Received: 12 August 2021 | Revised: 2 September 2021 | Accepted: 3 September 2021

DOI: 10.1002/jmv.27320

SHORT COMMUNICATION

JOURNAL OF MEDICAL VIROLOGY WILEY

# Occurrence of COVID-19 in priority groups receiving ChAdOx1 nCoV-19 coronavirus vaccine (recombinant): A preliminary analysis from north India

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## Abstract

The ChAdOx1 nCoV-19 vaccine (Oxford University-Astra Zeneca) has demonstrated nearly 70% efficacy against symptomatic COVID-19 in trials and some real-world studies. The vaccine was the first to be approved in India in early January 2021 and is manufactured by the Serum Institute of India. Favorable short-term safety data of the vaccine in India in a real-world setting has been recently demonstrated. Here, we report secondary objective (COVID-19 occurrence) measures of the same ongoing prospective observational study in prioritized recipients of the vaccine. The findings are based on participants who could complete at least 2 months of follow-up ($n = 1500$; female/male: 472/1028; mean age: 38.8 years). Laboratory confirmed SARS-CoV-2 infection was observed in 27/65 participants (41%) who received a single dose and 271/1435 (19%) who received both doses. Specifically, among doctors, 18/27 (66.7%) one dose recipients and 131/377 (34.7%) fully vaccinated developed SARS-CoV-2 infection. The majority of the cases were mild in all groups, and most were breakthrough infections. The occurrence of "severe" COVID-19 was 7.7 times lower (0.4%) in fully vaccinated participants compared to partially vaccinated (3.1%). Four deaths were observed in the study. One of the four deaths was due to sepsis, two due to unspecified cardiac events, and one due to unspecified post-COVID-19 complications. The results of this preliminary analysis necessitate vigorous research on the performance of vaccines against variants, optimal timing of vaccination, and also optimal timings of effectiveness studies to guide future vaccination policy.

**KEYWORDS**
breakthrough, cardiac, healthcare workers, real world

## 1 | INTRODUCTION

In randomized controlled settings, efficacy close to 70% against symptomatic COVID-19 has been demonstrated for the ChAdOx1 nCoV-19 vaccine which uses a recombinant chimpanzee adenovirus coding for the SARS-CoV-2 spike protein. Post-approval studies are, however, necessary to validate the findings in the real world. A prospective observational study is being conducted among the vaccinated individuals in a tertiary hospital of north India since February 5, 2021 with the primary objective of determining the safety of COVID-19 vaccines and the secondary objective of assessing the rate of occurrence of COVID-19. Healthcare workers, other frontline workers (police, sanitary workers, etc.) and elderly citizens who were initially focus groups for vaccine roll-out in India constituted the target population of the study. As per government

  

policies, COVISHIELD, based on the ChAdOx1 platform, was the designated vaccine for the study center during the enrollment period. The authors recently demonstrated a favorable safety profile of COVISHIELD when assessed up to 7 days after the second dose.[1] Here, we report the preliminary findings regarding our secondary outcome measure of post-vaccination SARS-CoV-2 infections. The data are based on at least 2 months of follow-up since the second dose of vaccine in enrolled participants who could be successfully contacted telephonically.

## 2 | MATERIALS AND METHODS

The study included all vaccine recipients who provided consent and were enrolled at the time of receiving the first or second dose of the COVISHIELD vaccine. The recipients included predominantly medical and paramedical personnel as they were the initial beneficiaries of vaccine roll-out. In the later stages of enrollment, elderly non-healthcare workers who visited the study center for vaccination were also enrolled. Baseline demographic details of each participant were collected in a pre-designed case report form.[1] Enrollment was continued till the target sample size ($n = 1650$) was reached. As part of the ongoing prospective observational study, each participant is being monitored telephonically at specific intervals following the second dose, for a total duration of 1 year (study duration). Those who received only one dose are also being followed up similarly. For the secondary objective, details pertaining to development of COVID-19 such as symptoms, reverse-transcription polymerase chain reaction (RT-PCR) positivity, or rapid antigen test positivity for SARS-CoV-2 at any time following vaccination, need for hospitalization, and oxygen requirement details were collected. In case of deaths of the vaccine recipients, telephonic ascertainment of the cause of death was done using information collected from family members, and a request was made to provide medical certification documents. This interim analysis is being performed after at least 2 months of follow-up since the second dose.

