Measuring the impact of a single dose of ChAdOx1 nCoV-19 (recombinant) coronavirus vaccine on hospital stay, ICU requirement, and mortality outcome in a tertiary care centre

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ABSTRACT

Objective: To comparatively evaluate ICU requirement, length of stay, and mortality between single-dose vaccinated and non-vaccinated hospitalized COVID-19 patients.

Design: A retrospective observational study was carried out in a tertiary care hospital in western Indian, from April 1 to June 30, 2021.

Results: Of the 569 patients who fulfilled the eligibility criteria and were enrolled in the study, 137 (24.08%) patients had received a single dose of ChAdOx1 nCoV-19 vaccine, while 432 (75.92%) patients had not received any form of vaccination. The overall length of stay in hospital was similar for both groups; however, a significant difference was seen in length of stay in the ward and in the ICU. Vaccinated patients were admitted to the ward for 6.21 ± 3.204 days, while non-vaccinated patients were admitted for 5.56 ± 4.55 days ($p < 0.001$). The mean length of ICU stay for the 21 vaccinated patients requiring intensive care was 4.47 ± 2.3 days, while that for the 145 non-vaccinated patients was 6.29 ± 2.19 days ($p < 0.001$). Mortality was observed in four patients in the vaccinated group and in 95 patients in the non-vaccinated group.

Conclusion: A single dose of ChAdOx1 nCoV-19 vaccine was associated with a significantly lower severity of SARS-CoV-2 infection compared with no vaccination.

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Introduction

On March 11, 2020, WHO declared COVID-19 to be a pandemic [World Health Organization, 2020]. Most of countries have since faced significant challenges in combating this disease. By June 2021, the cumulative number of cases reported globally had exceeded 180 million, and the number of global deaths had reached almost 4 million across 216 countries.

India has been among the highest-ranked countries in terms of sharp surges in identified cases, as well as death rates. During the first wave of the pandemic, the rate of SARS-CoV-2 infection was somewhat controlled by the nationwide lockdown imposed by the Indian Government in March, 2020 [Singh and Adhikari, 2020]. However, due to an increase in community transmission of the virus, the 7-day average of daily cases in India reached 93 617 on September 16, 2020, which at that point was the highest recorded so far [Pujari and Shekatkar, 2020].

The global vaccination development efforts by leading pharmaceutical companies have shown positive outcomes in terms of providing immunity, as well as decreasing the severity of the disease with up to 94% efficacy [World Health Organization COVID tracker, 2020]. The Government of India has approved emergency authorization for two of the eight vaccine candidates currently under clinical trials. First is the non-replicating chimpanzee adenovirus vaccine vector ChAdOx1, manufactured by the Serum Institute of India in collaboration with the University of Oxford and AstraZeneca, under the trade name Covishield™ [Voysey et al., 2021]. The second is the inactivated-virus vaccine BBV152, developed by Bharat Biotech International under the trade name Covaxin™ [Ella et al., 2021a]. At the height of the crisis, India gave restricted approval to the Russian vaccine SPUTNIK-V [ICMR New Delhi, 2021].

Despite India's extensive vaccination campaign, only a fraction of the population has been vaccinated due to the country very large population [Bagcchi, 2021 and Ranjan et al., 2021]. Towards the end of June 2021, 370 million doses had been administered, resulting in roughly 5% of the total population being fully vaccinated and 22% receiving at least a single dose. Of these, 321.4 million doses of Covishield™ and 45.47 million doses of Covaxin™ had been administered [ICMR New Delhi, 2021].

On April 26, 2021, India saw the highest daily tally of new SARS-CoV-2 infections ever recorded in the world (360 960), taking its pandemic total to 16 million cases — second only to the US — and more than 200 000 deaths. The devastating second wave came a year after the country imposed one of the most rigid lockdown restrictions in the world, and just 3 months after the health ministry declared that infections and mortality were at an all-time low [Thiagarajan, 2021].

The second wave of COVID-19 in India has had severe consequences in the form of spiraling cases, reduced supplies of essential treatments, and increased deaths — particularly in the young population. Studies have identified various circulating double- and triple-mutant strains of the original B.1.617 lineage of SARS-CoV-2, known as Delta AY.1 and Delta AY.2, across different regions of India, which are more pathogenic than the initial strains [Asrani et al., 2021 and Lancet, 2021]. The Delta variant has been reported to be 60% more transmissible than the Alpha variant (B.111.7), and WHO has designated the Delta variant as a variant of concern (VOC) [Kale et al., 2021].

