





Chest HRCT Assessment of COVID-19 Patients in Vaccinated versus Nonvaccinated Patients: A Comparative Study in a Tertiary Care Hospital

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Abstract

Keywords

- computed tomography severity score
- ► COVID-19
- delta variant
- herd immunity
- ► high-resolution computed tomography
- vaccine

Coronavirus disease 2019 (COVID-19) has turned out to be the most devastating viral disease that the world has encountered for the past century. The World Health Organization (WHO) declared it a pandemic on March 11, 2020. The disease mainly spreads through respiratory droplets which makes social distancing a primary tool of prevention. Many variant strains have emerged up since the pandemic started and the Delta variant is responsible for recent surge of cases in second wave of COVID-19 in India. Mass vaccination is the most efficacious precautionary measure that can be applied to stop the transmission and generate herd immunity. Vaccination does not give 100% prevention from infection, but it halts the severity of infection. Vaccine is the boon amidst the mayhem. Our study highlights that those vaccinated (particularly two doses) had clinically mild symptoms and mild computed tomography severity score (CTSS) with a speedy recovery. Those unvaccinated had moderate to severe symptoms with moderate to severe CTSS (>8) often requiring hospital admission and having poor prognosis. Thus, vaccine helps reduce the health burden of the already strained health care system. Immunization visit can also be used as an opportunity to disseminate message to encourage behavior, to reduce transmission risk of COVID-19 virus, to identify the signs and symptoms of disease, and to provide guidance on what to do.

Introduction

Coronavirus disease 2019 (COVID-19) has turned out to be the most cataclysmic viral disease that the world has encountered for the past century. The disease was first notified in December 2019 in Wuhan, China. The World Health Organization (WHO) proclaimed it a Public Health Emergency of International Concern on January 30, 2020, and later declared a pandemic on March 11, 2020. The apex case of COVID-19 in India was reported on January 30, 2020.²

The disease is mainly transmitted via the respiratory route when people inhale droplets and particles that the

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infected people release while breathing, talking, coughing, sneezing, or singing. Infected people are more likely to transmit COVID-19 when they are in close physical contact, which makes social distancing as one of the important preventive measure in controlling the spread of the virus. High-grade fever with dry cough and tiredness were the common prodrome at starting but in the past 1 year, many atypical symptoms were seen which may be the presenting complaint.³ These can be aches and pains, sore throat, diarrhea, conjunctivitis, headache, loss of taste or smell, and abdominal pain. People having existing comorbidities such as diabetes mellitus, hypertension, heart disease, and chronic obstructive pulmonary disease (COPD) have increased risk of severe ailment.

Generally, every symptomatic patient has to undergo a computed tomography (CT) scan to see the pattern and severity of lungs involvement. On high-resolution CT (HRCT), the common finding is ground-glass opacity (GGO) and consolidation being the next common.

The different pattern of virulence may be due to its rapidly mutating ability and forming different strains. Many variant strains have emerged up since the pandemic started and delta variant responsible for recent surge in cases in second wave of COVID-19 in India.⁴ Mass vaccination is the most efficacious precautionary measure that can be applied to stop the transmission and generate herd immunity.⁵ So far in India, we have mainly Covishield and Covaxin vaccines which are authorized by the government both having almost equal efficacy.⁶ Other vaccine which has been recently authorized is Sputnik V vaccine. Vaccination does not give 100% prevention from infection, but it halts the austerity of infection⁵ and according to recent statistical data released in June 2021, India stands 16th among 30 most populous countries of world with 18.9% people vaccinated per 100%⁷ and according to data released on 15 January by Ministry of Health and Family Welfare, India has administered 1.56 billion doses (including first, second, and precautionary doses) accounting to 64% of total vaccinated population, so the need of hour is to increase rate of vaccination.

Purpose of Our Study

Due to lower rate of vaccination in India despite efficient vaccines for COVID-19 with promising herd immunity and encouraging results, we here provide a substantial evidence of effectiveness of vaccination on severity of disease and clinical outcome.

