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Effectiveness of BBV152 vaccine and ChAdOx1-S vaccine in preventing severe disease among vaccinated patients admitted to a designated COVID-19 hospital in India

Rajaraman Nivetha[1], Ramesh Anshul[2], Subbarayan Sarojini[3], Chinnaian Sivagurunathan[1], Chandrasekar Janaganbose Maikandaan[4]

[1]Department of Community Medicine, Tagore Medical College and Hospital, Chennai; [2]Department of Psychiatry, Sri Muthukumaran Medical College Hospital and Research Institute, Chennai; [3]Department of Paediatrics, Sri Muthukumaran Medical College Hospital and Research Institute, Chennai; [4]Department of Psychiatry, Melmaruvathur Adhiparasakthi Institute of Medical Sciences & Research, Melmaruvathur, India

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Corresponding author:
Chinnaian Sivagurunathan, MD
Department of Community Medicine, Tagore Medical College and Hospital, Chennai, Tamil Nadu, India
Tel: +91-9790474787
E-mail: drsivaguru85@gmail.com

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Purpose: Coronavirus disease 2019 (COVID-19) is a highly formidable disease. Globally, multiple vaccines have been developed to prevent and manage this disease. However, the periodic mutations of severe acute respiratory syndrome coronavirus 2 variants cast doubt on the effectiveness of commonly used vaccines in mitigating severe disease in the Indian population. This study aimed to assess the effectiveness of the BBV152 vaccine and ChAdOx1-S vaccine in preventing severe forms of the disease.

Materials and Methods: This retrospective study, based on hospital records, was conducted on 204 vaccinated COVID-19 patients using a consecutive sampling approach. Data on their vaccination status, comorbidities, and high-resolution computed tomography lung reports' computed tomography severity scores were extracted from their medical records. Fisher's exact test and binomial logistic regression analysis were employed to assess the independent associations of various factors with the dependent variables.

Results: Of the 204 records, 57.9% represented males, with a mean age of 61.5±9.8 years. Both vaccines demonstrated effective protection against severe illness (90.2%), with BBV152 offering slightly better protection compared to ChAdOx1-S. Male gender, partial vaccination, comorbid conditions, and the type of vaccine were identified as independent predictors of severe lung involvement.

Conclusion: This study indicates that both vaccines were highly effective (90%) in preventing severe forms of the disease in fully vaccinated individuals. When comparing the two vaccines, BBV152 was slightly more effective than ChAdOx1-S in preventing severe COVID-19.

Keywords: COVID-19 vaccine, Vaccination, SARS-CoV-2, CT severity score, Aged

Introduction

Coronavirus disease 2019 (COVID-19) is one of the most devastating infectious diseases in recent history. The World Health Organization (WHO) officially declared COVID-19 a pandemic on March 11, 2020 [1]. COVID-19 has significantly increased mortality and morbidity worldwide, causing substantial economic, social, and political disruptions [2]. Globally, extensive efforts have been made to develop safe and effective vaccines for preventing and controlling COVID-19. Currently, approximately 13 different COVID-19 vaccines have been approved by WHO under the Emergency Use Authorization protocol [3]. In India, 12 COVID-19 vaccines are currently approved for use. However, the whole virion inactivated BBV152 coronavirus vaccine (COVAXIN; Bharat Biotech International

Ltd., Hyderabad, India) and the recombinant ChAdOx1-S vaccine (COVISHIELD; Serum Institute of India Pvt. Ltd., Pune, India) are the most commonly administered vaccines to adults in India [4].

