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Original Article

Radiology Section

Comparison of Severity of Lung Involvement between Vaccinated and Unvaccinated COVID-19 Patients Assessed using HRCT Scan of Thorax: A Cross-sectional Study

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ABSTRACT

Introduction: The Coronavirus Disease-2019 (COVID-19) pandemic, as we all know has wreaked havoc in many countries due to its high rate of infectivity. A High-Resolution Computed Tomography (HRCT) thorax scan is a must to determine the extent of lung involvement, which is helpful in further management.

Aim: To compare the severity of lung involvement in COVID-19 patients with double dose, single dose vaccinated and unvaccinated patients, and thus assess the role of vaccination in limiting the severity of lung involvement in infected patients.

Materials and Methods: This was cross-sectional study conducted on 244 patients in the Department of Radiology of Adichunchungiri Institute of Medical Sciences, Bellur, Karnataka, India. The patients were divided into three groups based on their vaccination status. Group A constituted patients who had received two doses of vaccine, group B constituted patients vaccinated with only one dose and group C constituted unvaccinated patients. The Computed Tomography Severity Index (CTSI) score of each patient was assessed. CTSI score of these three groups were compared to know the role of vaccine in preventing or limiting the severity of the disease. The chi-square test, Analysis of Variance (ANOVA) test and t-test were used to compare two means to compare two independent groups.

Results: The HRCT scans of a total of 244 patients (166 males and 78 females) were included in the study, analysed and divided into three groups. Group A (n=30) had patients with only mild CTSI score. Group B (n=34) had patients with both mild and moderate CTSI score. Group C (n=180) had patients with mild, moderate and severe CTSI scores. There were no patients with severe lung involvement in group A and group B. The mean CTSI scores in group A, B and C were 0.8, 7.2 and 9.3 respectively (p-value <0.001). Group A and B had less severe lung involvement in comparison to group C.

Conclusion: Complete vaccination is essential in preventing severe lung disease due to COVID-19 infection, and to limit complications and long-term sequelae.

Keywords: Coronavirus disease-2019, Covishield, Computed tomography severity score index, Ground glass opacity, High resolution computed tomography, Severe acute respiratory syndrome- coronavirus-2

INTRODUCTION

In December 2019, a novel coronavirus meanwhile named Severe Acute Respiratory Syndrome- Coronavirus-2 (SARS-CoV-2) was isolated in several patients with acute severe lower respiratory tract illness in Wuhan, Hubei Province, China [1]. Initially, restricted to Wuhan, the infection spread rapidly in a couple of months reaching the status of a pandemic in March 2020. The infection had high transmission rate and led to tremendous burden on health care infrastructure world-wide. Early identification of the infected, asymptomatic patients is very crucial in limiting the spread of the disease. However, the clinical picture of the disease is not helpful for early detection, since a vast majority of the patients are asymptomatic or have only mild symptoms. Infected individuals usually have non specific symptoms like fever, sore throat, cough and dyspnoea. However, 15% develop severe pneumonia, and 5% end up in having critical disease including Acute Respiratory Distress Syndrome (ARDS), septic shock and multiorgan failure, eventually leading to death [2]. Patients aged more than 60 years of age or those with associated co-morbidities are at increased risk of serious illness from COVID-19 [3].

Countries like United Kingdom, India, United States of America, and South Africa were affected by deadlier second waves due to highly infectious mutated strains of the COVID-19. One such strain is B1617 or Delta variant, which is crippling the already constrained healthcare infrastructure in India and other developing countries. There are also some patients who have symptoms of COVID-19 but have a negative Reverse Transcription-Polymerase Chain Reaction (RT-PCR) or Rapid Antigen Test (RAT). These patients need a HRCT thorax scan to diagnose COVID-19 pneumonia and to determine the extent of lung involvement, which is very helpful in further management [4].

The RT-PCR is presently considered the gold standard investigation for the diagnosis of COVID-19. Several studies reporting the morphology of COVID-19 pneumonia on HRCT thorax scan have been published [5]. Computed Tomography (CT) findings of COVID-19 are highly suggestive of the diagnosis, and it is relatively easy for the radiologists to distinguish COVID-19 pneumonia from other lung infections [6].