COVID-19 cases were defined as "confirmed" and "suspect" based on investigators' assessment and guided by recommendations issued by the Ministry of Health and Family Welfare, Government of India.[2] Any person with laboratory confirmation of SARS-CoV-2 infection, irrespective of clinical signs or symptoms, was considered a confirmed case. COVID-19 suspect cases are those having a suggestive clinical pattern of symptoms, and exposure to confirmed/probable cases of COVID-19 within the past 14 days. They were divided into COVID-19 suspects (not tested)—in the absence of rapid antigen test or RT-PCR test reports, and RT-PCR negative COVID-19 suspects- with a negative RT-PCR test.

### 2.1 | Ethical permission

Ethical approval was obtained from the ethics committee of the Institute of Medical Sciences, Banaras Hindu University. No human experimentation was performed. Written informed consent was taken from all participants in this observational study.

## 3 | RESULTS

Among 1650 enrolled vaccine recipients, 1500 participants of the study (female/male: 472/1028) completed at least 2 months of follow-up, after the second dose (baseline characteristics in Table 1). Among these 1500, 1435 participants received both doses and 65 received only one dose.

### 3.1 | Occurrence and severity of COVID-19 after single dose of vaccine

In single-dose recipients ($n = 65$), laboratory-confirmed SARS-CoV-2 infection was observed in 27 individuals (41.5%). Two individuals (3.1%) were labeled as "suspects," and one (1.5%) was an RT-PCR negative suspect. Severity-wise, infections were mild in 21 out of 30 (70%) cases. Three individuals (10% of cases, 4.6% of vaccinees) required hospitalization for oxygen requirement (details in Table 1). Two deaths were observed in this group, one in an elderly male with pre-existing coronary artery disease who died because of an unspecified cardiac event following recovery from COVID-19, and the other in an elderly male with comorbid diabetes and congestive heart failure who succumbed to unspecified post-COVID-19 complications. Details of both events were based on history provided by family members (Table S1).

### 3.2 | Occurrence and severity of COVID-19 after both doses of vaccine

Of those who received both doses of vaccine ($n = 1435$), 388 (27%) were diagnosed as confirmed or suspect cases of SARS-CoV-2 infection. Of these 388, RT-PCR positivity was seen in 271 (18.9%) individuals. Severity wise, majority of SARS-CoV-2 infections were "mild" (331/388, 85.3%). Infection occurred within ≤14 days of receiving the second dose in 31 and after 14 days of receiving the second dose in 357. The breakthrough infection rate was determined to be close to 25% (357/1435), and 17.2% (247/1435) if only laboratory-confirmed cases were considered. Nineteen individuals (1.3% of vaccinees) needed hospitalization, of whom six (0.4% of vaccinees) were admitted because of respiratory distress or oxygen requirements (details in Table 1). Two deaths were reported in this group. One was a middle-aged man with comorbid diabetes who developed cellulitis of the lower limb leading to sepsis and encephalopathy and died due to multiorgan failure. He was assessed twice for SARS-CoV-2 infection but tested negative. The other death was of a healthcare worker with comorbid diabetes and hypertension who died of an unspecified cardiac event. Details of both events were based on history provided by family members (Table S1).

