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Clinical profile of ChAdOx1 nCoV-19- and BBV152-vaccinated individuals among hospitalized COVID-19 patients: a pair-matched study

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Abstract

Background: COVID-19 infections among severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-vaccinated individuals are of clinical concern, especially in those requiring hospitalization. Such real-world data on ChAdOx1 nCoV-19- and BBV152-vaccinated individuals are scarce. Hence, there is an urgent need to understand their clinical profile and outcomes.

Methods: A 1:1 pair-matched study was performed among vaccinated and unvaccinated COVID-19 patients admitted between March 2021 and June 2021 at a tertiary care centre in New Delhi, India. The vaccinated group (received at least one dose of ChAdOx1 nCoV-19 or BBV152) was prospectively followed till discharge or death and matched [for age (±10 years), sex, baseline disease severity and comorbidities] with a retrospective group of unvaccinated patients admitted during the study period. Paired analysis was done to look for clinical outcomes between the two groups.

Results: The study included a total of 210 patients, with 105 in each of the vaccinated and unvaccinated groups. In the vaccinated group, 47 (44.8%) and 58 (55.2%) patients had received ChAdOx1 nCoV-19 and BBV152, respectively. However, 73 patients had received one dose and 32 had received two doses of the vaccine. Disease severity was mild in 36.2%, moderate in 31.4% and severe in 32.4%. Two mortalities were reported out of 19 fully vaccinated individuals. All-cause mortality in the vaccinated group was 8.6% (9/105), which was significantly lower than the matched unvaccinated group mortality of 21.9% (23/105), $p = 0.007$. Vaccination increased the chances of survival (OR = 3.8, 95% CI: 1.42–10.18) compared to the unvaccinated group.

Conclusion: In the second wave of the pandemic predominated by delta variant of SARS CoV-2, vaccination reduced all-cause mortality among hospitalized patients, although the results are only preliminary.

Keywords: BBV152, ChAdOx1 nCoV-19, COVID-19, hospitalization, vaccine

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Highlights

- One of the initial studies reporting the clinical profile of breakthrough infections requiring hospitalization due to COVID-19.
- The study period coincides with the surge in cases due to the delta variant of SARS CoV-2.
- Vaccination increased the chances of survival (OR = 3.8, 95% CI: 1.42–10.18) compared to the matched unvaccinated group.
- At least one dose of both ChAdOx1 nCoV-19 and BBV152 was able to reduce mortality, although the study was not designed and adequately powered to explore this.

Introduction

Researchers across the globe have been constantly working to come out with effective vaccines to battle the pandemic of COVID-19. India began one of the world's largest vaccination campaigns against COVID-19 on 16 January 2021 with two approved vaccines, namely Covishield (ChAdOx1 nCoV-19) (by Serum Institute of India Ltd.) and Covaxin (BBV152) (by Bharat Biotech International Ltd.). Recently, heterologous recombinant adenovirus (rAd)-based vaccine, Gam-COVID-Vac (Sputnik V) and mRNA-1273 (Moderna) vaccine received emergency use approval in India.[1,2] By the beginning of July 2021, India had administered more than 335 million vaccine doses with 4.2% of the population being fully vaccinated according to the Ministry of Health and Family Welfare, Government Of India (MoHFW).[3]

Reports of COVID-19 infections in vaccinated individuals are alarming and of urgent concern to add granularity to our understanding of the post-vaccine immunology and further preventive strategies. During the inceptive phase of its vaccination drive, India was hit hard by the second wave of the COVID-19 pandemic with an exponential rise in cases during the middle of March 2021.[4] During this period, a study done at the Post Graduate Institute of Medical Education and Research, Chandigarh among healthcare workers reported 1.6% breakthrough infections in those vaccinated with ChAdOx1 nCoV-19.[5] Indian Council for Medical Research (ICMR) reported that post-vaccination breakthrough infections in India for ChAdOx1 nCoV-19 was 0.03% and BBV152 was 0.04%.[6] Similar studies have been reported from across the globe.[5,7] However, data after the end of this wave demonstrated that the breakthrough infection rate was much higher. About 13.1[8]–42.4%[9] of healthcare workers vaccinated with either one or two doses of ChAdOx1 nCoV-19 during the delta wave developed symptomatic COVID-19.

The most important vaccine efficacy endpoints are the severity of disease and mortality which are difficult to assess in phase III clinical trials.[10] Hence, there is a need for real-world vaccine effectiveness data with respect to preventing hospitalizations, disease severity and mortality. Currently, there is not much data available on the clinical profile of hospitalized COVID-19 patients who are vaccinated. In this study, we aim to understand the clinical profile and outcomes of admitted COVID-19 patients who had received at least one dose of either ChAdOx1 nCoV-19 or BBV152.