The government of India has imposed multiple measures to reduce the spread and flatten the curve. The 'test-track-treat' protocol has been implemented since April 2021 [Ministry of Home Affairs, 2021]. This includes RT-PCR testing, isolating/quarantining positive cases, tracing all possible contacts within 72 hours, imposing curfews in major cities, containment zoning in high-volume areas, bans on religious/political gatherings, travel restrictions, and prioritizing vaccinations for certain population groups.

Developing an infection after vaccination is known as a 'breakthrough infection'. So far, 2–4 breakthrough infections per 10 000 people have occurred, which is a very low number [Tyagi et al., 2021]. Patients infected with SARS-CoV-2 in the first wave were predominantly older than 60 years, and those with comorbid conditions were at increased risk of death. However, surprisingly, younger adults appear to be prone to infection during this second wave, and many patients have died at a young age, including those aged 25–50 years [Jain et al., 2021].

Our study aimed to estimate the real-life impact of a single dose of ChAdOx1 nCoV-19 vaccine on hospitalized patients infected with SARS-CoV-2. Our primary outcome was to determine the efficacy of a single vaccine dose in reducing the severity of SARS-CoV-2 infection. It is hoped that our results will have some impact in decreasing vaccine hesitancy in the population and encouraging more people to become vaccinated, so that maximum immunity can be achieved.

Materials and methods

Study design

This was a retrospective, single-centre, descriptive observational study based on secondary clinical data analysis of patients admitted to a tertiary COVID care centre (CCC) from April 1 to June 30, 2021 in western India. The subjects were categorized into two cohorts based on their ChAdOx1 nCoV-19 vaccination status. The protocol, performa, case record form, and informed consent form were reviewed by the Institutional Ethics Committee (IEC). The study was initiated after receiving written approval from the IEC and written informed consent of participants in vernacular language. Confidentiality of all the data was maintained.

Study participants

Consenting patients aged 18 years and above, with symptomatic SARS-CoV-2 infection and a positive polymerase chain reaction, were considered eligible; these accounted for about 94% of total admissions. Patients who had received a single dose of ChAdOx1 nCoV-19 vaccine were placed in one group, while those who had not received any vaccine were in the control group. Patients vaccinated with any vaccine other than those defined in the inclusion criteria were excluded from the study. Patients vaccinated with both doses of ChAdOx1 nCoV-19 were also excluded because the sample size for that cohort was very low. The criteria for admission to the ward and the ICU for the SARS-CoV-2 patients were predetermined, based on presenting symptoms and clinical signs.

Data collection

Demographic data, such as age and gender, were recorded on the case record form. Next, the following data were recorded: date of admission; date of positive RT-PCR test, fresh infection, or re-infection; vaccination details, including date of vaccination; length of stay in hospital; duration of stay in ward and/or intensive care unit; and the number of days requiring ventilator support. The subsequent section contained details on comorbid conditions that may have aggravated COVID-19 symptoms, including diabetes mellitus, hypertension, cardiac diseases, thyroid disorders, renal diseases, liver diseases, respiratory diseases, cancer, previous history of surgery, and pregnancy. The final section comprised the final outcome of the treatment.

Table 1
Baseline characteristics of patients with SARS-CoV-2 infection, and vaccination status

		Enrolled patients($n = 569$)	Vaccinated group($n = 137$)	Non-vaccinated group($n = 432$)	*p*-value
Age (years)		55.55 ± 15.769	61.71 ± 11.93	53.59 ± 16.32	0.001
Gender	Male (%)	347 (61%)	84 (61.3%)	263 (60.9%)	0.505
	Female (%)	222 (39%)	53 (38.7%)	169 (39.1%)	
Diabetes (%)		149 (26.2%)	40 (29.2%)	109 (25.2%)	0.373
Hypertension (%)		214 (37.6%)	63 (46%)	151 (35%)	0.026
IHD (%)		37 (6.5%)	11 (8%)	26 (6%)	0.427
Thyroid diseases		26 (4.6%)	8 (5.8%)	18 (4.2%)	0.480
Kidney diseases		26 (4.6%)	2 (1.5%)	24 (5.6%)	0.058
Liver diseases		3 (0.5%)	1 (0.7%)	2 (0.5%)	0.563
Respiratory diseases		15 (2.6%)	2 (1.5%)	13 (03%)	0.540
Neoplasms		6 (1.1%)	1 (0.7%)	5 (0.7%)	1.000