**TABLE 1** Demographic characteristics and details of COVID-19 in vaccinated individuals

| **Demographic characteristics of all vaccine recipients (*n* = 1500)** | | |
|---|---|---|
| Male, female | 1028, 472 | |
| Age (years) (mean ± SD) | 38.8 ± 12.8 | |
| Diabetes mellitus, *n* (%) | 142 (9.5) | |
| Hypertension, *n* (%) | 170 (11.3) | |
| Heart diseases, *n* (%) | CAD: 21 (1.4) | |
| | RHD: 1 (0.1) | |
| | ASD: 1 (0.1) | |
| Hypothyroidism, *n* (%) | 54 (3.6) | |
| Respiratory diseases, *n* (%) | Asthma/COPD: 41 (2.7) | |
| | ILD: 1 (0.1) | |
| **Characteristics of COVID-19 (*n* = 1500)** | | |
| | **Participants who received single dose of vaccine (*n* = 65)** | **Participants who received both doses of vaccine (*n* = 1435)** |
| Confirmed or suspect cases, *n* (%) | 30 (46.1) | 388 (27) |
| | | ≤14 days after second dose: *n* = 31 |
| | | >14 days after second dose: *n* = 357 |
| RT-PCR confirmed SARS-CoV-2 infections | 27 (41.5) | 271 (18.9) |
| COVID-19 suspect (not tested)[a] | 2 (3.1) | 82 (5.7) |
| RT-PCR negative COVID-19 suspect[b] | 1 (1.5) | 35 (2.4) |
| Efficacy (two doses of vaccine vs. single dose) against confirmed or suspect COVID-19 | 41.3% | |
| Severity[c] (all confirmed or suspect) | (*n* = 30) | (*n* = 388) |
| Asymptomatic | 1 (3.3) | 18 (4.6) |
| Mild | 21 (70) | 331 (85.3) |
| Moderate | 5 (16.7) | 33 (8.5) |
| Severe | 2 (6.7), including one death | 6 (1.5) |
| Unsure of severity | 1 (3.3), one death (other cause) | – |
| Efficacy (Two doses of vaccine vs. one dose) against severe COVID-19 | 86.4% | |
| Hospitalization needed | 3 (all for oxygen requirement) | 19 (6 for oxygen requirement, 12 for observation, 1 for general caregiver support) |
| Median time of onset following vaccine dose in days (Q1,Q3; range) | 45 (29,55; 1–73) | 39 (28,47; 0–99) |
| Death due to other cause | 1 | 2 |
| **Characteristics of COVID-19 in doctors (*n* = 404)** | | |
| | **Doctors who received single dose (*n* = 27)** | **Doctors who received both doses (*n* = 377)** |
| Confirmed or suspect cases, *n* (%) | 19 (70.4) | 160 (42.4) |
| | | ≤14 days after second dose: *n* = 12 |
| | | >14 days after second dose: *n* = 148 |
| RT-PCR confirmed SARS-CoV-2 infections | 18 (66.7) | 131 (34.7) |

(Continues)

**TABLE 1** (Continued)

| Characteristics of COVID-19 in doctors ($n$ = 404) | Doctors who received single dose ($n$ = 27) | Doctors who received both doses ($n$ = 377) |
|---|---|---|
| COVID-19 suspect (not tested)[a] | 0 (0) | 17 (4.5) |
| RT-PCR negative COVID-19 suspect[b] | 1 (3.7) | 12 (3.2) |
| Severity[c] (all confirmed or suspect) | ($n$ = 19) | ($n$ = 160) |
| Asymptomatic | 1 (5.3) | 9 (5.6) |
| Mild | 14 (73.7) | 130 (81.3) |
| Moderate | 3 (15.8) | 16 (10) |
| Severe | 1 (5.3) | 5 (3.1) |
| Hospitalization needed | 1 (for oxygen requirement) | 13 (5 for oxygen requirement, 7 for observation, 1 for general caregiver support) |
| Death due to other cause | 0 | 1 |

*Note*: COVID-19 suspect cases are those in whom the investigators suspected COVID-19 based on a clinical pattern of symptoms, exposure to confirmed/probable cases of COVID-19 within the past 14 days, and general guidance from the clinical guidelines issued by the Ministry of Health and Family Welfare (MoHFW), Government of India. They were divided into: [a]COVID-19 suspect (not tested)—in the absence of rapid antigen test or RT-PCR test report; [b]RT-PCR negative COVID-19 suspect—with a negative RT-PCR test report; [c]as defined by the MoHFW, Government of India (for severity, all percentages are out of a total of confirmed and suspect infections).