Methodology

This study was conducted in the dedicated COVID-19 healthcare facility of a tertiary care hospital in Northern India between March 2021 and June 2021. The main aim was to understand the clinical outcomes of vaccinated COVID-19 patients requiring hospitalization. The study was undertaken after approval by the Institute Ethics Committee (IECPG-337) with a protocol revision done in May 2021 to retrospectively include an unvaccinated control cohort. The study population included patients with confirmed SARS CoV-2 infection admitted to the COVID-19 centre, positive by nucleic acid amplification test or a rapid antigen test. We performed a 1:1 matched study between two groups of patients – the vaccinated COVID-19 group and the unvaccinated COVID-19 group of patients – to compare their clinical outcomes. Informed consent was taken from the study participants. Similarly, for the retrospective cohort, consent was taken *via* phone call, either from the patient or family members.

Group 1 – vaccinated COVID-19 patients

This group consisted of admitted COVID-19 patients who had received at least one dose of either ChAdOx1 nCoV-19 or BBV152 prior to hospitalization. After admission, they were classified to have mild (upper respiratory tract symptoms and fever without shortness of breath or hypoxia), moderate

(respiratory rate $\geq$ 24/min, or $SpO_2 \leq 93\%$ on room air) or severe disease (respiratory rate $>$ 30/min, or $SpO_2 < 90\%$ on room air) as per institutional protocol. This group was prospectively followed up to discharge or death. Demographic details, clinical data (symptoms, admission vitals), baseline laboratory parameters (including inflammatory markers), the treatment received (highest oxygen delivery devices used, steroids, antivirals, anticoagulation) and clinical outcomes (all-cause mortality and duration of hospital stay) of patients were recorded in a pre-designed proforma.

Group 2 – unvaccinated COVID-19 patients (controls)

Details of all admitted COVID-19 patients at our facility during the study period were retrieved from electronic medical records. Vaccination status was re-verified telephonically. All confirmed COVID-19 patients who had not received any dose of SARS CoV-2 vaccine and were admitted during the same study period were recruited as the control group. This was the group with which all clinical outcomes of the vaccinated group were compared.

Paired matching

We performed a 1:1 matching between the two groups. The matching variables included age ($\pm$10 years), sex, the severity of disease at presentation and comorbidities. Wherever possible, exact comorbidities were matched; in the absence of exact matches, we tried to match the number of comorbidities and the best possible pair was taken including at least the major comorbidities (diabetes mellitus, hypertension, chronic kidney disease and coronary artery disease). Codes were generated for both groups based on the matching variables. An independent investigator blinded for all other variables except for matching variables performed the matching.

Statistical analysis

All statistical analysis was done using SPSS version 23 software. Descriptive data are presented as mean $\pm$ standard deviation, median (IQR) for continuous variables and frequency (percentages) for categorical variables. A matched analysis was done to compare clinical outcomes between the vaccinated and the unvaccinated control groups. Paired analysis was done using McNemar and paired-sample *t*-test/Wilcoxon signed-rank test for categorical and continuous variables, respectively. Chi-square/Fisher's exact and Student's *t*-test/Mann–Whitney U test were used for analysis within the group to see for any difference in clinical variables between vaccine types and the number of vaccine doses. Statistical significance was considered at $p < 0.05$ for all tests. Conditional logistic regression was used to obtain the odds ratio for paired data.

Results

This study included a total of 210 patients, with 105 in each of the vaccinated and unvaccinated groups who were matched 1:1 as per the criteria described earlier.

Characteristics of vaccinated COVID-19 patients

The mean age of the study population was 59.5 $\pm$ 13.9 years and 70 (66.7%) were males. Hypertension (44.8%) and diabetes mellitus (37.1%) were the most common comorbidities. The median duration of symptom onset was 15 (7–28) days post any dose of vaccine and a median duration between symptom onset to hospitalization was 5 (3–9) days.

Out of 105 vaccinated patients, 47 (44.8%) had received ChAdOx1 nCoV-19 and 58 (55.2%) had received BBV152. However, 73 patients (69.5%) were vaccinated with a single dose and 32 (30.5%) had received two doses of the vaccine. Also, 19 patients were fully vaccinated with two doses of vaccine and had symptom onset after 14 days of vaccination (Supplementary Appendix-Table S1). However, 46 patients (43.8%) had mild disease, 36 (34.3%) had moderate disease and 23 (21.9%) had severe disease at admission. In addition, 8 out of 19 (42.1%) patients in the fully vaccinated group had severe disease. Severity progression was noted in 18% (19/105) of the patients in the vaccinated group during their hospital course with 32.4% of patients ultimately developing severe disease.

