

Association of Chest CT Severity Scores and Vaccination Status in COVID-19 Infection: A Cross-sectional Study

TT VISHWANATH¹, BR RAJALAKSHMI², KS SADANANDA³, CN MANJUNATH⁴

ABSTRACT

Introduction: Coronavirus Disease-2019 (COVID-19) has emerged as a pandemic with substantial morbidity and mortality. While global efforts towards mitigating the infection are focused on the vaccination of population, studies are warranted to prove the efficacy of vaccine in prevention of infection or reducing the severity of infection in affected patients. The 25-point High Resolution Computed Tomography (HRCT) severity score has proved to be an effective tool in estimating the severity of lung infection and correlates with laboratory parameters and disease outcome. The HRCT scores hence provide an objective evidence to prove the efficacy of vaccines in vaccinated individuals by assessing the extent of lung involvement.

Aim: To compare the chest CT severity score in vaccinated and unvaccinated COVID-19 infected patients.

Materials and Methods: This cross-sectional study was conducted in the Department of Radiology, at Sri Jayadeva Institute of Cardiovascular Sciences and Research, Mysuru, Karnataka, India. The data of HRCT scores and vaccination status was collected during the month of April 2021 from patients who were suspected to have COVID-19 infection and underwent a chest HRCT scan. The severity of lung infection in vaccinated and unvaccinated individuals were compared based on the HRCT scores and the association between these variables were

analysed. The association between the respective variables were studied using Fisher's-exact and Kruskal-Wallis tests.

Results: The study involved a total of 178 subjects (males were 98), where 127 (71.3%) were unvaccinated and 51 (28.6%) were vaccinated with one or both doses {Covaxin (Bharat Biotech) vaccine or Covishield (Oxford-AstraZeneca) vaccine approved by Emergency Use Authorisation (EUA)}. The frequency of disease was least in 14 (7.9%) among fully vaccinated subjects. Severe COVID-19 associated pneumonia with severity score of 18 or more was seen in 7% of unvaccinated individuals, while none of the partial/fully vaccinated individuals had severe disease. The median CT severity score was significantly higher among unvaccinated patients compared to partially and fully vaccinated patients (p -value=0.001). Fully vaccinated patients had almost low CT severity score indicating mild form of disease.

Conclusion: To the best of authors knowledge, this study was the first to describe the chest CT severity scores of vaccinated individuals in comparison with the unvaccinated COVID-19 infected patients. The disease severity was significantly higher among unvaccinated patients compared to partially or fully vaccinated patients. The present study has provided substantial evidence of vaccine efficacy in reducing the disease severity in COVID-19 infected patients.

Keywords: Coronavirus disease-2019, Computed tomography, Infection, Lung damage, Pandemic, Vaccine efficacy

INTRODUCTION

Coronavirus Disease-2019 (COVID-19) is a pandemic caused by a strain of coronavirus {Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2)} ranging from mild clinical course to severe COVID-19 pneumonia with or without Acute Respiratory Distress Syndrome (ARDS) [1-3]. Measuring the extent and severity of pulmonary involvement in COVID-19 pneumonia is possible by High Resolution Computed Tomography (HRCT) scan of lung. The clinical severity of COVID-19 infection has correlated well with 25-point HRCT score. Recent data has suggested that chest Computed Tomography (CT) score can predict the outcome of COVID-19 disease and also correlates significantly with laboratory parameters and oxygen requirements [4,5]. The use of chest HRCT has been advised by the World Health Organisation (WHO) as part of diagnostic workup of COVID-19 disease whenever Reverse Transcription-Polymerase Chain Reaction (RT-PCR) testing is not available; in case of delayed test results or in suspected cases with initial negative RT-PCR test result [4]. The current global strategies are focused on prevention of viral transmission by maintaining social distance, use of masks and promotion of mass vaccination.