COVAXIN is produced by Bharat Biotech and formulated by the National Institute of Virology, in collaboration with the Indian Council of Medical Research. COVAXIN includes whole-virion inactivated severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) antigen (strain: NIV-2020-770), and the other inactive ingredients such as aluminium hydroxide gel, toll-like receptor 7/8 agonist (imidazoquinolinone), 2-phenoxyethanol, and phosphate buffer. COVISHIELD is developed by the University of Oxford and produced by the Serum Institute of India. It is a recombinant, replication-deficient chimpanzee adenovirus vector encoding the SARS-CoV-2 spike (S) glycoprotein. COVISHIELD contains L-histidine, L-histidine hydrochloride monohydrate, magnesium chloride hexahydrate, polysorbate 80, ethanol, sucrose, sodium chloride, and disodium edetate dihydrate. Initial statements indicated that the pooled efficacy of ChAdOx1-S against moderate or severe illness was 85%, while BBV152's efficacy against severe COVID-19 was 93.4% [5,6]. However, the recurrent mutations of SARS-CoV-2 variants raise concerns about the vaccines' effectiveness against COVID-19, with evidence suggesting reduced efficacy against certain mutated strains [7,8]. For example, against the Delta variant of SARS-CoV-2 (B.1.617.2), the effectiveness of the BBV152 vaccine and the ChAdOx1 vaccine was only 65.2% and 70.4%, respectively [9,10]. Against this backdrop, the present study was conducted to evaluate the effectiveness of the whole virion inactivated BBV152 coronavirus vaccine (COVAXIN) and the recombinant ChAdOx1-S vaccine (COVISHIELD) in preventing severe forms of the disease, as indicated by high-resolution computed tomography (HRCT) lung reports, among vaccinated patients admitted to a designated COVID-19 hospital during the second wave.

Materials and Methods

Study design and setting

This retrospective study was conducted among COVID-19 patients admitted to a designated COVID-19 center in Chennai, Tamil Nadu, from April 1, 2021 to June 30, 2021. The study utilized hospital records. The study was approved by the Institutional Research Committee and Institutional Ethics Committee (IEC) under the reference (IEC no., 15/APR/2023). A waiver of consent was obtained from the Dean and Medical Superintendent for this retrospective record-based study.

Selection criteria

The study involved a review of medical records and the analysis of HRCT scans of the lungs for individuals who tested positive for COVID-19 using reverse transcription-polymerase chain reaction (RT-PCR) and were admitted to the hospital during the study period. The study specifically focused on individuals aged 45 years and older who had received a COVID-19 immunization at least 14 days before their positive RT-PCR test result. Records of patients under the age of 45 years, patients with chronic respiratory tract diseases or infections, individuals with unknown vaccination status, unvaccinated patients, and cases with HRCT chest reports not available or taken within 14 days of immunization were excluded from the study (Fig. 1). According to the type of COVID-19 vaccination received, patients were categorized into two groups: those who received COVAXIN (BBV152 vaccine) were designated as Group 1, and those who received COVISHIELD (ChAdOx1-S vaccine) were designated as Group 2.

Data collection

All relevant information was extracted from the selected case sheets using a semi-structured abstraction form. This form consisted of three sections: section A: demographic details, including Medical Records Department number, age, gender, and comorbidities; section B: the patient's vaccination history, including the type of COVID vaccine and the number of doses administered (one dose for partial vaccination and two doses for full vaccination); and section C: the patient's CO-RADS (COVID-19 Reporting and Data System) and CT severity scores (CTSS) from their HRCT lung reports.

Since CT imaging provides a more objective evaluation of lung parenchymal involvement compared to non-specific inflammatory indicators, the severity of lung involvement was categorized using the CTSS of the HRCT report, following the criteria set out in the AIIMS (All India Institute of Medical Sciences) protocol for COVID-19 management, revised version 2.1, issued on May 3, 2021 [11]. CTSS 8 was defined as mild lung involvement, CTSS 9–15 as moderate lung involvement, and CTSS >15 as severe lung involvement [12].

Data analysis

The raw data collected was entered into Microsoft Excel 2019 (Microsoft Corp., Redmond, WA, USA), and IBM SPSS ver. 20.0 software (IBM Corp., Armonk, NY, USA) was used to con-

duct descriptive and inferential statistics. Descriptive statistics such as frequency and percentage were employed for categorical variables, while mean and standard deviation were used for continuous variables. Fisher's exact test and binary logistic regression were used to assess the association between vaccinated COVID-19 patients and their illness severity outcomes based on their explanatory variables. The significance level for the tests was set at 5%, with a p-value less than 0.05 considered as statistically significant.