Six patients had extrapulmonary manifestations in the form of non-ST segment elevation myocardial infarction (NSTEMI; 2), myocarditis (1), bradycardia (1), deep vein thrombosis (DVT) (1) and ischaemic middle cerebral artery (MCA) infarct with hemorrhagic transformation (1). The patients who developed NSTEMI and DVT had received ChAdOx1 nCoV19 and the others

BBV152. The median CT severity score was 10/25 (8–17). The highest oxygen delivery devices that were required in most patients included nasal prongs/face mask (28.6%) and high-flow nasal cannula (HFNC; 16.2%). Eight patients required invasive mechanical ventilation.

The median duration of hospital stay was 10 (7–14) days. All-cause mortality was 8.6% (9/105). Two deaths were noted in patients who had received two doses and completed 14 days post-vaccination. Detailed mortality data have been presented in Supplementary Appendix-Table S2. Detailed demographic, clinical, baseline laboratory, treatment and clinical outcome data are presented in Tables 1–3.

Results of 1:1 matched analysis with unvaccinated COVID-19 patients

Matched analysis was performed to look for any difference in clinical outcome (all-cause mortality and duration of hospital stay) among vaccinated and unvaccinated groups. Age, sex, severity and major comorbidities were the matching variables. Among the laboratory parameters, median baseline C-reactive protein (16.7 mg/litre) was higher in the unvaccinated group but not statistically significant ($p = 0.13$). HFNC use was significantly higher in the vaccinated patients (16.2%, $p = 0.008$), while a significantly higher proportion of patients in the unvaccinated group required mechanical ventilation (21.9%, $p = 0.003$). Low-molecular-weight heparin administration was significantly more ($p = 0.04$) in the unvaccinated group. There is a possibility of physician bias in the prescription, which cannot be ruled out. Among the clinical outcomes, all-cause mortality was significantly higher in the unvaccinated group 23/105 (21.9%, $p = 0.007$) compared to the 9/105 (8.6%) vaccinated group. The median duration of hospital stay was similar among the two groups ($p = 0.84$). Conditional logistic regression showed that vaccinated patients had higher odds of survival during hospitalization (OR = 3.8, 95% CI: 1.42–10.18) than their unvaccinated counterparts (Table 3).

Subgroup analysis within the vaccinated patients – based on the type of vaccine and number of doses

Participants in both the vaccine groups (ChAdOx1 nCoV-19/BBV152) were similar in demographic profile, baseline severity, baseline laboratory parameters, baseline inflammatory markers and the treatment received except that the patients with coronary artery disease were more in the ChAdOx1 nCoV-19 group. There was no statistically significant difference in duration of hospital stay ($p = 0.14$) and all-cause mortality ($p = 0.98$) between the two vaccines.

All baseline data were similar between those who received one-dose vaccine and two-dose vaccines except that the number of patients with malignancy was higher in those who received two doses and median platelet count was lower in individuals who received one-dose vaccine than those who received two doses of vaccine. All-cause mortality ($p = 0.57$) and duration of hospital stay ($p = 0.88$) were not statistically different between one-dose and two-dose vaccine groups (Tables 1–3).

Discussion

The current efficacy data for various COVID-19 vaccines are calculated using the primary endpoint of preventing symptomatic illness. This varies from > 90% with the mRNA-based vaccines[11,12] to about 70% with the adenovirus-vectored vaccines such as ChAdOx1 nCoV-19.[13] Real-world data on vaccine effectiveness of BBV152 in a test-negative case–control study were 50%.[14] Arguably, the most important measure would be to know how effective the vaccines are in preventing moderate-to-severe COVID-19 or death, especially in high-risk individuals. This is demonstrated in the fact that the focus of surveillance has now shifted to identifying and investigating only hospitalized or fatal cases of breakthrough infections. ICMR has also recommended all hospitals to provide systematic data on hospitalizations after vaccination.