Vaccines act by two main mechanisms. They can prevent infection occurring entirely or they can halt the progression to symptomatic disease after infection occurs [6]. Though the effectiveness of

vaccine has been studied by vaccine trials prior to public use, much of its efficacy can be definitively assessed in patients infected by COVID-19 in postvaccination phase, whether vaccines are effective in preventing infection or are beneficial in reducing the disease severity, thereby preventing mortality. Considering the usefulness of HRCT scores in evaluating the severity of lung involvement, the objectives of the study were, to evaluate the severity of lung involvement in COVID-19 infection through HRCT scan and to compare the chest CT severity score in vaccinated and unvaccinated COVID-19 patients.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of Radiology, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Mysuru, Karnataka, India. The data was collected in the month of April 2021 during the second peak of COVID-19 pandemic, from patients who were suspected to have COVID-19 infection and underwent a chest HRCT scan in the Department of Radiology, after obtaining clearance from Institutional Ethical Committee.

Inclusion criteria

1. Clinically suspected symptomatic COVID-19 patients (having one or more of the following: fever, sore throat, cough and shortness of breath) who underwent screening HRCT irrespective of RT-PCR test result.

2. Clinically suspected asymptomatic COVID-19 patients who underwent screening HRCT with positive RT-PCR test result.

Exclusion criteria

1. Suspected asymptomatic patients of COVID-19 infection with negative RT-PCR result and normal screening HRCT scan.
2. Suspected symptomatic/RT-PCR positive cases with normal HRCT scan within 6 days of illness.

Procedure

In accordance with the inclusion and exclusion criteria, 178 patients were included in the study. The information about the real-time Reverse Transcription-Polymerase Chain Reaction (RT-PCR) test result and vaccination status was collected using a proforma. All patients underwent chest HRCT examination at Sri Jayadeva Institute of Cardiovascular Sciences using Philips 128 slice CT scanner. Patients were placed in a supine position and with single breath hold scanning was performed. Sagittal and coronal reformatted images were subsequently obtained. Scanning parameters were as follows: scan direction (craniocaudal), tube voltage (120kV), tube current (251 mA), slice collimation (64x0.625), no contrast material was used. The results for the chest HRCT images were collected and evaluated using the Picture Archiving and Communication Systems (PACS).

HRCT image analysis: A Radiologist with more than 12 years of experience evaluated the CT images to determine the disease severity score (CO-RAD Score- Coronavirus disease-2019 Reporting and Data System) in each patient. The scans were first assessed whether negative or positive for typical findings of COVID-19 pneumonia (bilateral, multilobe, posterior peripheral ground-glass opacities) [4]. Severity was assessed using the 25 point scoring system through visual assessment of each lobe involved.

The severity of lung involvement was assessed using the following scoring system depending on the visual assessment of each lobe involved. The scores of 1 to 5 were assigned for lung involvement of <5%, 5%-25%, 26%-49%, 50%-75% and >75%, respectively. The sum of the lobar scores indicates the overall severity [7]:

- Mild disease with score ≤7
- Moderate disease with score 8-17
- Severe disease with total score ≥18

STATISTICAL ANALYSIS

The analysis was performed using Statistical Package for the Social Sciences (SPSS) version 21.0. Descriptive statistics of patient’s demographics details and vaccination status were reported as numbers and percentage. Frequencies of chest CT scores were calculated. The association between the respective variables were studied using Fisher’s-exact test and Kruskal-Wallis test.

RESULTS

Among 178 subjects included in the present study, majority of the study subjects were males 98 (55.1%) and 80 (44.9%) were females [Table/Fig-1].

Age group	Gender n (%)		Total n (%)
	Male	Female	
≤30	16 (66.7)	8 (33.3)	24 (13.5)
31-40	19 (48.7)	20 (51.3)	39 (21.9)
41-50	18 (52.9)	16 (47.1)	34 (19.1)
51-60	25 (50)	25 (50)	50 (28.1)
≥61	20 (64.5)	11 (35.5)	31 (17.4)
Total	98 (55.1)	80 (44.9)	178 (100)

[Table/Fig-1]: Age and gender wise distribution of study participants.