Results

Characteristics of COVID-19 patients

This retrospective study included 204 vaccinated patients diagnosed with COVID-19 who were admitted to a designated COVID-19 facility. With a mean age of 61.5±9.8 years, more than half of the participants (52.9%) were aged 61 years or older. The majority of participants (57.9%) were male. Among the 204 vaccinated patients, 63.7% received the ChAdOx1-S vaccine, while 36.3% received the BBV152 vaccine. More than two-thirds of patients (82.4%) were partially (one-dose) vaccinated. The CT severity was higher among partially vaccinated patients (6.9%) than among fully vaccinated patients (2.9%), regardless of the vaccine type (Fig. 2). Among vaccinated individuals, only 9.8% of participants had severe disease, as indicated by a CTSS of 15 or above in their HRCT lung report (Table 1).

Associations between demographics, vaccination status, and HRCT lung results

Table 2 presents the associations between the demographic profiles of COVID-19 patients, vaccination status, and HRCT lung results, analyzed using Fisher's exact test. CTSS were higher among males than females, with statistically significant results (p=0.001). A similarly significant statistical association was observed between the severity of lung involvement and patients with a prior history of comorbidities compared to those without such conditions (Table 2). Fully vaccinated patients with either of the two vaccines were found to have less severe lung involvement than partially vaccinated patients, which was also statistically significant. This study revealed that the severity of lung involvement was lower among patients who received the BBV152 vaccine (1%) compared to those who received the ChAdOx1-S vaccine (8.8%).