Materials and Methods

This study was done at the Department of Radiodiagnosis, SMS Hospital, Jaipur. This was a cross-sectional type of observational study. Since prevalence and incidence of disease have not been established, so all patients underwent chest HRCT imaging for COVID-19 swab positivity during the specified period of our study, which included 670 patients (150 vaccinated and 520 nonvaccinated). Random sampling technique was used. Written informed consent was taken

from all patients. Permission was taken from institutional ethical committee before conducting the study. Data collection was done from 15 April to 10 May. The equipment used was 128 slice Philips CT machine. Pretested, predesigned, and semistructured proforma were used to collect data. Reverse transcriptase–polymerase chain reaction (RT-PCR)positive patients whether vaccinated or nonvaccinated were included. RT-PCR-negative patients were excluded.

Data Collection

We retrospectively collected the clinical and chest imaging data. This included epidemiological data, vaccination status, comorbidities of patients, CT chest characteristics such as pattern of involvement and CT severity score (CTSS). After collection of all required data, the clinical data of laboratory confirmed patients were compiled and tabulated. The diagnosis of COVID-19 was made by positive RT-PCR samples of nasal and throat swab, which was based on the WHO interim guidance. The epidemiological data (age and sex) were recorded and clinical data, inclusive of comorbidities, were obtained. All 670 patients underwent a CT scan of the chest and the pattern of involvement and CTSS were obtained.

Review of CT Images

Thin section (0.625 mm) CT images were acquired on a 128-slice Ingenia machine. The CT images were assessed for the presence of ground-glass haziness (seen as increased attenuation with visible bronchovascular markings) and consolidation (increased attenuation of air space opacification).

CT findings were overall classified as typical, indeterminate, atypical, or negative for COVID-19 pneumonia on CT. Typical features were those that are reported in the literature to be frequently and more specifically in COVID-19 pneumonia such as bilateral, peripheral GGOs with or without consolidation, or crazy paving. Indeterminate features were those like multifocal, diffuse, central, or unilateral GGOs. Atypical features were those that are reported to be uncommon or not occurring in COVID-19 pneumonia such as consolidation without GGOs or cavitation or pleural effusion. Negative for pneumonia means that there are no lung parenchymal abnormalities that can be attributed to

The severity score was calculated based on lung parenchymal involvement. The percentage of each lobe involvement was seen individually and a score from 1 to 5 was given where

- 1: Representing less than 5% lobar involvement
- 2: 5 to 25% lobar involvement
- 3: 26 to 50% lobar involvement
- 4: 51 to 75% lobar involvement
- 5: > 75% lobar involvement.

Then, the final score will be given out of 25 by addition of individual lobar scores.8

The acquired HRCT images were read by two radiologists who were blinded for the vaccinated status. The interobserver reliability using Cronbach's alpha was 0.997(95% confidence interval [CI]: 0.995-0.998).

Nonvaccinated (N) Percentage Vaccinated Percentage Total Age in y <40 35 77.8 10 22.2 45 41-50 140 63.6 80 36.4 220 51-60 103 77.4 30 22.6 133 61-70 242 89.0 30 11.0 272 Total 520 77.6 150 22.4 670 Chi-square test = 44.929; df = 3; p < 0.001; highly significant

Table 1 Table showing percentage of age distribution among vaccinated and nonvaccinated patients

Abbreviation: COVID-19, coronavirus disease 2019.

Statistical Analysis

The study data were analyzed using SPSS software. Tables and pie charts were used wherever needed.

Results

A retrospective comparative analysis of 670 RT-PCR COVID-19-positive patients were evaluated for their clinical data, vaccination status, and HRCT findings to determine the severity of disease with respect to vaccination status of the patient and thereby determining the prognostic capability of chest HRCT in management of patient. A total of 670 patients were included in our study (excluding the patients with unknown vaccination status and negative RT-PCR status) from 15 April to 10 May among which 150 were vaccinated (103 patients received single dose and 47 received two doses of vaccine) (**Fig. 1**).