Majority 127 (71.3%) of the study subjects who were suffering from COVID-19 (clinically diagnosed and RT-PCR confirmed) were unvaccinated. The frequency of disease was least in 14 (7.9%) among fully vaccinated subjects, while 37 (20.8%) partially vaccinated subjects (taken atleast one dose of either of vaccine either Covishield or Covaxin approved by Emergency Use Authorisation (EUA) were suffering from the disease [Table/Fig-2].

Vaccination status	n	%
Unvaccinated	127	71.3%
Partially vaccinated (Covishield-31, Covaxin -6)	37	20.8%
Fully vaccinated (Covishield-13, Covaxin -1)	14	7.9%
Both partial and fully vaccinated	51	28.6%
Total	178	100%

[Table/Fig-2]: Distribution of study subjects based on the vaccination status.

Among 178 subjects included in the study, 139 (78.1%) were RT-PCR positive. Remaining 39 (21.9%) were clinically diagnosed with CT scan features suggestive of COVID-19 with median Coronavirus disease-2019 Reporting and Data System (CO-RADS) score of 6 [Table/Fig-3]. The RT-PCR negative cases were either symptomatic or showed CT findings suggestive of COVID-19 pneumonia. It can be observed that, there was no statistically significant association between RT-PCR positivity status and vaccination status of study subjects [Table/Fig-3]. This strengthens the hypothesis that, vaccination may not prevent the infection but has definite role in reducing the severity of the disease.

Vaccination	RT-PCR		Total	Chi-square	p-value
	Negative	Positive			
Unvaccinated	29 (22.8%)	98 (77.2%)	127 (71.3%)	0.569	0.562
Partially vaccinated	6 (16.2%)	31 (83.8%)	37 (20.8%)		
Fully vaccinated	4 (28.6%)	10 (71.4%)	14 (7.9%)		
Total	39 (21.9%)	139 (78.1%)	178 (100%)		

[Table/Fig-3]: Association between vaccination status and RT-PCR Positivity among study subjects. *Fischer’s-exact test

The HRCT scan showed no lung changes in 34 (19%) out of total 178 COVID cases. Among the remaining 144 cases, lung involvement was predominantly bilateral in 131 (91%) cases and peripheral in 120 (83.3%) cases. Both upper and lower lobes were involved in 88 (61.1%) cases out of 144 cases. The patterns of lung changes are depicted in [Table/Fig-4], showing ground glass densities in a majority of 136 out of 178 cases (76%).

CT findings	Number of cases	Percentage
Ground glass densities	136	76
Interstitial/septal thickening	110	62
Parenchymal/sub-pleural bands	81	45
Sub-segmental consolidation	55	31
Crazy paving pattern	13	7
No lung changes	34	19

[Table/Fig-4]: Spectrum of lung changes in High Resolution Computed Tomography (HRCT), n=178.

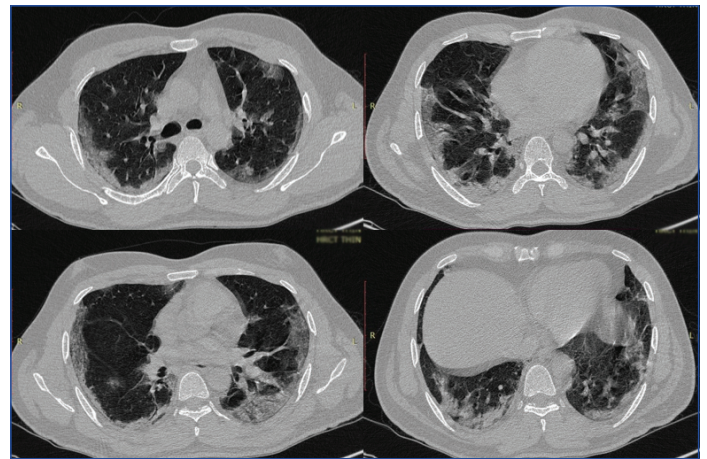
The study shows that severe COVID-19 associated pneumonia with CT severity score of 18 or more was seen in 7% of unvaccinated individuals, while none of the partial/fully vaccinated individuals had severe disease [Table/Fig-5]. The data [Table/Fig-6] also shows that median CT severity score was significantly higher among unvaccinated patients compared to partially and fully vaccinated patients. Fully vaccinated patients had almost nil CT severity score indicating milder form of disease. The corresponding lung changes of varying severity are shown in [Table/Fig-7-10].