Table 2
In-hospital stays and outcome differences between the two groups

	Enrolled patients($n = 569$)	Vaccinated group($n = 137$)	Non-vaccinated group($n = 432$)	*p*-value
Length of ward stay in days	6.11 ± 4.816	6.21 ± 3.20	5.56 ± 4.55	0.257
Length of hospital stay in days	8.35 ± 6.418	8.53 ± 5.89	8.30 ± 6.58	0.179
Length of ICU stay in days (n)*	7.67 ± 5.29 (166)	4.47 ± 2.3 (21)	6.29 ± 2.19 (145)	0.001
Duration of mechanical ventilation in days (n)**	4.49 ± 2.29 (128)	3.77 ± 2.20 (9)	6.83 ± 2.28 (119)	0.001
Mortality	99 (17%)	4 (2.9%)	95 (22%)	0.001

* Mean calculated for the number of subjects admitted to the ICU, excluding those who were not.
** Mean calculated for the number of subjects requiring mechanical ventilation, excluding those who did not.

Statistical analysis

Numerical variables were presented as mean ± SD. Discrete variables were summarized as percentages. The qualitative data were evaluated using Pearson's chi-square test or Fisher's absolute-value chi-square test, while comparisons of quantitative variables between two groups were performed using an independent-sample t-test or the Mann-Whitney test, depending on normality of data, and results with a *p*-value < 0.05 were considered to be statistically significant. The long-term survival for each study group was assessed using Kaplan-Meier analysis with log-rank testing. The results were expressed as hazard ratios (HR) with associated 95% confidence intervals. Cox regression analysis was used to determine variables predictive of survival. All analyses were performed using IBM SPSS Statistics, version 26.

Results

This was a retrospective observational study conducted at a single tertiary COVID care center in western India. Between April 1 and June 30, 2021, 569 patients were enrolled in the study, based on the eligibility criteria described previously. There were 347 males and 222 females, with a mean age of 55.55 ± 15.769 years, with a diagnosis of SARS-CoV-2 infection confirmed by RT-PCR via an oropharyngeal and nasopharyngeal swab. Among the vaccinated patients, mean ± SD age was 61.70 ± 15.7 years, while that for the non-vaccinated group was 53.59 ± 12.1 years, giving a statistically significant difference.

One hundred and sixty-nine patients had no chronic comorbidity. On the other hand, 476 patients presented one or more comorbidities (diabetes 26.2%, hypertension 37.6%, IHD 6.5%, thyroid diseases 4.6%, kidney diseases 4.6%, liver diseases 0.5%, respiratory diseases 2.6%, and neoplasms 1.1%), as shown in Table 1.

Of the 569 patients, 137 (24.08%) had been vaccinated with a single dose of ChAdOx1 nCoV-19 vaccine, while 432 (75.92%) had not received any form of vaccination. Table 2 shows the differences between the two groups regarding the lengths of stay and outcomes during the hospital stay. There were no significant differences in total hospital stay or average length of stay in a ward ($p = 0.179$ and 0.257, respectively). However, there were significant differences between both groups in terms of length of ICU stay

($p = 0.001$) and duration of mechanical ventilation ($p = 0.001$). Twenty-one vaccinated patients were admitted in the ICU, with a mean stay of 4.47 ± 2.3 days, while 145 patients in the non-vaccinated group were admitted to the ICU, with a mean stay of 6.29 ± 2.19 days [Figure 1]. Similarly, nine patients in the vaccinated group required mechanical ventilation, with a mean of 3.77 ± 2.20 days of support, while 119 non-vaccinated patients required mechanical ventilation, with a mean of 6.83 ± 2.28 days of support [Figure 2]. A high rate of mortality was observed in the non-vaccinated group (95/432; 22%) as compared with the vaccinated group (4/137; 2.9%), showing a significant difference ($p < 0.0001$). To investigate whether high differences between the groups in terms of age, gender, and comorbidities could obscure an association with prognosis in COVID-19 patients, a multinomial logistic regression analysis was performed, with mortality as the outcome. After correcting for gender, age, and comorbidities, vaccination was found to be independently associated with a lower risk of mortality ($p < 0.001$; HR 0.142; 95% CI 0.051–0.390). This indicated that vaccinated individuals had an additional 86% protection against mortality after a positive COVID-19 test result [Figure 3].