Most of the patients were in the fifth decade of age with average age being 58.2 years in vaccinated group and 55.6 in nonvaccinated group, which was highly statistically significant between the two groups (**Table 1**). Majority of the patients were males both in vaccinated group (56% males and 44% females) and in nonvaccinated group (58% males and 42% females). Out of 670 patients, 482 (72%) were symptomatic with most common symptoms being fever, cough, malaise among both groups. The average duration of symptoms in vaccinated group and nonvaccinated group was 5 and

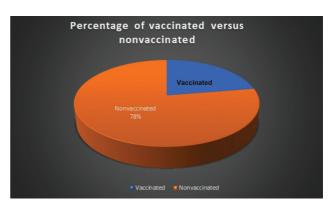


Fig. 1 Pie-chart depicting percentage of vaccinated versus non-vaccinated patients.

12 days, respectively. Among the vaccinated group, the most prevalent comorbidity was diabetes (52%), followed by hypertension (48%) and K-chest/COPD (14%), while in other group, most prevalent comorbidity was hypertension (30%), followed by diabetes (28%)and K-chest/COPD (7%). However, it did not show any significant difference between the two groups (**FTable 2**) (**Fig. 2**).

Among the 150 patients in vaccinated group, 83 (55%) had typical HRCT findings for COVID-19 pneumonia, indeterminate (unilateral) were 42 (28%), atypical 18 (12%), and negative 7 (4%). Among 520 nonvaccinated patients, 320 (61.5%) had typical findings, indeterminate were 83 (16%),

Table 2 Table showing percentage of comorbidities among vaccinated and nonvaccinated groups

Comorbidities		Vaccinated		Nonvaccinated		
DM		52		145		
HTN	HTN		76		156	
K-chest/COPD		21		36		
Others		8		62		
Comorbidities	Vaccina	ted Nonvaccin		nated Tota		
	N	Percentage	N	Percentage		
No	99	24.1	312	75.9	411	
Yes	51	19.7	208	80.3	259	
Total	150	22.4	520	77.6	670	
Chi-square test = 1.767; df = 1; p = 0.184; not significant						

Abbreviations: COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HTN, hypertension.

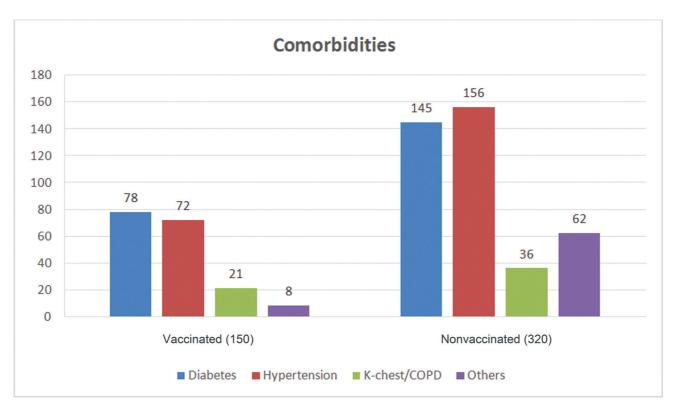


Fig. 2 Bar chart showing distribution of comorbidities among vaccinated and nonvaccinated groups.

Table 3 Table showing distribution of category of disease among vaccinated and nonvaccinated groups

HRCT	Vaccinated	Percentage	Nonvaccinated	Percentage
Negative	7	12.3	50	87.7
Typical	83	33.6	320	66.4
Atypical	18	21.2	67	78.8
Indeterminate	42	20.6	83	79.4
Total	150	22.4	520	77.6
Chi-square test = 13.212; df = 3; $p = 0.004$; significant				

Abbreviation: HRCT, high-resolution computed tomography.

atypical 67 (12.8%), and 50 (9.6%) were negative. There was statistically significant difference between the two groups (►Table 3) (►Fig. 3).