Vaccination status	Number of cases	CT severity scores			
		Normal scan	Mild CT score 7 or less	Moderate CT score 8-17	Severe CT score 18 or more
Unvaccinated	127	14 (11%)	23 (18%)	81 (64%)	9 (7%)
Partially vaccinated	37	9 (24%)	11 (30%)	17 (46%)	0
Fully vaccinated	14	11 (79%)	2 (14%)	1 (7%)	0
Both partially and fully vaccinated	51	20 (39%)	13 (25%)	18 (35%)	0

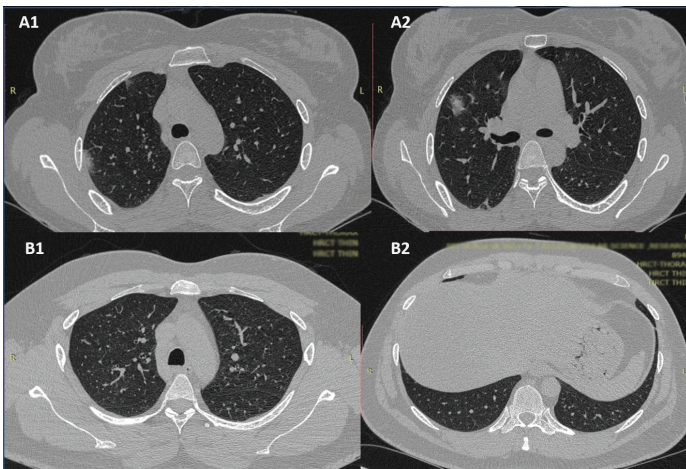
[Table/Fig-5]: CT severity scores in the study subjects.

Statistical measure	Unvaccinated	Partially vaccinated	Fully vaccinated	Chi-square	p-value
Median CT score	10	7	0	25.847	0.001
Interquartile range	6-14	1-11	0-1		

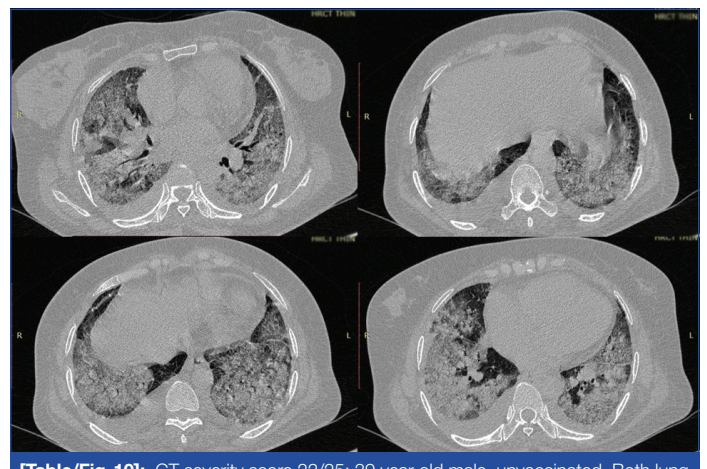
[Table/Fig-6]: Comparison of severity scores among unvaccinated, partially and fully vaccinated patients.
*Kruskal Wallis test