In response to the COVID-19 pandemic, tremendous efforts to develop and test vaccines against SARS-CoV-2 have led to an unprecedented number of candidate vaccines by various pharmaceutical companies globally starting clinical trials during 2020. Phase III clinical trials of Covishield vaccine in Brazil, South Africa, and the UK showed significant vaccine efficacy of about 70.4% after two doses and protection of 64.1% after at least one standard dose, against symptomatic disease, with no safety concerns [7].

The main purpose of this study was to compare the severity of lung involvement in double dose, single dose vaccinated and in unvaccinated patients.

MATERIALS AND METHODS

The present study was a cross-sectional study conducted at the the Department of Radiology, Adichunchungiri Institute of Medical Sciences, Bellur, Karnataka, India, by reviewing the HRCT thorax scans of 335 COVID-19 patients done in the department from 1st April to 31st May 2021. The vaccination status of the patients was recorded at the time of CT scan as a routine protocol. All vaccinated patients in this study had received only Covishield vaccine.

Approval from the Institutional Ethics Review Committee was obtained (IEC number: AIMS/IEC/498/2021). The procedures followed were in accordance with the ethical standards of the Institutional committee on human experimentation and with the Helsinki Declaration of 1975 that was revised in 2000.

Inclusion Criteria

1. All patients diagnosed with RT-PCR positive for COVID-19.
2. All patients who had got HRCT thorax study done during 1st April to 31st May 2021 in the department.
3. Patients with known vaccination status:

- Zero dose- unvaccinated;
- Single dose vaccinated and 2nd dose of vaccine administered within one week of HRCT scan considered as single dose vaccinated patients;
- Patients who received two doses of the vaccine and getting HRCT scan done after two weeks of 2nd dose of vaccine-double dose vaccinated.

Exclusion criteria: Patients aged less than 18 years (n=23), those with unknown vaccine status or ones who received vaccination within one week of CT scan (n=52), those with other co-existing lung infections (n=16) were excluded from the study.

The final study sample consisted of 244 patients.

The patients were divided into three groups based on their vaccination status:

- Group A constituted patients who had received two doses of vaccine;
- Group B constituted patients vaccinated with only one dose of vaccine and;
- Group C constituted unvaccinated patients.

All patients in group A and group B were vaccinated with Covishield vaccine.

Study Procedure

Imaging protocol: The HRCT images of the chest were obtained on a 16 slice (GE BRIVO CT 385) Multi-Detector CT scanner. After explaining the procedure to the patient and obtaining consent, the patients were positioned supine in the gantry with both arms resting by the head. Patients were asked to hold their breath at inspiration. Images were acquired in axial sections in a cranio-caudal direction. The imaging parameters were as follows: Tube voltage: 120 kVp; Tube current: 30-70 mAs; slice thickness: 5 mm; and Field of view: 300 mm. Images were then reconstructed with a slice thickness of 0.625-1.250 mm with the same increment.

Safety procedures followed for COVID-19: All patients undergoing CT scan were masked.CT technicians were equipped with a mask, face shield, surgical cap and gloves, and an isolation gown. After each CT scan, the table was disinfected using isopropyl alcohol surface cleaner. The CT room was ventilated and the time gap between each patient was at least 10-15 minutes.

Image analysis: The HRCT thorax findings of each patient were assessed for typical imaging features of COVID-19 pneumonia like unifocal or multi-focal Ground Glass Opacities (GGO) with or without consolidations in subpleural locations or along the bronchovascular bundles, interlobular septal thickening with crazy-paving pattern and reverse halo sign [8].

Severity of lung involvement was then assessed using the scoring system, based on the percentage of visual assessment of each lobe involved. The total CT score is the sum of the individual lobar scores and can range from 0 (no involvement) to 25 (maximum involvement), when all the five lobes show more than 75% involvement [Table/Fig-1] and then the sum of each lobar scores gives overall severity score (maximum is 25), which is again categorised into mild, moderate and severe [Table/Fig-2] [9].

Lobar involvement	Score
No involvement	0
<5%	1
5-25%	2
26-49%	3
50-75%	4
>75%	5

[Table/Fig-1]: Individual lobar scores based on percentage of involvement [9].