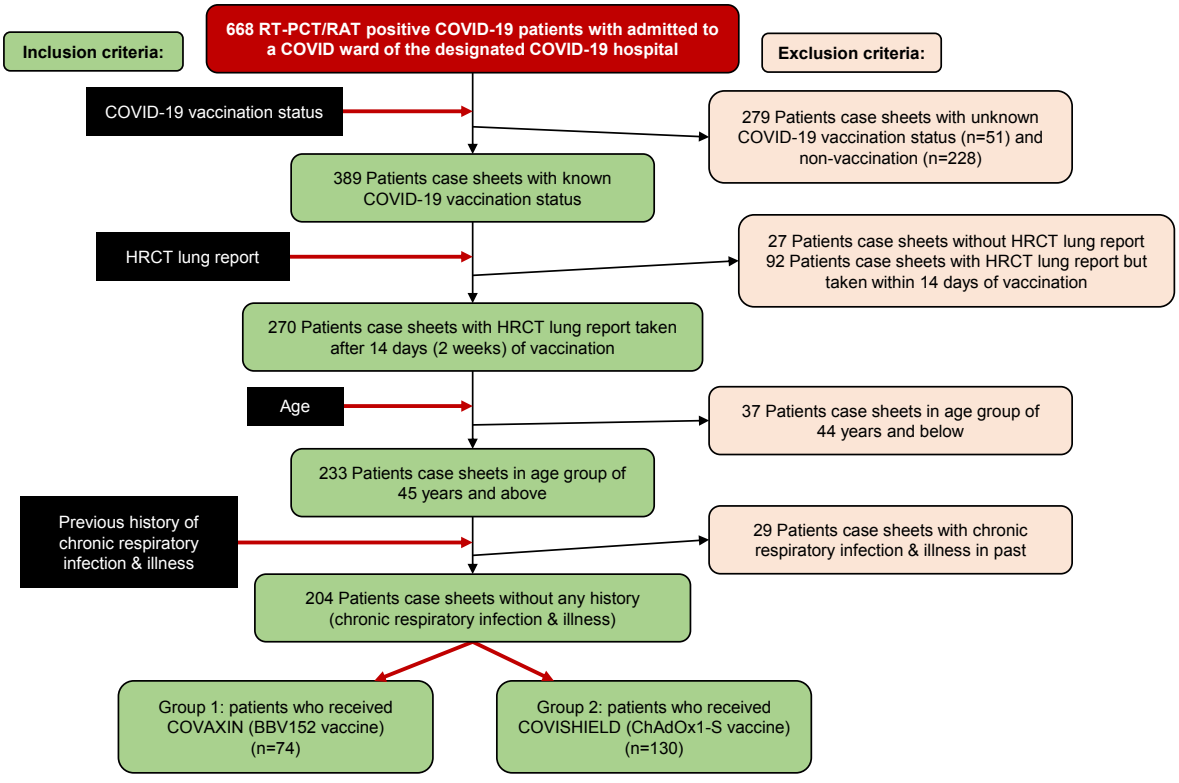

Fig. 1. Flowchat showing selection ctriteria of the study participants. RT-PCR, reverse transcription-polymerase chain reaction; RAT, rapid antigen test; HRCT, high-resolution computed tomography; COVID-19, coronavirus disease 2019.

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Binary logistic regression on severity of lung involvement and vaccination

Binary logistic regression was performed to investigate the relationship between the severity of lung involvement, as indicated by HRCT reports, and the type and dosage of COVID-19 vaccination (Table 3). The overall regression model fit was statistically significant, with a Nagelkerke R^2 of 7%–9%. Patients who received the BBV152 vaccine exhibited less severe lung involvement than those who received the ChAdOx1-S vaccine, a statistically significant finding. Similarly, fully vaccinated individuals (two doses) with the ChAdOx1-S vaccine had a 1.6 times lower likelihood of developing severe illness compared to those who were partially vaccinated (one dose).

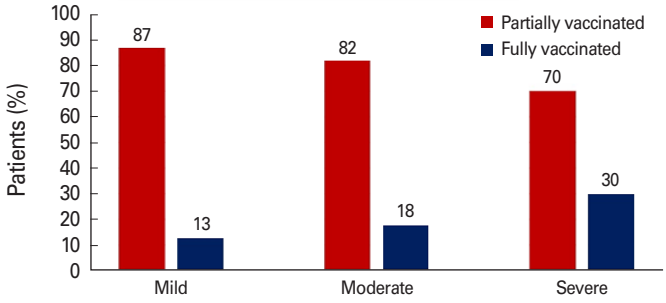

Fig. 2. Catogeries of patients and their vaccination status.

Discussion

This study was conducted among COVID-19 patients who were

Table 1. Distribution of demographic profile, vaccination status, and severity of illness among COVID-19 patients

Variable	Category	No. of frequency (%)
Age (yr)	45–60	96 (47.1)
	≥61	108 (52.9)
Gender	Female	88 (42.2)
	Male	118 (57.8)
Comorbidity	No	132 (64.7)
	Yes	72 (35.3)
Type of vaccine	COVIDSHIELD	130 (63.7)
	COVAXIN	74 (36.3)
Dose of vaccine	Partially vaccinated	168 (82.4)
	Fully vaccinated	36 (17.6)
CT severity score of HRCT lung report	Mild (<8)	60 (29.4)
	Moderate (9–15)	124 (60.8)
	Severe (>15)	20 (9.8)

COVID-19, coronavirus disease 2019; CT, computed tomography; HRCT, high-resolution computed tomography.

Table 2. Associated between CT severity score of HRCT lung report and demographic factors & vaccination status among COVID-19 patients

Variable	CT severity score category			Fisher's exact test value	p-value
	Mild (<8)	Moderate (9–15)	Severe (>15)		
Age (yr)				3.237	0.189
45–60	32 (15.7)	58 (28.4)	6 (2.9)		
≥61	28 (13.7)	66 (32.4)	14 (6.9)		
Gender				13.075	0.001***
Male	38 (18.6)	62 (30.4)	18 (8.8)		
Female	22 (10.8)	62 (30.4)	2 (1.0)		
Comorbidity				43.217	0.001***
No	46 (22.5)	86 (42.2)	0		
Yes	14 (6.9)	38 (18.6)	20 (9.8)		
Type of vaccine				26.989	0.001***
COVIDSHIELD	50 (24.5)	62 (30.4)	18 (8.8)		
COVAXIN	10 (4.9)	62 (30.4)	2 (1.0)		
COVIDSHIELD				9.446	0.007**
Partially vaccinated	48 (36.9)	54 (41.5)	12 (9.2)		
Fully vaccinated	2 (1.5)	8 (6.2)	6 (4.6)		
COVAXIN				5.890	0.037*
Partially vaccinated	4 (5.4)	48 (64.9)	2 (2.7)		
Fully vaccinated	6 (8.1)	14 (18.9)	0		

Values are presented as number (%).
CT, computed tomography; HRCT, high-resolution computed tomography; COVID-19, coronavirus disease 2019.
*p<0.05. **p<0.01. ***p<0.001.