Abbreviations: ASD, atrial septal defect; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; ILD, interstitial lung disease; RHD, rheumatic heart disease; RT-PCR, reverse-transcriptase polymerase chain reaction.

### 3.3 | Occurrence of COVID-19 in doctors

Four hundred and four out of the 1500 total participants were doctors (registered medical practitioners) including consultant/teaching faculty, resident doctors, and those in general practice. Among these, 27 had received one dose and 377 had received both doses at the time of analysis. Among the 27 having received a single dose, RT-PCR confirmed SARS-CoV-2 infection occurred in 18 (66.7%) and one participant was labeled as RT-PCR negative "suspect." Infection was mild in 14 out of these 19 (73.7%).

Among the 377 doctors who received both doses of vaccine, 160 (42.4%) were diagnosed as confirmed or suspect cases of SARS-CoV-2 infection. Of these, 131 (34.7%) were laboratory-confirmed cases. The infection was mild in 130 out of 160 (81.3%). Breakthrough infections occurring at >14 days after receiving the second dose were seen in 148 doctors (39.2%), or 119 doctors (31.6%), if only laboratory-confirmed cases were considered (details in Table 1).

## 4 | DISCUSSION

ChAdOx1 nCoV-19 vaccine has been found to reduce the rate of symptomatic COVID-19 by around 70% in randomized controlled trials and in some real-world studies.[3–5] The percentage of individuals developing COVID-19 after vaccination has been low and has varied from 0.6% to 1.2%.[3,6] However, there may be differences in vaccine effectiveness and breakthrough infection rates depending on the timing of surveillance. In a relatively quiescent period after the downslope of a wave, there may be few cases, while the case numbers, including breakthrough, maybe higher during an ongoing wave. Victor et al. reported a close to 10% rate of occurrence of COVID-19 in fully vaccinated healthcare workers from a tertiary care hospital in southern India. Rates of hospitalization and oxygen requirement in the vaccinated group were 0.9% and 0.06%, respectively.[7] In our study, 4.6% of individuals who received one dose and 0.4% who received both doses were hospitalized for oxygen needs. Some participants who developed hypoxemia preferred home-based management, including oxygen supplementation. Another Indian study from a tertiary hospital in northern India has reported a rather low rate (2.6%) of occurrence of COVID-19 after two doses of COVISHIELD vaccine.[8] Even after excluding RT-PCR negative and untested suspects, the rates of SARS-CoV-2 infection were much higher (close to 19%) in the fully vaccinated participants in our study, and nearly 35% among fully vaccinated doctors.

This disproportionately high occurrence of SARS-CoV-2 infection and COVID-19 in our study can be explained to some extent by the existence of variants such as the delta which might have escaped immune protection. Though state-wise data on the prevalence of delta variant is scarce, percentage positivity for delta variant among the sequenced samples was maximum for the Uttar Pradesh state of India.[9] Furthermore, a report suggested a close to 35% rate of occurrence of delta variant in the sequenced samples from Varanasi city

in April.[10] Our study design did not incorporate a lab component to determine variants in breakthrough cases and routine determination of variants is not performed in most institutes in India. The data from Varanasi included samples tested at our institute, but being for general surveillance, these do not necessarily represent our participants. Internationally, an outbreak of the delta variant was reported following the first dose of VAXZEVRIA (also ChAdOx1 based) in an elderly care home in London.[11] A reduced protection against the delta variant has been shown for the ChAdOx1 nCoV-19 vaccine recently.[12,13]