Initial data during the delta wave from Eastern India reported that 9.9% (27/274) of patients with breakthrough infections required hospitalization.[15] Other studies which described breakthrough infections from India mainly reported either mild or asymptomatic infections, with healthcare workers as their major cohort. Among about 7000 healthcare workers in Vellore, vaccination with two doses of ChAdOx1 nCov-19 reduced hospitalization (Relative Risk = 0.23), need for oxygen therapy (Relative Risk = 0.08) and intensive care admission (Relative Risk = 0.06) significantly.[16] Prospective data from another cohort in Northern India

Table 1. Demographic profile and baseline clinical characteristics.

Characteristics		Vaccination status (paired analysis)			Type of vaccine			No. of vaccine doses		
		Vaccinated (*N* = 105)	Unvaccinated (*N* = 105)	*p* value	ChAdOx1 nCoV-19 (*N* = 47)	BBV152 (*N* = 58)	*p* value	One dose (*N* = 73)	Two doses (*N* = 32)	*p* value
Age, years (M ± SD)		59.5 ± 13.9	59.8 ± 14.4	0.35	61.5 ± 12.4	57.9 ± 14.9	0.18	57.6 ± 13.3	63.7 ± 14.6	0.05
Male, *N* (%)		70 (66.7)	70 (66.7)	1	31 (66)	39 (67.2)	0.89	49 (67.1)	21 (65.6)	0.88
Baseline severity, *N* (%)	Mild Moderate Severe	46 (43.8) 36 (34.3) 23 (21.9)	46 (43.8) 36 (34.3) 23 (21.9)	1	19 (40.4) 19 (40.4) 9 (19.1)	27 (66.6) 17 (29.3) 14 (24.1)	0.48	31 (42.5) 29 (39.7) 13 (17.8)	15 (46.9) 7 (21.9) 10 (31.3)	0.14
Severity progression, *N* (%)		19 (18.1)			8 (17)	11 (19)	0.8	11 (15.1)	8 (25)	0.22
Maximum severity, *N* (%)	Mild Moderate Severe	38 (36.2) 33 (31.4) 34 (32.4)			16 (34) 17 (36.2) 14 (29.8)	22 (37.9) 16 (27.6) 20 (34.5)	0.64	28 (38.4) 24 (32.9) 21 (28.8)	10 (31.3) 9 (28.1) 13 (40.6)	0.49
Median duration between symptom onset to hospitalization, days (IQR)		5 (3–9)	7 (3–9)	1	6	5	0.15	5	7	0.47
Median days of symptom onset post-vaccination (IQR), days		15 (7–28)			17	14	0.29	15	17	0.93
Comorbidities, *N* (%)										
Diabetes mellitus		39 (37.1)	47 (44.8)	0.10	18 (38.3)	21 (36.2)	0.83	27 (37)	12 (37.5)	0.96
Hypertension		47 (44.8)	46 (43.8)	1	20 (42.6)	27 (46.6)	0.68	30 (41.1)	17 (53.1)	0.25
Chronic kidney disease		4 (3.8)	6 (5.7)	0.69	3 (6.4)	1 (1.7)	0.32	4 (5.5)	0	0.31
Coronary artery disease		14 (13.3)	20 (19)	0.21	10 (21.3)	4 (6.9)	0.04	10 (13.7)	4 (12.5)	1
Chronic liver disease		3 (2.9)	1 (1)	0.63	0	3 (5.2)	0.25	1 (1.4)	2 (6.3)	0.22
Cerebrovascular disease		4 (3.8)	2 (1.9)	0.69	0	4 (6.9)	0.13	3 (4.1)	1 (3.1)	1
Chronic obstructive pulmonary disease		4 (3.8)	3 (2.9)	1	2 (4.3)	2 (3.4)	1	2 (2.7)	2 (6.3)	0.58
Bronchial asthma		5 (4.8)	2 (1.9)	0.38	4 (8.5)	1 (1.7)	0.17	3 (4.1)	2 (6.3)	0.64
Malignancy		4 (3.8)	2 (1.9)	0.63	2 (4.3)	2 (3.4)	1	0	4 (12.5)	0.008
Rheumatological disorder		2 (1.9)	1 (1)	1	2 (4.3)	0	0.2	2 (2.7)	0	1
Hypothyroidism		12 (11.4)	5 (4.8)	0.14	6 (12.8)	6 (10.3)	0.76	6 (8.2)	6 (18.8)	0.12
Clinical features, *N* (%)										
Fever		79 (75.2)	78 (74.3)	1	34 (72.3)	45 (77.6)	0.54	56 (76.7)	23 (71.9)	0.60
Cough		72 (68.6)	59 (56.2)	0.07	36 (76.6)	36 (62.1)	0.11	50 (68.5)	22 (68.8)	0.98
Breathlessness		47 (44.8)	54 (51.4)	0.32	21 (44.7)	26 (44.8)	0.99	34 (46.6)	13 (40.6)	0.57
Vitals, M ± SD										
Pulse rate (bpm)		87 ± 16	88 ± 11	0.70	89 ± 14	85 ± 17	0.17	87 ± 13	86 ± 21	0.85