Typical COVID-19 findings on chest HRCT were divided based on CTSS into mild (<8), moderate (9–15), and severe (>15) (R). There were 320 typical COVID-19 patients in nonvaccinated group and 83 in vaccinated group, among which 75 (23.4%) and 29 (34.9%) had mild CTSS, respectively, which was statistically significant (>Table 4). Similarly, 111 (34.6%) and 19 (22.8%) had severe CTSS among nonvaccinated and vaccinated groups, respectively, showing statistical significance (►Fig. 4).

Predominant pattern of chest HRCT findings in vaccinated group was GGOs (55.4%) and in nonvaccinated group was consolidation (78.1%). There was statistically significant difference between two groups (►Table 7) (►Fig. 5).

The involvement of opacities with respect to lung fields was predominantly peripheral (52%) in vaccinated group and involving both central and peripheral regions (56%) in nonvaccinated patients. There was statistically significant difference between the two groups (►Table 6) (►Fig. 6).

Forty-two patients in vaccinated group showed unilateral involvement of lung in comparison to 83 patients in nonvaccinated group which was statistically significant (**Table 8**). Among the vaccinated group, comparison of severity of disease between those who received single shot with those who received two doses of vaccine was done. There was statistically significant difference between the two groups with majority of mild CTSS (56.4%) in those who received two doses and moderate score (45.3%) in those who had a single shot (►**Table 5**) (►**Fig. 7**).

Discussion

Coronaviruses (CoVs) are a large group of viruses that cause illness ranging from common cold to more severe diseases

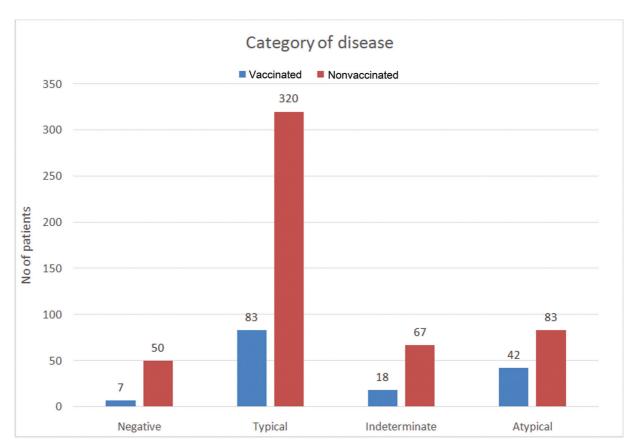


Fig. 3 Bar chart showing distribution of category of disease among vaccinated and nonvaccinated groups.

Table 4 Table showing distribution of severity of disease among vaccinated and nonvaccinated groups

HRCT	Vaccinated	Percentage	Nonvaccinated	Percentage
Mild (CTSS <8)	29	27.6	76	72.4
Moderate (8–15)	35	26.1	99	74.9
Severe (>15)	19	11.6	145	88.4
Total	83	20.6	320	79.4
Chi-square test = 13.809; df = 2; $p = 0.001$; significant				

Abbreviations: CTSS, computed tomography severity score; HRCT, high-resolution computed tomography.

Table 5 Table showing statistical significance among single dose and double dose in vaccinated group

HRCT	Vaccin	Statistical	
	One dose Two doses		significance
Negative	3	4	
Mild	15	14	p < 0.05
Moderate	29	6	p < 0.05
Severe	17	2	p < 0.05

Abbreviation: HRCT, high-resolution computed tomography.

such as Middle East respiratory syndrome (MERS-CoV) and severe acute respiratory syndrome (SARS-CoV). A novel CoV/COVID-19 is a new strain that has not been previously identified in humans. In March 2020, the WHO declared the COVID-19 outbreak as "pandemic." ¹

The first pandemic wave of COVID-19 in India started in mid-March 2020 which lasted for 3 months causing health crisis and challenging health care system and thereby requiring social distancing, home confinement, and strict lockdown. Being it the menacing disease which caused alarming number of casualties, the only way to incarcerate it was through creation of herd immunity by effective vaccination. India began its vaccination drive on January 16, 2021, after nearly 1 year of first reported case. However, by early April 2021, a major second wave of infections took hold of the country: on April 9, India surpassed 1 million active cases, and by April 12, India overtook Brazil becoming the second-most COVID-19-affected country worldwide. Multiple factors have been put forward to have potentially contributed to the spike in cases, including highly infectious variants of concern such as lineage B.1.617 and lack of preparations as temporary hospitals were dismantled after