Table 3. Relationship between severity of lung involvement based on HRCT report and vaccination status among COVID-19 patients by using binary linear regression

Variable	B	Exp B	SE	95% CI for Exp B	p-value (<0.05)
Type of vaccine					
COVAXIN	Ref	Ref	Ref	Ref	
COVIDSHIELD	-1.755	0.173	0.761	0.039–0.767	0.021***
Constant	3.584	36.00	0.717		0.001***
COVAXIN					
Fully vaccinated	Ref	Ref	Ref	Ref	
Partially vaccinated	17.94	62,133.62	8,987.42	0.001	0.998
Constant	-21.2	0.001	8,987.42		0.998
COVIDSHIELD					
Fully vaccinated	Ref	Ref	Ref	Ref	
Partially vaccinated	1.629	5.100	0.600	1.574–16.525	0.007***
Constant	0.511	1.667	0.516		0.323

Dependent reference group: mild to moderate lung involvement (CTSS<15).
HRCT, high-resolution computed tomography; COVID-19, coronavirus disease 2019; CI, confidence interval; Ref, reference; CTSS, computed tomography severity scores.
***p<0.001.

vaccinated and aged 45 years and above to evaluate the association between lung involvement, as indicated by HRCT reports, and the effectiveness of two commonly used vaccines. This age group was chosen because, during the study period, the Government of India approved vaccination only for individuals aged 45 and above in the general population. Additionally, COVID-19 severity was found to be higher among the elderly population [13]. The study found that the mean age of participants was 61.5±9.8 years, with the majority being 61 years or older. However, there was no statistically significant association between age and disease severity. Similar results have been reported in a study conducted in the Indian Himalayan foothills, which included patients ranging in age from 18 to 78 years, with the majority in their 60s [14]. This may be attributed to the increasing rate of COVID-19 positivity with age, although the exact mechanisms behind this phenomenon remain unknown. People aged 60 years and above were found to have higher rates of positivity, which could be related to shorter incubation periods, pre-existing comorbidities, and age-dependent reduced T-lymphocyte immune responses, all of which make the elderly population more susceptible to the disease [15-17].

The study identified that the severity of illness was significantly higher among males (8.8%) than females (1%). Similar findings were reported in studies conducted by Kushwaha et al. [17], Jin et al. [18], and Betron et al. [19], among COVID-19 patients. This difference could be attributed to behaviors such as sharing cigarettes or bidis and prior smoking, which are more common risk factors among men. In the case of women, the XX chromosome, which contributes to enhancing humoral immunity, has been shown to be protective [17-19]. Previous studies suggest that comorbidities significantly contribute to the poor progression of COVID-19 illness [14,20,21], and this study also reported similar findings. Patients with comorbid conditions exhibited higher CTSS than those without such conditions. This could be due to the age-related decline in adaptive immunity, making individuals less effective at responding to viral infections and more susceptible to severe disease. The study also found that patients who received two doses of either the BBV152 or ChAdOx1-S vaccine had considerably lower CTSS than those who received only one dose. This aligns with the results of studies conducted in Rajasthan by Gurumurthy et al. [22] and in Uttar Pradesh by Verma et al. [23]. It emphasizes the importance of receiving the recommended doses (full vaccination) to maximize protection and significantly reduce the risk of developing severe forms of the disease.