(Continued)

Table 1. (Continued)

Characteristics	Vaccination status (paired analysis)			Type of vaccine			No. of vaccine doses		
	Vaccinated (*N* = 105)	Unvaccinated (*N* = 105)	*p* value	ChAdOx1 nCoV-19 (*N* = 47)	BBV152 (*N* = 58)	*p* value	One dose (*N* = 73)	Two doses (*N* = 32)	*p* value
Mean arterial pressure (mmHg)	93 ± 10	95 ± 9	0.32	93 ± 10	93 ± 10	0.95	94 ± 10	93 ± 9	0.52
Respiratory rate (cpm)	22 ± 5	23 ± 5	0.1	23 ± 6	22 ± 5	0.62	22 ± 6	22 ± 5	0.92
Oxygen saturation (%)	92 ± 5	92 ± 6	0.44	92 ± 5	92 ± 5	0.62	92 ± 4	91 ± 7	0.32

bpm, beats per minute; mmHg, millimeter of mercury; cpm, cycles per minute; IQR, Inter-quartile range; M, Mean; SD, Standard deviation.

Table 2. Baseline laboratory parameters and radiological investigations.

Characteristics (Median, IQR)	Vaccination status (paired analysis)			Type of vaccine			No. of vaccine doses		
	Vaccinated	Unvaccinated	*p* value	ChAdOx1 nCoV-19 (*N* = 47)	BBV152 (*N* = 58)	*p* value	One dose (*N* = 73)	Two doses (*N* = 32)	*p* value
Haemoglobin (g/dl)	12.8 (11.9–14.1)	12.3 (11.1–13.7)	0.24	12.6	13	0.15	12.8	12.8	0.87
Total leukocyte count (cells/dl)	7270 (4965–10,715)	7810 (5500–11,975)	0.49	7910	6885	0.12	7420	7000	0.67
Neutrophil–lymphocyte ratio	5.1 (3.1–9.2)	6.6 (3.9–12)	0.20	6.8	4.8	0.10	5.7	4.5	0.3
Platelets (cells/dl) lakhs	1.63 (1.20–2.14)	1.8 (1.28–2.5)	0.43	1.62	1.65	0.22	1.50	1.84	0.01
AST (IU/litre)	34 (27–53)	45 (28–62)	0.02	32	40.5	0.05	35	32	0.69
ALT (IU/litre)	33 (22–52.5)	40 (25–66)	0.007	30	33	0.23	35	30	0.67
Bilirubin (mg/dl)	0.7 (0.5–0.8)	0.6 (0.5–0.8)	0.35	0.7	0.7	0.74	0.7	0.7	0.46
ALP (IU/litre)	70 (56–93.5)	81 (62–102)	0.37	70	72	0.81	73	67	0.46
Urea (mg/dl)	40 (29.5–54)	38 (26–57)	0.23	39	40.9	0.73	41	39	0.35
Creatinine (mg/dl)	0.85 (0.7–1.1)	0.9 (0.7–1.14)	0.41	0.8	0.9	0.38	0.82	0.9	0.91
CRP (mg/litre)	6.7 (1.8–20.5), *n* = 99	16.7 (2.9–87.5), *n* = 103	0.13	7.5, *n* = 44	4.2, *n* = 55	0.11	7.05	4.43	0.72
Ferritin (mg/litre)	327 (138.7–596), *n* = 101	406 (233–696), *n* = 91	0.45	321, *n* = 44	325, *n* = 56	0.98	318	332	0.92
D-dimers (mcg/ml)	0.8 (0.4–3.5), *n* = 32	1.9 (0.8–4.4), *n* = 34	1	0.8, *n* = 17	0.8, *n* = 15	0.58	0.88	0.69	0.58
LDH (IU/litre) (91)	317 (227–406)	324 (241–432)	0.23	306, *n* = 39	319.5, *n* = 52	0.83	333	271	0.09
CT score (out of 25)	10 (8–17), *n* = 69	11 (5–15), *n* = 44	0.68	11, *n* = 30	10, *n* = 39	0.56	11	10	0.47

ALP, Alanine aminotransferase; ALT, Alkaline phosphatase; AST, Aspartate aminotransferase; CRP, C-Reactive protein; CT, Computed tomography; g/dl, gram/decilitre; IL-6, Interleukin-6; IQR, Inter-quartile range; IU/litre, international unit/litre; LDH, Lactate dehydrogenase; mcg/ml, microgram/millilitre; mg/dl, milligram/decilitre; pg/ml, picogram/millilitre.