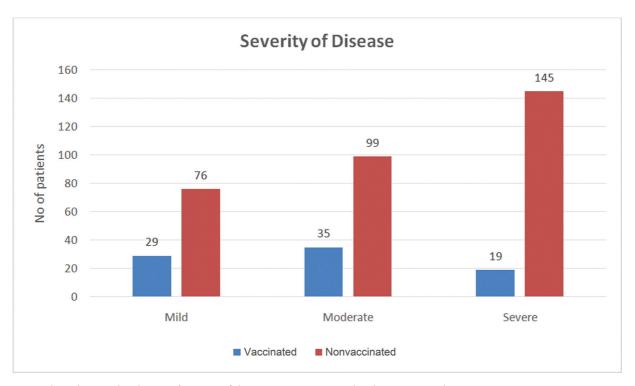


Fig. 4 Bar chart showing distribution of severity of disease among vaccinated and nonvaccinated groups.

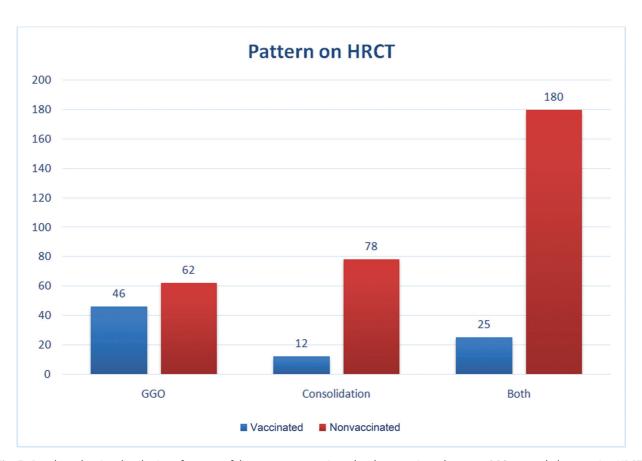


Fig. 5 Bar chart showing distribution of pattern of disease among vaccinated and nonvaccinated groups. GGO, ground-glass opacity; HRCT, high-resolution computed tomography.

Table 6 Table showing distribution of lung involvement among vaccinated and nonvaccinated groups

HRCT	Vaccinated (83)	Nonvaccinated (320)	
Hilar	8	51	
Peripheral	43	90	
Diffuse	32	179	
Chi-square test = 7.628; df = 1; $p = 0.006$; significant			

Abbreviation: HRCT, high-resolution computed tomography.

cases started to decline, new facilities were not built, and health and safety precautions were poorly implemented during weddings, festivals, sports events, state and local elections, and in public places.²

Simultaneously, vaccine trials and efficacy were tested by various virology laboratories. Two versions of the vaccine—produced by AstraZeneca-SKBio (Republic of Korea) and the Serum Institute of India—have been granted emergency use by WHO. When the vaccine underwent SAGE consideration,

it had undergone analysis by the European Medicines Agency (EMA). The EMA has rigorously evaluated the data on the quality, safety, and efficacy of the vaccine and has recommended granting marketing authorization for people aged 18 and older. The Covishield vaccine against COVID-19 has an efficacy of 88% against symptomatic SARS-CoV-2 infection. Longer dose intervals within the 8 to 12 weeks range are associated with greater vaccine efficacy. SAGE currently recommends the use of AZD1222 vaccine according to the WHO Prioritization Roadmap, even if virus variants are present in a country. No substantive data are available related to impact of AZD1222 on transmission or viral shedding. In the meantime, we must sustain and build public health measures that work: masking, social distancing, handwashing, respiratory and cough hygiene, avoiding gathering, and ensuring good ventilation. As of April 19, 2021, the AstraZeneca vaccine is safe and efficacious at safe-guarding people from the extremely serious perils of COVID-19, including death, hospitalization, and severe disease. The vaccine is not recommended for persons younger than 18 years. The recommended dosage being two doses given