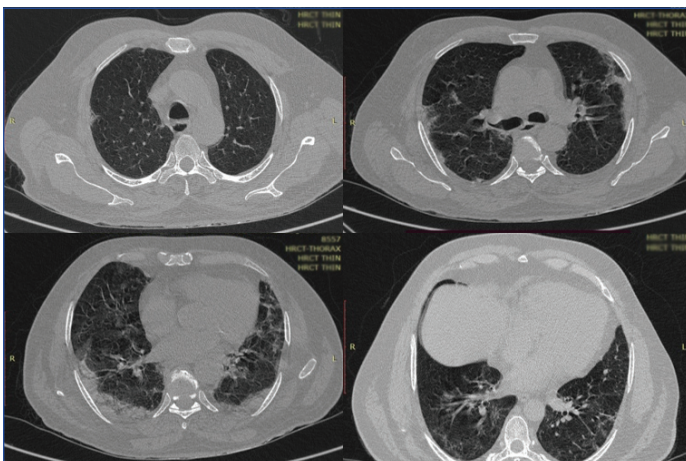
[Table/Fig-9]: CT severity score 14/25: 61 year old female, unvaccinated. Both lung parenchyma show areas of ground glass densities, crazy paving pattern, interstitial thickening and sub segmental consolidation, predominantly at sub pleural location and basal segments of both lower lobes, RT-PCR positive.



[Table/Fig-7]: A1, A2: CT severity score -3/25: 43 year old male fully vaccinated with two doses. CT scan shows small patchy areas of sub pleural ground glass densities, RT-PCR negative.
B1, B2: CT severity score 0/25: 54 year old male fully vaccinated with two doses of vaccine CT shows normal appearing both lung parenchyma, RT-PCR positive



[Table/Fig-10]: CT severity score 22/25: 39 year old male, unvaccinated. Both lung parenchyma show areas of ground glass densities with consolidation, predominantly at basal segments of both lower lobes, RT-PCR positive.



[Table/Fig-8]: CT severity score 10/25: 51 year old female partially vaccinated with one dose. Both lung parenchyma shows areas of ground glass densities with interstitial thickening and sub segmental consolidation, predominantly at sub pleural location, RT-PCR negative.

DISCUSSION

The HRCT of lung has been an effective imaging modality in the diagnosis of COVID-19 associated lung changes, being more sensitive than RT-PCR in suspected cases (98% vs 71%) and also to quantitate the extent of lung involvement in COVID-19 pneumonia [8]. Chest CT scan is used to screen for COVID-19 associated viral pneumonia in patients with clinical and epidemiologic features compatible with COVID-19 infection, particularly when results of RT-PCR tests are negative [9].

Various studies have obtained positive correlation of HRCT scores with other laboratory parameters of inflammatory markers and oxygen requirement in defining disease severity [4,5,8,10]. The extent of lung abnormalities detected at CT scan is maximum during days 6-11 of illness [11]. The lung changes detected by HRCT showed involvement of bilateral and multiple lobes in 91% of patients, with ground glass opacity [Table/Fig-4] being the most common pattern of lung infection. This is similar to the study by Salaffi F et al., where they found 90.9% showing bilateral lung involvement and 76.3% cases with ground glass opacities [8]. The study by Hafez MA has also showed ground glass opacities, bilateral lung involvement with peripheral and lower lobe predominance similar to our study [10].

The approximate RT-PCR test sensitivity for COVID-19 infection is reported to be around 50-62% [1]. The accuracy of RT-PCR results is affected by number of factors including the respiratory tract viral load, samples source and timing of samples acquisition. The RT-PCR positivity was 71.5% (123 out of 172) in a study by Al-Mosawe AM et al., [1], while in our study, 78.1% of study subjects were RT-PCR positive.

The frequency of disease in the present study was least in 14 (7.9%) of fully vaccinated subjects, compared to 127 (71.3%) unvaccinated COVID-19 infected patients. This is similar to the data by Hall VJ et al., in UK where they found 80 infected participants (3.8%) among vaccinated and 977 (38%) among unvaccinated healthcare workers [12]. The study also found 140 (14%) asymptomatic COVID-19 positive cases in the unvaccinated cohort, compared to 15 (19%) asymptomatic in the vaccinated cohort. A single dose of vaccine showed vaccine effectiveness of 70% (95% CI 55-85) after first dose and 85% (74-96) after two doses in the study population [12].