Other potential explanations for the discrepancy in the rate of occurrence of SARS-CoV-2 infection between our study and other Indian studies can be related to the study designs and regional variations. The study by Rana et al. mentions the minimum follow-up period of 2 weeks following a second dose but does not mention the total duration of follow-up. Further, the study period was from January 16, 2021, to April 17, 2021. The second wave of COVID-19 hit India significantly after mid-April, and hence the infection rates in this study are expectedly lower. The possibility of infections that may have been detected on longer follow-up, being missed cannot be ruled out.[8] Other studies which reported a relatively higher rate of infections coincided in timing with ours, and with the peak of the second wave in India.[7,14] Apart from variant and study-timing/design-related factors, regional variations and genetic factors may also be explored in the future to explain the differences in breakthrough rates in various parts of India. Pre-existing immunity by virtue of prior SARS-CoV-2 infection in the first wave may also drive observed vaccine effectiveness.

Despite the high rate of occurrence of SARS-CoV-2 infections in vaccinated individuals, the severity of COVID-19 was observed to be low. The occurrence of "severe" COVID-19 was 7.7 times lower (0.4%) in fully vaccinated participants compared with the partially vaccinated group (3.1%). These rates might reflect a dose–response relationship of the vaccine in reducing disease severity. Similarly, 41% of individuals who received only one dose of the vaccine and 19% of those who received both doses developed laboratory-confirmed SARS-CoV-2 infection, suggesting a probable dose–response relation with infection rates. Of the four deaths observed, one was possibly related to COVID-19 and occurred in a partially vaccinated elderly patient. No deaths due to COVID-19 were observed in fully vaccinated individuals.

Registered medical practitioners (doctors) in our study had a higher rate of breakthrough infections. It is possibly because of their relatively higher exposure to patients. Although other frontline workers mostly deal with in-patients with the use of full personal protective equipment, doctors have to manage both out-patients and in-patients, often using only N95 masks while managing out-patients.

As the ongoing study was primarily focused on adverse events following immunization (AEFIs) and enrolled only vaccinated individuals, the secondary outcome results lack a control unvaccinated group. Hence, we cannot comment upon the effectiveness of vaccines against infection, hospitalization, and death. A separate study has been initiated by the authors to analyze this aspect. Compared to a single dose of the COVISHIELD vaccine, two doses provided 41% efficacy against COVID-19 and 86% efficacy in preventing severe disease.

## 5 | CONCLUSION

The second wave of the COVID-19 pandemic hit large parts of India in April and May. The findings of the present study suggest that real-world protection by the ChAdOx1 vaccine against symptomatic COVID-19 may not be as high as observed in clinical trial settings. Differences may also exist depending on the prevailing variants. The rate of infection in vaccinated individuals was over 20 times higher than what has been observed in randomized controlled settings and severe COVID-19 occurred in 0.4% of fully vaccinated individuals. Detailed analysis of the cause of death in the four cases with mortality could not be performed due to the observational nature of the study. Healthcare workers constituted a significant part of the study population. This attains significance, as, being at high risk of acquisition of infection by SARS-CoV-2, they need to be vaccinated on a priority basis. The finding regarding a higher rate of breakthrough infections in doctors would compel a strategic rethink to protect this important segment of the healthcare team. The results of this preliminary analysis necessitate vigorous research on the performance of vaccines against variants, optimal timing of vaccination, and also optimal timings of effectiveness studies to guide future vaccination policy.

### CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

### AUTHOR CONTRIBUTIONS

*Generated idea, designed study protocol, supervised data collection, performed literature search, performed the statistical analysis, wrote the first draft*: Upinder Kaur. *Assisted in data collection, data management, and literature search*: Sapna Bala. *Assisted in data collection, data management, and literature search*: Bisweswar Ojha. *Assisted in data collection and data management*: Sumit Jaiswal. *Finalized study protocol, supervised data collection, and edited the first draft*: Sangeeta Kansal. *Supervised data management, performed the statistical analysis, edited the final draft and final revised version*: Sankha S. Chakrabarti.