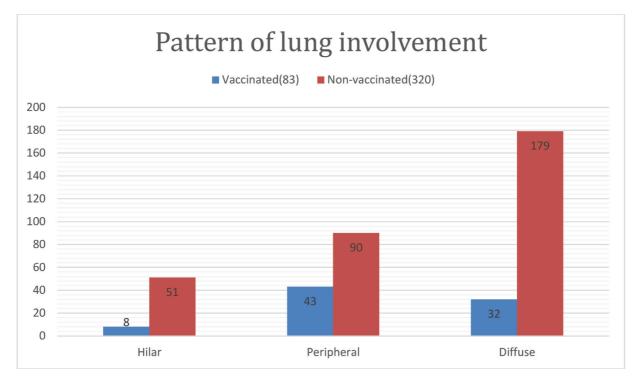


Fig. 6 Bar chart showing pattern of lung involvement among vaccinated and nonvaccinated groups.

Table 7 Table showing percentage of pattern on HRCT among vaccinated and nonvaccinated groups

Pattern on HRCT	Vaccinated	Percentage	Nonvaccinated	Percentage
GGO	46	42.2	62	57.8
Consolidation	12	13.3	78	86.7
Both	25	12.3	180	87.7
Total	83	20.6	320	79.4
Chi-square test = 42.695; df = 2; $p < 0.001$; highly significant				

Abbreviations: GGO, ground-glass opacity; HRCT, high-resolution computed tomography.

Table 8 Comparison of chest HRCT patterns between both the groups

CT features	Vaccinated	Nonvaccinated		
Opacity distribution (axial)				
Central	8	51		
Peripheral	43	90		
Both	32	179		
GGO and consolidation				
GGO present	46	62		
Consolidation present	12	78		
GGO and consolidation both present	25	180		
Unilateral involvement	42	83 (p < 0.05)		
Bilateral involvement	83	320		
CT severity score				
Mild (<8)	29	75 (<i>p</i> < 0.05)		
Moderate (8–15)	35	99		
Severe (>15)	19	111 (p < 0.05)		

Abbreviations: CT, computed tomography; GGO, ground-glass opacity; HRCT, high-resolution computed tomography.

intramuscularly (0.5 mL each) with a gap of 8 to 12 weeks, additional research is needed to understand longer term potential protection after a single dose.9

Our study included 670 RT-PCR confirmed COVID-19 patients who visited SMS Hospital, Jaipur for COVID-19related symptoms. In the present study, an attempt was

made to evaluate demographic data, vaccination status, comorbidities, and chest HRCT findings in these patients.

Patients included in vaccinated group were those who received either a single dose or two doses of vaccine (irrespective of type of vaccine either being Covishield or Covaxin) and compared it with the nonvaccinated group in terms of severity and pattern of lung involvement. There were 150 patients who were vaccinated and 520 patients who were unvaccinated. We included patients of all age groups excluding the pediatric age group, majority of them were in the fifth decade of life. Greater number of patients were males with a sex ratio of male:female 1.27 in vaccinated group and 1.39 in nonvaccinated group. Among vaccinated group, larger number of patients were asymptomatic or had mild symptoms such as fever and cough and those in nonvaccinated group had moderate to severe symptoms ranging from cough, malaise, to breathlessness. We also found that there were few cases who were asymptomatic (12%) but had positive HRCT findings for COVID-19, thereby highlighting the importance of radiological diagnosis more superior for crucial patient management as they are major source of disease spread to susceptible population. Comorbidities on the other hand played a role of catalyst in both disease morbidity and mortality. The most common comorbidity observed in vaccinated group was diabetes (found in 52% of patients) and hypertension (30%) in nonvaccinated group. Those patients having multiple comorbidities had poor prognosis which necessitated for hospital admission, oxygen therapy, and steroid administration.

