest computed tomography (HRCT) chest score, Sahu et al. compared the imaging findings of patients with coronavirus disease (COVID-19) and those with well-controlled, poorly-controlled, and non-diabetic patients. In the study population, diabetes was present 71.5% of the time. Of these, 126 (63%) patients were male, the median age was 54.45 years (95% CI: 54.45 15.53). They discovered that in patients with COVID-19, the existence of diabetes, the presence of ground-glass appearance with mixed consolidation, consolidation, and reverse halo sign in the HRCT findings were significant predictors of the HRCT scores.^[7]

The above results coincided with the current study where diabetes was present in 46.15% of the total patient population. Majority (45.2%) of the diabetic patients showed moderate CT severity changes followed by severe changes (23.8%). With lab-confirmed COVID-19 infection, diabetes status is substantially correlated with the severity of HRCT results.

Monica Fung et al. examined the research that has been published on COVID-19 in immunocompromised individuals, including cancer patients, solid-organ transplant recipients, HIV patients, and people taking immunomodulatory medication for autoimmune illness. The risk of severe COVID-19 disease and poor prognosis may be raised in cancer patients and in those who have received solid-organ transplants, but the evidence is less with other evident for patients kinds of immunocompromised.^[8]

In our study, we included the chest HRCT scans of patients with co-morbidities such as chronic kidney disease (CKD), diabetes (DM) & AIDS. In comparison with patients without such immunocompromising co-morbidities, these patients showed higher risk for moderate and severe CT severity scores.

Characterizing normal and atypical pulmonary and extrapulmonary HRCT features in patients with COVID-19 infection was the goal of Monika Sharma et al.^[9] Patients with high CT severity scores had abnormal pulmonary and extra-pulmonary findings, which may have been brought on by an aggravated inflammatory response or a subsequent bacterial infection. But the truth is that difficult patients frequently have uncommon but aberrant observations.^[9]

In contrast to the above study, the typical findings in our study were ground glass opacities followed by subpleural fibrosis being the second most common finding. However, patients with higher CT severity scores had pulmonary and extra-pulmonary complications such as pleural effusion, pneumomediastinum and pneumothorax in agreement with the above study.

Ye et al. aimed to improve radiologists' detection of these findings by reviewing the typical and somewhat atypical CT presentations with representative COVID-19 cases at their hospital. The usual CT symptoms of COVID-19 include consolidation, reticular pattern, crazy paving pattern, and ground glass opacities. Patients with COVID-19 showed emerging atypical CT symptoms, such as pleural alterations, fibrosis, nodules, and airway changes^[10] In our study, the typical features studied included ground glass opacification, subpleural lines, consolidatory changes, crazy paving. Atypical features such as traction bronchiectasis was seen in 6 patients (7%) in our study.^[10,11]

According to the study by Reshad et al.^[12] a significant number of the COVID 19 patients with comorbidities who were hospitalised and admitted to the ICU were found to be diabetic. As a result, studies had suggested an association between COVID-19 and diabetic mellitus (DM). Additionally, a summary of the relationship between COVID-19 and diabetic patients was provided with DM having the potential to increase the severity of COVID-19 instances. Patients with diabetes experience various related issues such as a weakened immune system, a decreased virus clearance rate, abnormal metabolic activity, and elevated blood glucose levels. This does not make the patients more likely to get COVID-19 infection. However, the comorbidity of DM can make COVID-19 more severe.^[12]

Similar understanding can be seen in the present study where diabetic patients tended to have higher severity on HR CT, more variety of CT morphological features of COVID-19.

Jdiaa et al.^[13] analyzed 69 systematic reviews and 66 primary studies to determine the impact of chronic kidney disease (CKD) on acquiring COVID-19, hospitalization, mortality, and disease severity. The prevalence of CKD among COVID-19 patients was reported in 28 reviews and ranged from 0.4 to 49.0%. In one systematic analysis, patients with CKD and COVID-19 had a higher chance of being hospitalized (RR = 1.63, 95% CI 1.03-2.58). (Moderate certainty). Additionally, primary research revealed a statistically significant rise in hospitalizations among these patients. 37 systematic reviews evaluated the mortality risk in CKD and COVID-19 individuals. A HR of 1.48 (95% CI 1.33-1.65), an OR of 1.77 (95% CI 1.54-2.02), and an RR of 1.6 (95% CI 0.88-2.92) were the pooled values from primary studies for mortality in patients with CKD and COVID-19. The study emphasises the association between CKD and the poor COVID-19 outcomes, highlighting the significance of developing preventative measures for COVID-19 infection in CKD patients.^[13]

There were 12 chronic kidney disease (CKD) patients (23.52%) in the immunocompromised group of patients in our study. Of them, 8 patients (66.66%) had moderate CT severity followed by 2 patients (16.66%) who had severe CT changes. Only 1 patient had mild disease. This is in

agreement with the study done by Jdiaa et al.

Shirani et al.^[14] introduced typical & atypical CT features of COVID-19 pneumonia. The main differential diagnosis were discussed. The most frequent symptom of corona pneumonia (40–83%) is the ground virus glass opacification with the bilateral lower lobes being the most commonly affected. The reverse halo sign (also known as Atoll sign) is assumed to be secondary to disease progression, which can consequently result in the development of consolidation around GGO. This may also result in the absorption of the lesion with consequent decreased central density. There were several different imaging abnormalities in this viral pneumonia, however, pathognomonic imaging findings for COVID-19 pneumonia were not found.^[14]

Similarly in our study the most frequent CT feature was ground glass opacification predominantly involving the bilateral lower lobes. Reverse halo sign was seen only in 2 cases of which 1 showed progression form moderate to severe form upon follow up.

Limitations

The predominant immunocompromising conditions in the current study were diabetes mellitus and chronic kidney disease. Patients with various other conditions causing immunosuppression such as organ transplantation and cancer chemotherapy could not be studied as they were beyond the catchment area of the hospital. More studies including other such patients must be carried out to understand the effects of immunosuppression on Corona virus pneumonia.

The CT severity score is a semi-quantitative scoring system, therefore, there is some degree of scope for subjective bias.

Conclusion

HRCT chest demonstrates various typical lung features of the corona virus pneumonia such a ground glassing, crazy pavement, consolidation, reverse halo along with few atypical features and complications with excellent spatial resolution. There is bilateral pulmonary involvement with lower lobe predominance. Ground glassing, followed by subpleural lines were the most frequent CT features in our current study.

CT severity score is a semi-quantitative scoring system to determine the severity of the corona virus disease on HRCT chest.

Patients with immunosuppressing conditions such as diabetes mellitus and chronic kidney disease had significantly more severe CT scores as compared to patients with no such background.

Immunosuppressed patients are at higher risk for more severe corona virus disease and complications such as pneumothorax and pneumomediastinum. High Resolution CT is an important imaging modality to determine the disease extent and severity. Prioritizing those patients who have COVID-19 and immunosuppression is crucial since the severity of HRCT results has been shown to be higher in these patients.

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