An interesting finding was that the BBV152 vaccine was significantly more effective in fully vaccinated individuals compared to the ChAdOx1-S vaccine. This finding is consistent with the results reported by Fiolet et al. [24]. This difference may be attributed to the mutated variants present in the study area, which primarily involve spike-mutated variants of SARS-CoV2 (Alpha, Beta, Gamma, Delta, and Lambda). As a result, the nucleocapsid protein vaccine demonstrated better effectiveness in preventing severe forms of the disease compared to the spike glycoprotein vaccine [25-27].

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Conclusion

This study demonstrates that both vaccines were highly effective (>90%) in preventing severe forms of the disease after two doses. When comparing the two vaccines, the BBV152 vaccine was found to be slightly more effective than the ChAdOx1-S vaccine in preventing severe COVID-19.

Limitations and recommendations

This retrospective study had a relatively small sample size. Therefore, we recommend conducting larger-scale, longitudinal studies to gain a better understanding of the natural disease progression and vaccine effectiveness. Future studies should consider incorporating clinical and serological parameters to provide a more detailed analysis of the disease process.

ORCID

Rajaraman Nivetha *https://orcid.org/0000-0002-2094-1161*
Ramesh Anshul *https://orcid.org/0009-0008-7469-0979*
Subbarayan Sarojini *https://orcid.org/0000-0003-4729-1637*
Chinnaian Sivagurunathan *https://orcid.org/0000-0002-4152-8982*
Chandrasekar Janaganbose Maikandaan *https://orcid.org/0000-0002-9137-3624*

References

1. WHO Director-General's opening remarks at the media briefing on COVID-19: 11 March 2020 [Internet]. Geneva: World Health Organization; 2020 [cited 2023 May 6]. Available from: https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020
2. Chang D, Chang X, He Y, Tan KJ. The determinants of COVID-19 morbidity and mortality across countries. Sci Rep 2022;12:5888.
3. World Health Organization (WHO) Emergency Use Authorization (EUA) qualified COVID-19 vaccines [Internet]. Vancouver (BC): BC Centre for Disease Control; 2023 [cited 2023 May 6]. Available from: http://www.bccdc.ca/Health-Info-Site/Documents/COVID-19_vaccine/WHO-EUA-qualified-covid-vaccines.pdf
4. India: 12 vaccines approved for use in India [Internet]. [place unknown]: COVID19 Vaccine Tracker; c2023 [cited 2023 May 6]. Available from: https://covid19.trackvaccines.org/country/india/
5. Harder T, Kulper-Schiek W, Reda S, et al. Effectiveness of COVID-19 vaccines against SARS-CoV-2 infection with the Delta (B.1.617.2) variant: second interim results of a living systematic review and meta-analysis, 1 January to 25 August 2021. Euro Surveill 2021;26:2100920.
6. Geddes L. India's "Covaxin" vaccine shows high efficacy against COVID-19 infections in phase 3 trial [Internet]. Geneva: Gavi; 2021 [cited 2023 May 6]. Available from: https://www.gavi.org/vaccineswork/indias-covaxin-vaccineshows-high-efficacy-against-covid-19-infections-phase-3
7. Tartof SY, Slezak JM, Fischer H, et al. Effectiveness of mRNA BNT162b2 COVID-19 vaccine up to 6 months in a large integrated health system in the USA: a retrospective cohort study. Lancet 2021;398:1407-16.
8. Hadizadeh N, Naderi M, Khezri J, Yazdani M, Shamsara M, Hashemi E. Appraisal of SARS-CoV-2 mutations and their impact on vaccination efficacy: an overview. J Diabetes Metab Disord 2022;21:1763-83.
9. COVAXIN: India's first indigenous COVID-19 vaccine [Internet]. Hyderabad: Bharat Biotech; 2022 [cited 2023 May 6]. Available from: https://www.bharatbiotech.com/covaxin.html
10. Press statement by the Drugs Controller General of India (DCGI) on restricted emergency approval of COVID-19 virus vaccine [Internet]. New Delhi: Press Information Bureau, Government of India; 2021 [cited 2023 May 6]. Available from: https://www.icmr.gov.in/pdf/press_realease_files/HFW_DCGI_energency_use_authorisation_03012021_2.pdf
11. All India Institute of Medical Sciences. Protocol for COVID-management: updated version 2.1 – AIIMS 3rd May 2021 [Internet]. New Delhi: AIIMS; 2021 [cited 2023 May 6]. Available from: https://police.py.gov.in/AIIMS%20-%20Version%202.1%20-%20Protocol%20for%20COVID-Management%20-%20Dt%2003.05.21.pdf
12. Francone M, Iafrate F, Masci GM, et al. Chest CT score in COVID-19 patients: correlation with disease severity and short-term prognosis. Eur Radiol 2020;30:6808-17.
13. Guideline for COVID-19 vaccination of children between 12-14 years of age [Internet]. New Delhi: Ministry of Health and Family Welfare, Government of India; 2022 [cited 2023 May 6]. Available from: https://www.mohfw.gov.in/pdf/GuidelinesCovidvaccination12to14yrchildrenMarch2022.pdf
14. Sharma R, Thakker V, Bahri Sharma R, et al. Effect of vaccination on the HRCT profile of COVID-19 patients: a sin-