Total score (numerical)	Severity (category)
≤7	Mild
8-17	Moderate
≥18	Severe

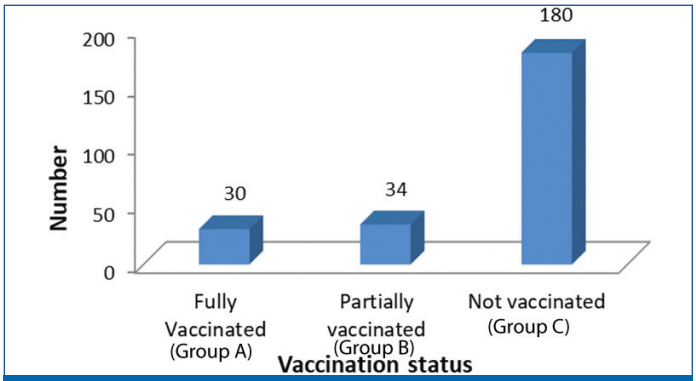
[Table/Fig-2]: Sum of the individual lobar scores indicates the overall severity of the five lobes.

STATISTICAL ANALYSIS

Statistical Package for Social Sciences (SPSS) was used to enter raw data of the present study and its analysis. Percentage analysis was used to display the percentage of observations that exist for each data point or grouping of data points. Descriptive statistics were used for continuous data. For categorical variables, chi-square test was used and it was tested at 5% level of significance. Analysis of Variance (ANOVA) test and t-test were used to compare two means to compare two independent groups and it was tested at 5% level of significance.

RESULTS

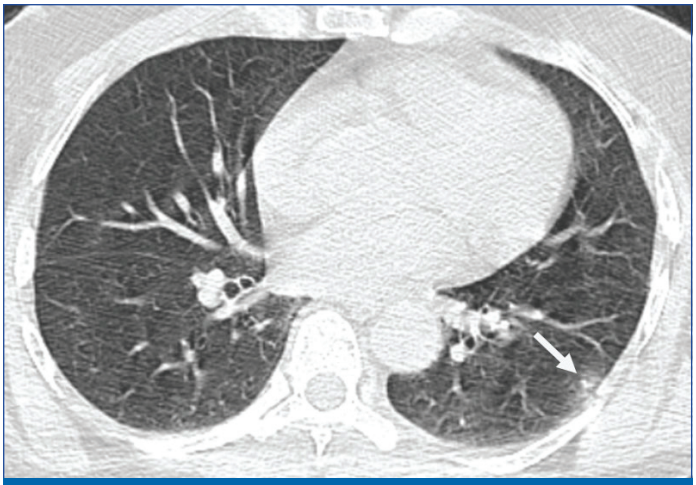
The final study group consisted of 244 patients (166 males and 78 females) diagnosed with COVID-19. There was a male predominance with a Male:Female ratio of 2:1. Group A consisted of 30 patients. Group B consisted of 34 patients and group C consisted of 180 patients [Table/Fig-3].



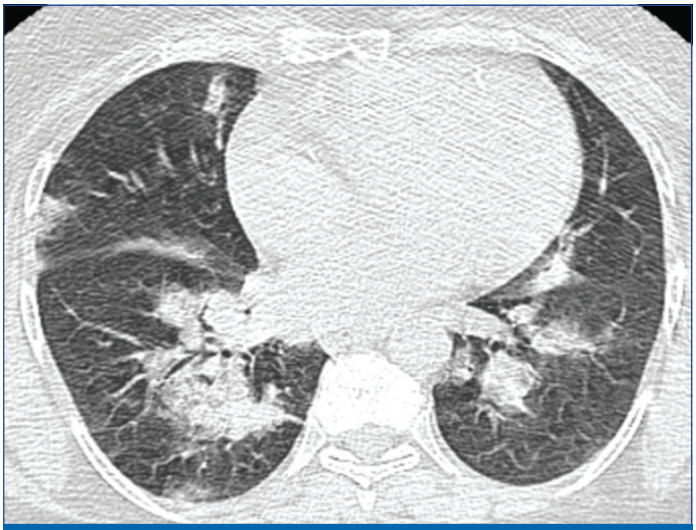
[Table/Fig-3]: Number of patients in each group.