Of the 292 patients with systemic comorbidities, 83 (60.5%) belonged to the vaccinated group and 209 (48.3%) to the non-vaccinated group. There were significant differences in ward stays and ICU stays between the two cohorts. Vaccinated patients with comorbidities had a mean length of stay in the hospital of 8.26 ± 4.57 days, while that of non-vaccinated patients was 8.94 ± 7.16 days; this difference was not significant ($p = 0.363$). However, the mean length of stay in the ward was 7.65 ± 4.14 days for the vaccinated patients, compared with 5.09 ± 4.80 days for non-vaccinated patients, giving a statistically significant difference ($p < 0.001$). The difference in length of ICU stay was also significant ($p < 0.001$), with vaccinated patients staying for a mean of 3.61 ± 2.06 days and non-vaccinated patients staying for a mean 6.51 ± 2.64 days.

Discussion

The COVID-19 pandemic has proven to be the biggest healthcare challenge of the 21st century, especially for a developing country like India. The first wave showed that timely lockdown measures can help in curbing the spread of the disease. However, the second wave involving the mutated Delta variant has overwhelmed
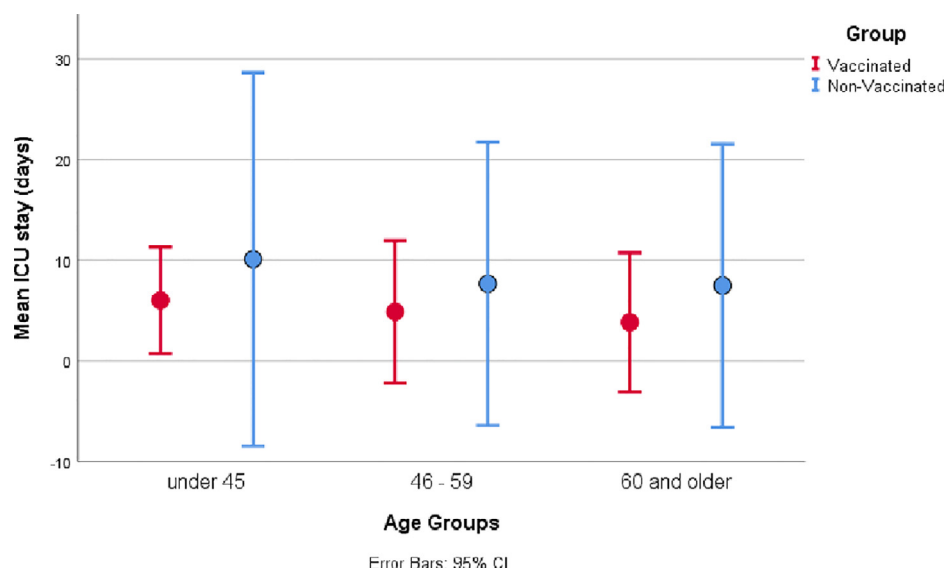
Figure 1. Mean ICU stay by age group, for the vaccinated and non-vaccinated groups
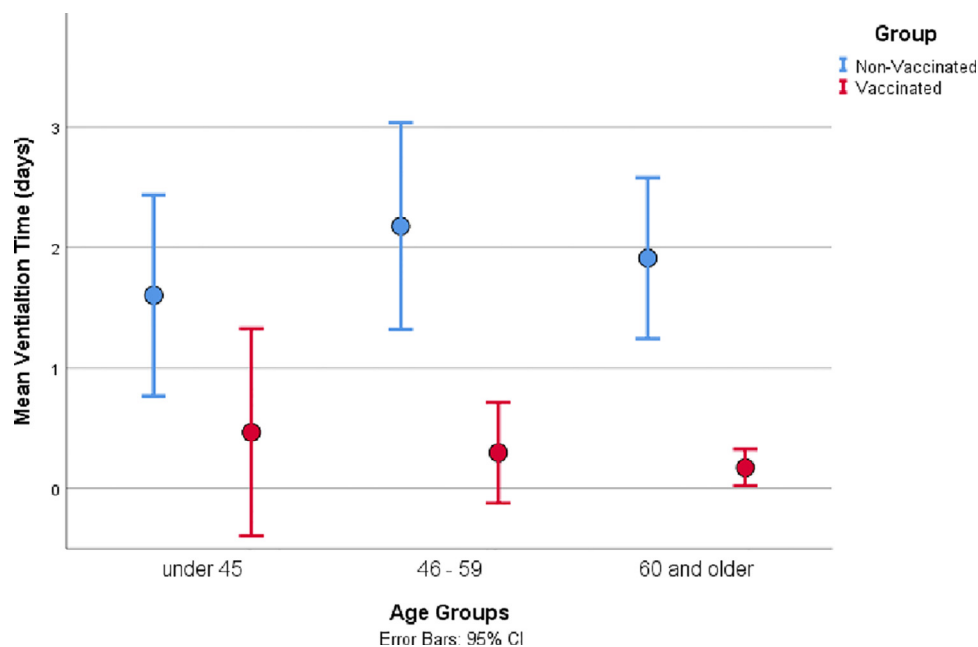