gle-center experience. J Family Med Prim Care 2022;11:2938-44.
15. Boehmer TK, DeVies J, Caruso E, et al. Changing age distribution of the COVID-19 pandemic: United States, May-August 2020. MMWR Morb Mortal Wkly Rep 2020;69:1404-9.
16. Nicoli F, Solis-Soto MT, Paudel D, et al. Age-related decline of de novo T cell responsiveness as a cause of COVID-19 severity. Geroscience 2020;42:1015-9.
17. Kushwaha S, Khanna P, Rajagopal V, Kiran T. Biological attributes of age and gender variations in Indian COVID-19 cases: a retrospective data analysis. Clin Epidemiol Glob Health 2021;11:100788.
18. Jin JM, Bai P, He W, et al. Gender differences in patients with COVID-19: focus on severity and mortality. Front Public Health 2020;8:152.
19. Betron M, Gottert A, Pulerwitz J, Shattuck D, Stevanovic-Fenn N. Men and COVID-19: adding a gender lens. Glob Public Health 2020;15:1090-2.
20. Gupta N, Kaur H, Yadav PD, et al. Clinical characterization and genomic analysis of samples from COVID-19 breakthrough infections during the second wave among the various states of India. Viruses 2021;13:1782.
21. Vaidiyanathan B, Dhanger S, Raajesh J, et al. To determine the clinical efficacy of COVID vaccine in post vaccinated individuals with severe pneumonia in preventing ICU mortality in a COVID designated tertiary care centre: a retrospective study. Arch Anesth Crit Care 2022;8:208-12.
22. Gurumurthy B, Das SK, Shetty S, Veerabhadrappa RC, Kosinepalli SS, Dharamaraju SH. CT severity score: an imaging biomarker to estimate the severity of COVID-19 pneumonia in vaccinated and non-vaccinated population. Egypt J Radiol Nucl Med 2022;53:88.
23. Verma A, Kumar I, Singh PK, et al. Initial comparative analysis of pulmonary involvement on HRCT between vaccinated and non-vaccinated subjects of COVID-19. Eur Radiol 2022;32:4275-83.
24. Fiolet T, Kherabi Y, MacDonald CJ, Ghosn J, Peiffer-Smadja N. Comparing COVID-19 vaccines for their characteristics, efficacy and effectiveness against SARS-CoV-2 and variants of concern: a narrative review. Clin Microbiol Infect 2022;28:202-21.
25. Das S, Kar SS, Samanta S, Banerjee J, Giri B, Dash SK. Immunogenic and reactogenic efficacy of covaxin and covishield: a comparative review. Immunol Res 2022;70:289-315.
26. Singh DD, Parveen A, Yadav DK. SARS-CoV-2: emergence of new variants and effectiveness of vaccines. Front Cell Infect Microbiol 2021;11:777212.
27. Mohammadi M, Shayestehpour M, Mirzaei H. The impact of spike mutated variants of SARS-CoV2 [Alpha, Beta, Gamma, Delta, and Lambda] on the efficacy of subunit recombinant vaccines. Braz J Infect Dis 2021;25:101606.