Table 3. Treatment and clinical outcomes.

Characteristics	Vaccination status (paired analysis)			Type of vaccine			No. of vaccine doses		
	Vaccinated	Unvaccinated	*p* value	ChAdOx1 nCoV-19 (*N* = 47)	BBV152 (*N* = 58)	*p* value	One dose (*N* = 73)	Two doses (*N* = 32)	*p* value
Oxygen device used, *N* (%)									
Face mask/nasal prongs	30 (28.6)	28 (26.7)	0.85	14 (29.8)	16 (27.6)	0.8	19 (26)	11 (34.4)	0.38
NRBM	12 (11.4)	11 (10.5)	1	6 (12.8)	6 (10.3)	0.7	9 (12.3)	3 (9.4)	0.75
HFNC	17 (16.2)	5 (4.8)	0.008	6 (12.8)	11 (19)	0.39	11 (15.1)	6 (18.8)	0.64
NIV	1 (1)	2 (1.9)	1	1 (2.1)	0	0.26	1 (1.4)	0	1
Mechanical ventilator	8 (7.6)	23 (21.9)	0.003	5 (10.6)	3 (5.2)	0.46	6 (8.2)	2 (6.3)	1
Medications (*N* = 103)									
Doxycycline	38 (36.9)	35 (34)	0.75	19 (40.4)	19 (32.8)	0.42	29 (39.7)	9 (28.1)	0.26
Ivermectin	41 (39.8)	33 (32)	0.27	22 (46.8)	19 (32.8)	0.14	31 (42.5)	10 (31.3)	0.28
Methylprednisolone	50 (48.5)	59 (57.3)	0.18	19 (40.4)	31 (53.4)	0.18	36 (49.3)	14 (43.8)	0.60
Dexamethasone	12 (11.7)	9 (8.7)	0.63	7 (14.9)	7 (12.1)	0.67	9 (12.3)	5 (15.6)	0.76
LMWH	52 (50.3)	65 (63.1)	0.04	24 (51.1)	30 (51.7)	0.95	36 (49.3)	18 (56.3)	0.51
Remdesivir	44 (42.7)	44 (42.7)	1	18 (38.3)	27 (46.6)	0.4	35 (47.9)	10 (31.3)	0.11
Clinical outcomes									
Median duration of hospital stays (IQR), days	10 (7–14)	10 (6–15)	0.84	9	11	0.14	10	9	0.88
Deaths, *N* (%)	9 (8.6)	23 (21.9)	0.007	4 (8.5)	5 (8.6)	0.98	7 (9.6)	2 (6.3)	0.57
Odds of survival (95% CI)	3.8 (1.42–10.18)								

CI, confidence interval; HFNC, High-flow nasal cannula; IQR, Inter-quartile range; LMWH, Low-molecular-weight heparin; NIV, Non-invasive ventilation; NRBM, Non-rebreathing face mask.

demonstrated similar results, with a statistically significant decrease in moderate-to-severe disease (1.2% *versus* 3.4%, adjusted Hazard Ratio = 0.35) between the two-dose vaccinated and unvaccinated cohort.[8] A study from South India on breakthrough infections among healthcare workers reported that 5.5% required hospitalization, none of them required supplemental oxygen and there was no mortality.[17]

Other real-world data regarding the effectiveness of BBV152 are limited to a large study done in India among BBV152-vaccinated individuals which demonstrated a vaccine effectiveness of 50% against symptomatic COVID-19. This was a test-negative case–control study done during the second wave of COVID-19 which was predominantly due to the delta variant.[14] Data from 553 patients studied in the same centre showed a dose-dependent protection against the development of disease following vaccination, and the odds of hospitalization and death were 0.12 and 0.07, respectively.[18]

Our study added light to the outcomes of vaccinated hospitalized patients, by describing the profile of patients who had received at least one dose of either ChAdOx1 nCoV-19 or BBV152 vaccine. Severe disease was observed in 32.4% of all vaccinated patients requiring admission with an

all-cause mortality of 8.6% in our study and two deaths among fully vaccinated individuals. Results of our matched analysis showed that vaccinated patients had more than threefold higher chances of survival. We were able to discharge 91.4% of vaccinated patients compared to 78.1% of unvaccinated patients. In a study of mRNA BNT162b2, the clinical effectiveness was 97.5% against severe or critical COVID-19-related hospitalization, and 96.7% against COVID-19-related deaths.[19]