### DATA AVAILABILITY STATEMENT

Since this is a preliminary analysis of a currently ongoing longitudinal study, associated data may be made available by the corresponding author on request.

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### REFERENCES

1. Kaur U, Ojha B, Pathak BK, et al. A prospective observational safety study on ChAdOx1 nCoV-19 corona virus vaccine (recombinant) use

in healthcare workers- first results from India. *EClinicalMedicine*. 2021;38:101038.
2. Ministry of Health and Family Welfare Government of India. Updated clinical management protocol for COVID-19. Accessed September 20, 2020. https://www.mohfw.gov.in/pdf/UpdatedClinicalManagementProtocolforCOVID19dated03072020.pdf
3. Voysey M, Clemens SAC, Madhi SA, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *Lancet*. 2021;397:99-111.
4. Lopez Bernal J, Andrews N, Gower C, et al. Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on covid-19 related symptoms, hospital admissions, and mortality in older adults in England: test negative case-control study. *BMJ*. 2021;373:n1088.
5. Shrotri M, Krutikov M, Palmer T, et al. Vaccine effectiveness of the first dose of ChAdOx1 nCoV-19 and BNT162b2 against SARS-CoV-2 infection in residents of long-term care facilities (VIVALDI study). *medRxiv*. 2021. 2021.03.26.21254391. http://medrxiv.org/content/early/2021/03/26/2021.03.26.21254391.abstract
6. Paris C, Perrin S, Hamonic S, et al. Effectiveness of mRNA-BNT162b2, mRNA-1273, and ChAdOx1 nCoV-19 vaccines against COVID-19 in healthcare workers: an observational study using surveillance data. *Clin Microbiol Infect*. 2021;S1198-743X(21):00379–00387.
7. Victor PJ, Mathews KP, Paul H, Murugesan M, Mammen JJ. 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.
8. Rana K, Mohindra R, Pinnaka L. Vaccine breakthrough infections with SARS-CoV-2 variants. *N Engl J Med*. 2021;385:e7.
9. Indian SARS-CoV-2 Genomics Consortium, (INSACOG). State-wise VOCs. 2021. Accessed 1 September 2021. https://dbtindia.gov.in/sites/default/files/INSACOGKeyAspects.pdf
10. Sadam R. Delta variant behind India's 2nd wave, 7 strains circulating in & around Varanasi, study finds. 2021. Accessed September 1, 2021. https://theprint.in/health/delta-variant-behind-indias-2nd-wave-7-strains-circulating-in-around-varanasi-study-finds/672288/
11. Williams SV, Vusirikala A, Ladhani SN, et al. An outbreak caused by the SARS-CoV-2 Delta (B.1.617.2) variant in a care home after partial vaccination with a single dose of the COVID-19 vaccine Vaxzevria, London, England, April 2021. *Euro Surveill*. 2021;26:2100626.
12. Lopez Bernal J, Andrews N, Gower C, et al. Effectiveness of Covid-19 vaccines against the B.1.617.2 (Delta) variant. *N Engl J Med*. 2021;385:585-594.
13. Planas D, Veyer D, Baidaliuk A, et al. Reduced sensitivity of SARS-CoV-2 variant Delta to antibody neutralization. *Nature*. 2021;596:276-280.
14. Satwik R, Satwik A, Katoch S, Saluja S. ChAdOx1 nCoV-19 effectiveness during an unprecedented surge in SARS COV-2 infections. *Eur J Intern Med*. 2021;S0953-6205(21):00271–00275.

## SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

**How to cite this article:** Kaur U, Bala S, Ojha B, Jaiswal S, Kansal S, Chakrabarti SS. 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. https://doi.org/10.1002/jmv.27320