Figure 2. Mean ventilation time by age group, for the vaccinated and non-vaccinated groups

the medical infrastructure, with hospitals struggling to cope with critical drugs and oxygen shortage. As of June 30, 2021, deaths had passed the 0.4 million mark, with 0.11 million in May 2021 alone [COVID-19 Dashboard, 2021]. Prior to April 1, 2021, in what can be loosely termed the first COVID-19 wave in India, little more than 0.16 million deaths had been reported [Worldometers, 2021].

The priority now is acquiring immunity, which can be either naturally or through vaccination. Given India's status as the second-most populous country in the world, it is understandable that the people of India have varying perceptions and concerns about COVID-19 vaccines. Distribution of public health information and education about vaccines had begun before the government approval of Covishield™ and Covaxin™. It is essential that distribution of vaccines and access to vaccination occur in an equal manner countrywide, to ensure that the maximum number of the population is immunized safely and effectively.

WHO has identified vaccine hesitancy as a cause of a global health risk [MacDonald and SAGE group, 2015]. Multiple factors play a role in determining whether a newly introduced vaccine will be accepted widely or not. Aside from these, problems of production, manufacturing, marketing, cold-chain maintenance, and cost also factor into the advent of new vaccines [Sallam, 2021]. Normally it would take months to years to complete the phases of a randomized controlled clinical trial, in order to prove the safety and efficacy of a vaccine. However, with a rapidly spreading and mutating virus, it is imperative that accelerated studies and emergency approvals are implemented as soon as possible.

The aim of our study was to establish the association of partial vaccination with the ChAdOx1 nCoV-19 vaccine with various parameters, such as comorbidity, ICU requirement, length of stay, and mortality in hospitalized COVID-19 patients. Our study found that the overall hospital stay for vaccinated patients was
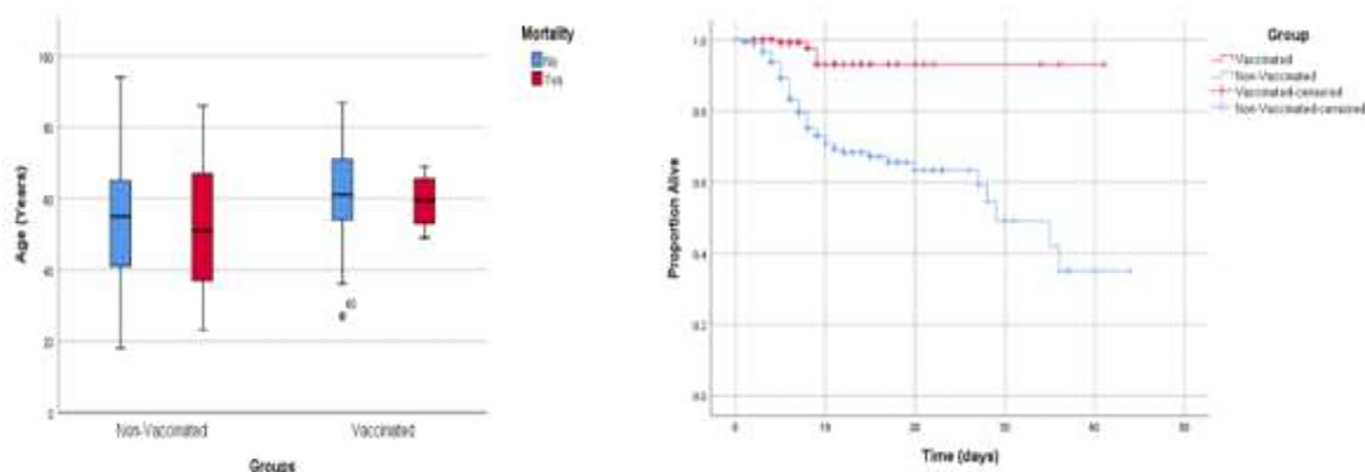
Figure 3. Mortality difference by age and vaccination status, with survival curves, for the vaccinated and non-vaccinated groups