Around 70% of the patients in our study were included 14 days after they had received only one dose of either vaccine. Satwik *et al.* demonstrated that the efficacy of one dose of ChAdOx1 nCoV-19 in preventing moderate to severe was just 7% as compared to an efficacy of 67% with two doses.[8] In a 2-month follow-up of 1400 patients vaccinated with ChAdOx1 nCoV-19, severe COVID-19 was 7.7 times lower in fully vaccinated individuals than partially vaccinated ones.[9] Data regarding BBV152 showed an adjusted OR of 1 (0.67–1.51) for symptomatic COVID-19 after one dose and 0.5 (0.38–0.67) after two doses.[14] Our study did not demonstrate a statistically significant difference between partially and completely vaccinated individuals, although 40.6% went on to develop severe disease in the one-dose group as compared to 28.8% in the two-dose group.

Severe disease and mortality were observed after complete vaccination. Comorbidities, such as diabetes mellitus, obesity, chronic lung disease including asthma, hypertension and chronic kidney disease, pose worse outcome in COVID-19. This has been previously elucidated from multiple well-powered studies.[20–22] Of the few patients who developed extrapulmonary complications, we did note that NSTEMI and DVT occurred in those who had received ChAdOx1 nCov-19. This vaccine has been implicated in a few case reports to have led to myocardial infarction in the absence of COVID-19 infection as well.[23,24]

Our study had few limitations. First, the severity profile and mortality may seem higher because the study was done at an apex COVID care facility which usually receives a high proportion of referred sick patients. However, the paired matching between vaccinated and unvaccinated patients takes care of this without affecting the outcome variable of mortality. Second, the data of our matched population were retrospective. All efforts were made to match the two groups for age, sex, comorbidities and baseline severity. However, we were unable to capture the data for severity progression among the unvaccinated group as it was retrospectively collected. There might be a possibility that the high all-cause mortality in the unvaccinated group may have been due to reasons other than progression to severe disease. Third, given the rapid turnover of patients along with a paucity of manpower during this study period, several vaccinated patients could have likely been missed in our recruitment. We included the maximum number of vaccinated individuals we could. The resulting sample size was small. Moreover, the number of patients who were fully vaccinated (post two doses and post 14 days) was considerably less. This can be understood as the study was started in March 2021 coinciding with the second wave of COVID-19 which was close to the inception of the vaccination campaign in India from the middle of January. Finally, data on random blood sugar, antibody levels and genomic sequencing are lacking and would have provided additional conclusive information. However, we are aware that the predominant variant circulating during the study period was the delta variant.

This is one of the initial prospective studies to investigate the clinical details and outcomes among a hospitalized cohort of vaccinated patients. While more such studies can throw further light on outcomes in vaccinated individuals, until then we urge to follow infection prevention strategies and COVID appropriate behaviour along with the vaccine jabs.

Conclusion

The study coincided with the second wave of the COVID-19 pandemic which was predominated by the delta variant of SARS CoV-2. The vaccinated cohort had better outcomes for survival than the unvaccinated matched controls in the study. However, the higher all-cause mortality in the unvaccinated group may be due to reasons other than mere progression to severe COVID-19. This being a preliminary study requires further exploration into this aspect.

Declarations

Ethical approval and consent to participate

Ethical clearance was obtained from Institute Ethics Committee, All India Institute of Medical

Sciences, New Delhi (IECPG-337). Informed consent to participate was obtained from participants.

Consent for publication
Not Applicable.

Author contributions
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References
1. Bagcchi S. The world's largest COVID-19 vaccination campaign. *Lancet Infect Dis* 2021; 21: 323.
2. COVID vaccines approved in India: Covishield, Covaxin, Sputnik V, Moderna; here's all you wish to know, https://www.timesnownews.com/health/article/covid-vaccines-approved-in-india-