In group A (n=30), only 20% (n=6) had lung involvement, of which six patients had mild CT severity [Table/Fig-4]. The remaining 24 patients had no lung involvement. We did not have any patients with moderate or severe CTSI score in this group. The Mean CTSI score was 0.8.

In group B (n=34) 29.4% (n=10) had no lung involvement, 11.7% (n=2) patients had mild CTSI score and 64% (n=22) had moderate CTSI score [Table/Fig-5]. We did not have patients with severe CTSI score in this group. The mean CTSI score was 7.2.



[Table/Fig-4]: HRCT thorax scan in a 72-year-old patient who had taken two doses of Covishield vaccine, showing a focal wedge shaped subpleural ground glass opacity in superior segment of left lower lobe (white arrow). CTSI: 1/25 (Mild).



[Table/Fig-5]: HRCT Thorax scan in a 59-year-old patient who had taken only one dose of Covishield vaccine, showing Multi-focal Ground Glass Opacities (GGO) with areas of early consolidatory changes along bronchovascular bundles and subpleural location in bilateral lung fields. CTSI: 11/25 (Moderate).

In group C (n=180) 33.3% of patients (n=60) had mild CTSI score, 47.7% (n=86) had moderate CTSI score and 11.11% of patients (n=20) had severe CTSI score [Table/Fig-6]. A 7.7% of patients (n=14) had no lung involvement. Mean CTSI score was 9.3 [Table/Fig-7].

[Table/Fig-6]: HRCT Thorax scan in a 37-year-old patient who had not received any vaccine showing Extensive Ground Glass Opacities (GGO) with air bronchograms along bronchovascular bundles and subpleural locations of bilateral lung fields. CTSI: 22/25 (Severe).

The study population was divided into three age groups viz., 18-44 years, 45-59 years and >60 years. There were 40.2% (n=98), 36.9% (n=90) and 23% (n=56) patients in each of the age groups respectively [Table/Fig-8].

Vaccination status	N	Mean	Standard deviation	p-value (ANOVA test)
Group A	30	0.8000	1.90100	0.001
Group B	34	7.2647	6.43056	
Group C	180	9.3833	5.58157	

[Table/Fig-7]: Vaccination status and mean CTSI Score.

Age group	N	Mean	Std. deviation	p-value (ANOVA test)
18-44	98	6.4898	5.65730	0.004
45-59	90	9.2889	5.76554	
≥60	56	8.7143	6.74123	
Total	244	8.0328	6.07353	

[Table/Fig-8]: Number of patients in each age group with mean CTSI score.

Mean CTSI score in patients of age group 18-44 years was 6.4, 45-60 years was 9.2 and >60 years was 8.7 [Table/Fig-8].

The CT severity was lesser in the younger age group compared to middle aged and elderly aged group which again reiterates the fact that more severe involvement of lung is seen with increase in age.

DISCUSSION

The Oxford-AstraZeneca COVID-19 vaccine, sold under two brand names- Covishield and Vaxzevria is a viral vector vaccine for prevention of COVID-19. The vaccine is made from modified version of a chimpanzee adenovirus, known as ChAdOx1, which is used to carry proteins from the SARS-CoV-2 coronavirus called spike glycoprotein. After vaccination, the adenovirus enters into the host cells and pushes its DNA into the nucleus.The adenovirus is engineered so it can't make copies of itself, but the gene for the coronavirus spike protein can be read by the cell and copied into a molecule called messenger RNA, or mRNA. The mRNA leaves the nucleus, and the cells start producing the spike proteins. The spike proteins are recognised by the immune system and generate a strong response even from a single dose. The vaccine is given by intramuscular injection. It has been shown to be safe and well tolerated, although it can cause temporary side-effects such as a temperature, flu-like symptoms, headache or sore arm [10,11].

The second wave of COVID-19 put a heavy burden on India's healthcare system, affecting younger patients. Vaccine effectiveness has been surveyed with emergence of new variants of COVID-19 such as B1617 (delta) or B117 (alpha) mutants, which appear to have higher transmissibility and case fatality than the earlier version of the virus [12]. Various studies conducted on vaccine efficacy in the current pandemic have suggested that vaccines are effective against variants in preventing severe disease [13].