In India, diagnosis of COVID-19 pneumonia is majorly clinical and confirmed by SARS-CoV-2 nucleic acid RT-PCR. However, the sensitivity of chest HRCT is greater than RT-

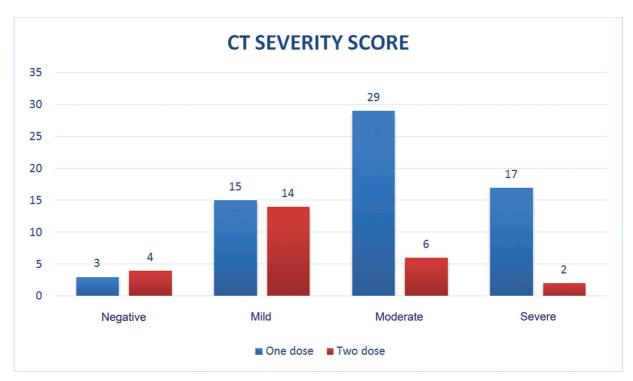


Fig. 7 Bar chart showing distribution of severity of disease among single dose and double dose of vaccinated groups.

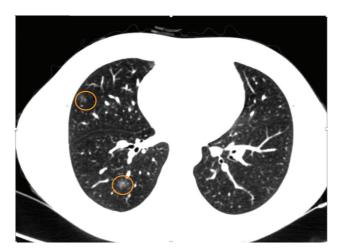


Fig. 8 Axial section of chest HRCT of a 49-year-old fully vaccinated (two doses) male patient RT-PCR positive shows subtle patches of ground-glass opacities in right middle and lower lobes suggesting indeterminate for COVID-19 pneumonia (unilateral involvement) with CTSS 3 (mild). COVID-19, coronavirus disease 2019; CTSS, computed tomography severity score; HRCT, high-resolution computed tomography; RT-PCR, reverse transcriptase–polymerase chain reaction.

PCR for diagnosis of COVID-19.¹⁰ The characteristic chest CT findings in COVID-19 is bilateral GGOs predominantly peripheral and basal in distribution. The Radiological Society of North America Expert Consensus proposed four categories for reporting CT imaging findings potentially attributable to COVID-19 each with suggested standardized language. Typical appearance designates commonly reported features of greater specificity for COVID-19 pneumonia. Indeterminate appearance indicates nonspecific imaging features in absence of typical features. Atypical appearance incorporates uncommonly reported or unrelated imaging features of COVID-19 pneumonia.⁸



Fig. 10 A 36-year-old female patient known hypertensive presented with complaints of fever, breathlessness who was unvaccinated. Coronal section of chest HRCT shows ground-glass opacities involving both lungs extensively with sparing of apical segments of both upper lobes suggesting typical for COVID-19 pneumonia (CTSS 21 [severe]). COVID-19, coronavirus disease 2019; CTSS, computed tomography severity score; HRCT, high-resolution computed tomography.

Our study depicted varied appearances of CT findings including typical GGO only (**Fig. 8**), mixed pattern of both GGO and consolidation (**Fig. 9**), typical bilateral peripheral involvement, both hilar and peripheral involvements, bilateral whiteout lungs (**Fig. 10**), unilateral GGO/mixed pattern of GGO and consolidation, atypical findings such as lobar pneumonia, pleural effusion, tree-in-bud opacities, centrilobular nodules, cavitation, and centrilobular/paraseptal emphysematous changes. Initial

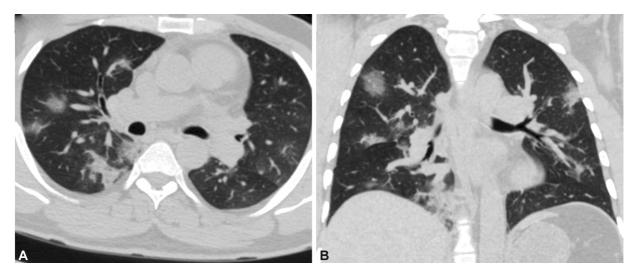


Fig. 9 (A, B) A 53-year-old male patient known case of type II diabetes mellitus who was vaccinated with single dose of Covaxin vaccine presented with fever, fatigue, and cough for 7 days was advised chest HRCT which reveals areas of ground-glass opacities in right upper, middle, lower, and left lower lobes with few areas of consolidation in right lower lobe suggesting typical for COVID-19 pneumonia (CTSS 9 [moderate]). COVID-19, coronavirus disease 2019; CTSS, computed tomography severity score; HRCT, high-resolution computed tomography.