covishield-covaxin-sputnik-v-moderna-heres-all-you-wish-to-know/778482

3. Cumulative coverage report of COVID-19 vaccination, https://www.mohfw.gov.in/pdf/CummulativeCovidVaccinationReport30thjune2021.pdf
4. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports
5. Hacisuleyman E, Hale C, Saito Y, *et al.* Vaccine breakthrough infections with SARS-CoV-2 variants. *N Engl J Med* 2021; 384: 2212–2218.
6. Only 2 to 4 in 10,000 breakthrough infections: ICMR chief Balram Bhargava, https://www.expresshealthcare.in/news/only-2-to-4-in-10000-breakthrough-infections-icmr-chief-balram-bhargava/428177/
7. CDC COVID-19 Vaccine Breakthrough Case Investigations Team. COVID-19 vaccine breakthrough infections reported to CDC – United States, January 1-April 30, 2021. *MMWR Morb Mortal Wkly Rep* 2021; 70: 792–793.
8. Satwik R, Satwik A, Katoch S, *et al.* ChAdOx1 nCoV-19 effectiveness during an unprecedented surge in SARS COV-2 infections. *Eur J Intern Med* 2021; 93: 112–113.
9. Kaur U, Bala S, Ojha B, *et al.* Occurrence of COVID-19 in priority groups receiving ChAdOx1 nCoV-19 coronavirus vaccine (recombinant): a preliminary analysis from north India. *J Med Virol* 2022; 94: 407–412.
10. Hodgson SH, Mansatta K, Mallett G, *et al.* What defines an efficacious COVID-19 vaccine? A review of the challenges assessing the clinical efficacy of vaccines against SARS-CoV-2. *Lancet Infect Dis* 2021; 21: e26–e35.
11. The Moderna COVID-19 (mRNA-1273) vaccine: what you need to know, https://www.who.int/news-room/feature-stories/detail/the-moderna-covid-19-mrna-1273-vaccine-what-you-need-to-know (accessed 1 May 2022).
12. The Pfizer BioNTech (BNT162b2) COVID-19 vaccine: what you need to know, https://www.who.int/news-room/feature-stories/detail/who-can-take-the-pfizer-biontech-covid-19–vaccine-what-you-need-to-know (accessed 1 May 2022).
13. Knoll MD and Wonodi C. Oxford–AstraZeneca COVID-19 vaccine efficacy. *Lancet* 2021; 397: 72–74.
14. Desai D, Khan AR, Soneja M, *et al.* Effectiveness of an inactivated virus-based SARS-CoV-2 vaccine, BBV152, in India: a test-negative, case-control study. *Lancet Infect Dis* 2022; 22: 349–356.
15. Dash GC, Subhadra S, Turuk J, *et al.* Breakthrough SARS-CoV-2 infections in an eastern state of India: a preliminary report. *Res Sq*. Epub ahead of print 23 June 2021. DOI: 10.21203/rs.3.rs-649914/v1.
16. Victor PJ, Mathews KP, Paul H, *et al.* Protective effect of COVID-19 vaccine among health care workers during the second wave of the pandemic in India. *Mayo Clin Proc* 2021; 96: 2493–2494.
17. Niyas VKM and Arjun R. Breakthrough COVID-19 infections among health care workers after two doses of ChAdOx1 nCoV-19 vaccine. *QJM* 2021; 114: 757–758. DOI: 10.1093/qjmed/hcab167.
18. Bhattacharya A, Ranjan P, Ghosh T, *et al.* Evaluation of the dose-effect association between the number of doses and duration since the last dose of COVID-19 vaccine, and its efficacy in preventing the disease and reducing disease severity: a single centre, cross-sectional analytical study from India. *Diabetes Metab Syndr* 2021; 15: 102238–102238.
19. Haas EJ, Angulo FJ, McLaughlin JM, *et al.* Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data. *Lancet* 2021; 397: 1819–1829.
20. Kaur U, Bala S, Ojha B, *et al.* Patterns and predictors of COVID-19 occurrence and severity in vaccinated priority groups. *Res Sq*. Epub ahead of print 28 December 2021. DOI: 10.21203/rs.3.rs-1204671/v1.
21. Mehta AA, Haridas N, Belgundi P, *et al.* A systematic review of clinical and laboratory parameters associated with increased severity among COVID-19 patients. *Diabetes Metab Syndr* 2021; 15: 535–541.
22. Zhu J, Ji P, Pang J, *et al.* Clinical characteristics of 3062 COVID-19 patients: a meta-analysis. *J Med Virol* 2020; 92: 1902–1914.
23. Chatterjee S, Ojha UK, Vardhan B, *et al.* Myocardial infarction after COVID-19 vaccination-casual or causal? *Diabetes Metab Syndr* 2021; 15: 1055–1056.
24. Singh R, Chakrabarti SS, Gambhir IS, *et al.* Acute cardiac events after ChAdOx1 nCoV-19 corona virus vaccine: report of three cases. *Am J Ther*. Epub ahead of print 11 January 2022. DOI: 10.1097/MJT.0000000000001472.