The RT-PCR still remains the gold standard test for diagnosis of COVID-19 pneumonia. But standby time for viral detection with RT-PCR tests, incomplete sampling techniques, new mutated strains of COVID-19 and inadequate viral load, can delay the diagnosis. Although the first test is negative in many patients, it has been reported that positivity develops in the second, third, or even subsequent tests [14]. The CT plays an important role in quantification of parenchymal involvement, detection of complications (like pulmonary embolism or superinfection), and even for triaging the COVID-19 patients in case of limited healthcare resources. Hence, CT has emerged as a widely used tool in diagnosing and treating patients with suspected or proven COVID-19.

In the present study, majority of the patients in group A did not have any lung involvement. Of the six patients who had lung involvement, all had mild CTSI score. In group B, majority of the patients had only mild and moderate CTSI score. There were no patients with severe lung involvement. In group C, there were patients with mild, moderate and severe CTSI score. Severe disease was seen only in group C patients. Group A and group B did not have any patient with severe lung involvement.

However, patients with no lung involvement were seen in all the three groups. This can be attributed to early diagnosis of the COVID-19 infection, younger age group, good immunity of the patients and also the effect of vaccination in group A and group B patients. Patients with double dose or single dose vaccination had less severe lung disease compared to unvaccinated patients which confirms the effectiveness of vaccine in preventing severe disease. This finding of reduced lung involvement with full or partial vaccination could be crucial in highlighting the role of vaccines as an effective tool in the fight against COVID-19 during these times of vaccine misinformation to motivate more people to get vaccinated.

Many studies have been done on efficacy of COVID-19 vaccines and emphasising their role in preventing severe disease and thereby reducing hospital admissions and mortality. In a study done in United Kingdom by Pritchard E et al., showed that 21 days after a single dose of either the AstraZeneca or the Pfizer vaccine, the rates of all new SARS-CoV-2 infections had fallen by 65%, symptomatic infections by 72%, and asymptomatic infections by 57%, ($p<0.0001$). Among people who had a second dose of the Pfizer vaccine, infections were 70% ($p<0.0001$) lower and symptomatic infections 90% ($p<0.0001$) lower [15]. In another study done in Southern California by Ebinger JE et al., showed that two vaccine doses achieved high responses across all age groups, and particularly increased the number of older people seroconverting to similar levels to those receiving one dose after prior infection [16].

One more study done in UK by Wei J et al., showed that postvaccine anti-spike Immunoglobulin G responses vary by prior infection status, age, sex, the vaccine type, and the number of doses received. In previously infected patients, all age groups achieved high antibody response after first vaccination. In those without evidence of prior infection, older participants had lower responses than younger participants after receiving a single dose of vaccine, with especially marked effects in those over 60 years. Two doses achieved high responses across all ages, particularly increasing seroconversion in older people, to similar levels to those achieved after prior infection followed by a single dose [3].

Lopez Bernal J et al., conducted a study on the older population of England and found that a single dose of the Covishield (ChAdOx1-S) vaccine was about 60-75% effective against symptomatic disease and provided an additional protective effect against hospital admission [17].

Limitation(s)

The authors did not have details of the exact duration of the patients' illness prior to CT scan. Patient details such as their oxygen saturation, hospital admission status, previous infection with COVID-19 and co-existing medical conditions were also not available.

CONCLUSION(S)

Patients vaccinated with two doses showed only mild CTSI score. Severe lung involvement was seen only in unvaccinated group. Hence complete vaccination with two doses in all individuals is crucial in limiting the spread of the COVID-19, and if infected it helps in preventing severe lung disease. The key to control the COVID-19 pandemic is to understand the benefits of the COVID-19 vaccines and it is essential to know that the benefits of vaccination greatly outweigh any associated potential side-effects. The present study was done on those patients vaccinated exclusively with Covishield vaccine. Further studies can be done with other vaccines, and also with other ethnic groups in other countries, which would also help to know the differences in vaccine efficacy.

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