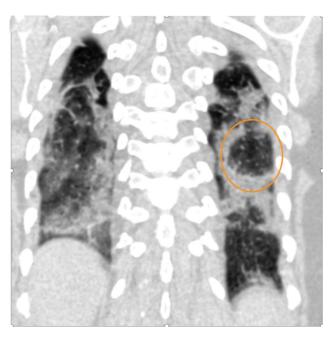


Fig. 11 Coronal section of chest HRCT of a 56-year-old male patient unvaccinated for COVID-19 shows bilateral ground-glass opacities with areas of consolidation with "reverse halo sign or atoll sign" in left lower lobe. COVID-19, coronavirus disease 2019; HRCT, high-resolution computed tomography.

days of illness showed GGO which later progresses to consolidation, vacuolation, reverse halo sign (atoll sign) (>Fig. 11), linear bands (>Fig. 12), and subpleural sparing which indicated organizing phase of the disease with corresponding clinical improvement.

Majority of symptomatic patients had positive HRCT findings for COVID-19 pneumonia and it well correlated with the CTSS. The average CTSS in vaccinated group was 4.5 and 13.8 in nonvaccinated group. Vaccinated group comparatively had mild symptoms, CTSS (<8), less duration of symptoms (average 5 days), and less hospital stay with speedy recovery. On the other hand, nonvaccinated group had moderate to severe symptoms, higher CTSS, longer duration of symptoms (12 days) with longer duration of hospital stay (even requiring intensive care unit admission) having significant morbidity and mortality.

Statistically significant difference between vaccinated and nonvaccinated groups was indeterminate imaging findings in vaccinated group on HRCT (unilateral involvement) and former group having mild CTSS (<8) while no statistical difference was jotted down with regard to pattern of involvement and lobe distribution.

HRCT findings in vaccinated group were predominantly GGO (55%) which were peripheral in distribution (52%), whereas primary pattern of involvement in nonvaccinated group was amalgamation of both GGO and consolidation (56%) having both hilar and peripheral distribution pattern (56%).

Those who received both the doses of vaccine were relatively asymptomatic or had mild symptoms with majority having mild CTSS (<8) compared with those who received single dose of vaccine (p < 0.05).



Fig. 12 Axial section of chest HRCT of a fully vaccinated patient aged 34 years shows areas of consolidation in bilateral lower lobes with subpleural sparing and linear bands. HRCT, high-resolution computed tomography.

Majority of the chest X-rays done early in the disease were near normal (and with the known fact that chest X-ray carries a lower sensitivity in detection of COVID-19 pneumonia) and the overall chest X-rays were quite less in number compared with the chest HRCT performed, so correlation was not possible.

Major limitations of the study included absence of followup of all patients, lesser study duration.

Conclusion

The life-threatening complications of COVID-19 pneumonia is devastating, thus effective vaccination is one of the way to contain the spread of disease, reduce severity, and associated mortality. Vaccine is the boon amidst the mayhem. Our study highlights that those vaccinated (particularly two doses) have clinically mild symptoms and mild CTSS with a speedy recovery. Those unvaccinated had moderate to severe symptoms with moderate to severe CTSS (>8) who often required hospital admission accompanied with poor prognosis, so to conclude, the lung parenchymal involvement was comparatively higher in nonvaccinated group than vaccinated group. 11 Thus, vaccine helps reduce the health burden of the already strained health care system. Immunization visit can also be used as an opportunity to disseminate message to encourage behavior, to reduce transmission risk of COVID-19 virus, to identify the signs and symptoms of disease, and to provide guidance on what to do.

Conflict of Interest None declared.

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