Hence, the beneficial role of single dose of vaccine can be inferred from our study as well, where majority were vaccinated with single dose, yet showing asymptomatic cases in 24% in vaccinated group, versus 11% in unvaccinated patients and no severe cases were documented in partially vaccinated group [Table/Fig-5].

Epidemiologists have opined that the threshold to achieve herd immunity is about 70% population protected by vaccination or previous infection. Accordingly, a one-dose strategy has been suggested as best for averting the most mortalities, but higher population immunity to prevent transmission will require a full course of two doses [6]. The present study corroborates these studies in proving the efficacy of vaccines in preventing disease severity.

The data in [Table/Fig-5] clearly shows that severe COVID-19 associated pneumonia with severity score of 18 or more was seen in 7% of unvaccinated individuals, while none of the partial/fully vaccinated individuals had severe disease, providing direct evidence on vaccine efficacy in reducing the severity of lung involvement. The incidence of moderate disease is noticed more in unvaccinated group (64%) compared to vaccinated (35%) group. A good number (39%) of vaccinated COVID-19 infected subjects showed no features of COVID-19 pneumonia with a normal CT scan, in contrast to only 11% of unvaccinated subjects. This will prove the hypothesis that vaccines are effective in preventing the disease progression and severity of infection [6]. Vaccines have a beneficial role in preventing lung damage and thereby reducing the morbidity and mortality associated with COVID-19 infection.

In SARS-CoV-2 immunity and Reinfection Evaluation (SIREN) study, 40% of the vaccinated SARS-CoV-2 infected patients reported typical COVID-19 symptoms compared with 63% in the unvaccinated group [6]. The study inferred that vaccinated subjects were less likely to progress symptomatic illness once infected, which is the second mechanism by which vaccines confer protection [6]. The study conducted in Christian Medical College, Vellore, showed that the risk of infection among fully vaccinated Healthcare Workers (HCW) was significantly lower compared to unvaccinated HCWs [13]. According to their study, the protective effect of vaccination in preventing infection, hospitalisation, need for oxygen and Intensive Care Unit (ICU) admission were 65%, 77%, 92% and 94%, respectively. Furthermore, subgroup analysis on the efficacy of the two vaccines was not possible as the number of Covaxin recipients were less, similar to the study by Victor PJ et al., [13].

Limitation(s)

The limitation of the present study is less number of fully vaccinated subjects were taken. Hence, studies involving more number of participants with two doses are warranted to support vaccine efficacy in prevention of disease severity. Also, as many of the patients in the present study could not remember the dates of vaccination because

of the rural background, the time interval between vaccination and HRCT could not be recorded for all the participants.

CONCLUSION(S)

Majority of COVID-19 diseased patients were unvaccinated, while the frequency of disease was least in fully vaccinated subjects, proving the protective effect of vaccine against infection. CT severity scores were significantly higher among unvaccinated patients compared to partially or fully vaccinated patients. Fully vaccinated patients showed mild form of disease and less frequency of lung involvement. HRCT must be used in the diagnosis of COVID-19 infection in suspected cases and useful in quantification of lung involvement, thereby giving substantial evidence of disease severity. The present study has proved that vaccines are beneficial in reducing the severity of lung involvement in COVID-19 infected patients. Vaccines have a definite beneficial role in flattening the epidemiological curve of COVID-19 pandemic and save the mankind.

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PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of Radiology, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Mysuru, Karnataka, India.
2. Associate Professor, Department of Pathology, JSS Medical College, Constituent College of JSS Academy of Higher Education and Research, Mysuru, Karnataka, India.
3. Professor, Department of Cardiology, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Mysuru, Karnataka, India.
4. Professor and Director, Department of Cardiology, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bangalore, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. B R Rajalakshmi,
Number 15, Block No. 8, First Stage, Jss Layout, Dr. Rajkumar Road,
Mysuru, Karnataka, India.
E-mail: dr.rajalakshmi2011@gmail.com

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