significantly lower than that for non-vaccinated patients. This finding was supported by an ongoing clinical trial, which showed that a single dose of the Ad26.COV2.S vaccine (Janssen) gave significant protection against symptomatic and asymptomatic SARS-CoV-2-infections, and was effective in reducing hospital stays and death rates for severe/critical disease cases [Sadoff et al., 2021].

The vaccinated patients in our cohort showed a mean stay of 6.21 days in the ward, compared with 5.56 days for non-vaccinated patients. This showed that a single shot of the vaccine not only made the patients less vulnerable to severe COVID-19 disease, but also allowed them to be treated without any need for intensive care. A similar study among healthcare professionals has shown improved efficacy of COVID-19 vaccination in terms of hospital stay [Swift et al., 2021]. Overall hospital stays for the two groups were similar, which could be accounted for by the higher mortality in the unvaccinated arm, effectively shortening their stay.

So far India has recorded 434 000 deaths from COVID-19, of which nearly 205 000 occurred in the second wave [Government of India, 2021; Bhattacharya, 2021]. Hospitals recorded 10.5 per cent mortality in the second wave, compared with 7.2 per cent in the first wave. With the advent of vaccination drives, the mortality rate has been under control. Our study showed 2.9% mortalities in the vaccinated cohort compared with 21.9% in the non-vaccinated cohort. This shows that our patients had a better survival rate, even with a single dose of vaccine. Multiple studies have shown that a single dose of vaccine is 70–80% effective in reducing mortality among COVID-19 patients, rising to 95–99% for two doses [Tyagi et al., 2021; Dagan et al., 2021; Vasileiou et al., 2021].

COVID-19 has had a major economic impact, especially among the lower socioeconomic classes in developing countries like India. Severe disease requires a long duration of intensive care admission, along with a need for supplemental life support, which can be expensive. Our study found that 15.32% of the vaccinated patients and 33.56% of the non-vaccinated patients were admitted in the ICU, of whom 42.85% of the vaccinated and 82.06% of the non-vaccinated patients required mechanical ventilation. This suggests that with a single vaccine dose the need for ICU admission and supplemental oxygen support is reduced, thereby decreasing the cost burden of hospitalization on the patients. A similar study reported a significant reduction in hospital expenses and ICU requirements after a first dose of any form of COVID-19 vaccine [Ramakrishnan and Subbarayan, 2021]. Moreover, our results showed that the numbers of patients with diabetes mellitus and hypertension were greater in the vaccinated group, with hospital

stay outcomes better for that group, indicating that partial vaccination leads to less severity of SARS-CoV-2 infection.

Our study had some limitations. In the absence of non-hospitalized patients, there could have been unmeasured differences between vaccinated and non-vaccinated patients. This study could therefore be extended to include non-hospitalized patients. The study could be further extended in the coming months to include more fully vaccinated patients, in order to evaluate the parameters more effectively. Moreover, SARS-CoV-2 antibody levels were tested only in a very small sample of patients due to financial constraints, hence these data were not included in our analysis. Various studies have shown higher levels of SARS-CoV-2 antibodies against different antigens in patients who have received a single dose of the vaccine [Jeewandara et al., 2021; Angyal et al., 2021]. The sample size of our study was also reduced due to study site limitations. A multicentric study could have provided a much larger sample size.

Conclusion

A single dose of ChAdOx1 nCoV-19 coronavirus vaccine (recombinant) was shown to be highly effective, with a pivotal role in reducing ICU stay, ventilator usage, and mortality, even at the peak of the COVID-19 pandemic. Safe vaccination is an effective and necessary measure to curb Delta variant or any other COVID-19 variant spread. In countries like India, a complete and early rollout of mass vaccination programs is the key to success in managing the COVID-19 pandemic. Our results are an encouraging indication of the power and promise of vaccines against COVID-19, especially ChAdOx1 nCoV-19.

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Conflicts of interest

None

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