Breakthrough SARS-CoV-2 infections in an eastern state of India: A preliminary report

Girish Chandra Dash
ICMR-Regional Medical Research Centre

Subhra Subhadra
ICMR-Regional Medical Research Centre

Jyotirmayee Turuk
ICMR-Regional Medical Research Centre

Debaprasad Parai
ICMR-Regional Medical Research Centre

Sonalika Rath
ICMR-Regional Medical Research Centre

Jyotsamayee Sabat
ICMR-Regional Medical Research Centre

Usha Kiran Rout
ICMR-Regional Medical Research Centre

Srikanta Kanungo
ICMR-Regional Medical Research Centre

Hari Ram Choudhary
ICMR-Regional Medical Research Centre

Rashmi R Nanda
ICMR-Regional Medical Research Centre

Matrujyoti Pattnaik
ICMR-Regional Medical Research Centre

Sanghamitra Pati (✉️ sanghamitra.pati@icmr.gov.in)
ICMR-Regional Medical Research Centre

Dr. Debdutta Bhattacharya (✉️ drdebdutta.bhattacharya@yahoo.co.in)
ICMR-Regional Medical Research Centre

Short Report

**Keywords:** COVID-19, Vaccination, COVAXIN®, COVISHIELDTM, Breakthrough

**DOI:** https://doi.org/10.21203/rs.3.rs-649914/v2

**License:** ☑️ ① This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](https://orcid.org/0000-0001-5199-5288)
Abstract

We recorded the vaccine breakthrough cases of Covaxin and Covishield through passive and voluntary reporting at various healthcare facilities of Odisha. A total of 274 samples were found to be COVID-19 positive after 14 days of receiving complete doses of the vaccines. Almost 83.2% of the individuals were found to be symptomatic with 9.9% of those required hospitalization and were having less median antibody titers than individual in home isolation.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which emerged in December 2019 has caused tremendous panic around the globe for the past one and half year. During a health crisis wherein the scientific community are trying to contain the effects of the first wave of coronavirus disease-19 (COVID-19), the world was recently struck by a second wave.¹ As of 20th June, 2021 more than 178 million individuals were infected with SARS-CoV-2 and 3.86 million SARS-CoV-2-associated deaths were reported.² USA, India and Brazil account for most of the cases worldwide with India recording about 29.88 million cases and 3.86 million deaths.²³

To tackle the ongoing pandemic, the Government of India initiated the world’s largest vaccination drive since 16th January 2021 in a phased manner with healthcare workers (HCWs) getting inoculated initially with either of the two vaccines named BBV-152 (COVAXIN®) and AZD1222 (COVISHIELD™) after the requisite approval for emergency use in the country. The vaccination of frontline workers (FLWs) was initiated on 2nd February. Subsequently, the Gam-COVID-Vac (Sputnik V) got approval and was launched in India on 14th May 2021.⁴⁵ India has administered 245.9 million citizens with at least a single dose of either BBV-152 or AZD1222 vaccine and among them, 52.1 million people got both the dosages (complete vaccination) and Odisha has vaccinated 9 million citizens with at least a single dose of either BBV-152 or AZD1222 vaccine and among them, 1.9 million people got both the dosages (complete vaccination) as of mid-June.⁶

During the early stages of the pandemic, scientists hypothesized that SARS-CoV-2 transmission would be slowed by herd immunity resulting from spontaneous infection, vaccination, or both.⁷ Although several studies have demonstrated that SARS-CoV-2 infection in vaccinated individuals present clinically mild symptoms, it is critical to determine whether severe symptoms can arise in others despite vaccination, as development of variants is a continuous process.⁸ A vaccine breakthrough infection is defined as the detection of SARS-CoV-2 RNA or antigen in a respiratory specimen collected from a person ≥14 days after receipt of all recommended doses of an approved COVID-19 vaccine.⁹

In the present study, we attempted to record the breakthrough cases reported through passive and voluntary reporting at various healthcare facilities from different districts of Odisha, their clinical presentation, requirement of hospitalization post infection and antibody titer against spike antigen.

Methodology

Study Design
During 1\textsuperscript{st} March to 10\textsuperscript{th} June 2021, nasopharyngeal swab and serum samples from vaccinated individuals were collected from various healthcare facilities of Odisha state and sent to ICMR-Regional Medical Research Centre, Bhubaneswar for testing. Individuals who tested positive by RT-PCR after \( \geq 14 \) days of complete doses of either BBV-152 (Covaxin) or AZD1222 (Covishield) vaccine were considered as breakthrough cases and included in the study. Demographic characteristics, symptoms present, medical history, vaccination details, duration of hospital/home isolation of the individuals were collected using a questionnaire. Institutional Human Ethics Committee of ICMR- Regional Medical Research Centre, Bhubaneswar approved the study.

**Laboratory Testing**

All nasopharyngeal swab samples were tested in an automated machine Cobas 6800 (Roche Molecular Systems, NJ, USA) which targets two genes i.e., the ORF1 gene (target 1), and E gene (target 2). Spike RBD IgG antibodies against SARS-CoV-2 were quantitative estimated in an automated chemiluminescence electro assay (CLIA) based platform, ARCHITECT i1000SR (Abbott Diagnostics, Chicago, USA) using a commercial quantitative kit ARCH SARS-CoV-2 IgG II Quant. The cut-off value for this kit was 50 AU/ml.

**Statistical Analysis**

Statistical Analyses were performed using SPSS version 24 (IBM) and GraphPad Prism 7.00 for Windows (GraphPad Software, La Jolla, California, USA). Qualitative data were described using frequencies and percentages and analysed using chi-square test. Quantitative data were described using median and inter quartile range (IQR) and analysed using Mann-Whitney U test. A p-value of less than 0.05 was considered as statistically significant.

**Ethics approval**

The study was ethically approved by the institutional human ethical committee of ICMR – Regional Medical Research Centre, Bhubaneswar.

**Results**

A total of 361 samples from vaccinated individuals were referred to our centre for confirmation of infection and quantitative antibody estimation. All these 361 individuals were found to be RT-PCR positive, however, 87 individuals were excluded as they were either not fully vaccinated or were found positive within 14 days of completing 2\textsuperscript{nd} dose of their vaccination. Out of the 274 samples with confirmed breakthrough infection, 35 (12.8\%) individuals received Covaxin and 239 (87.2\%) individuals received Covishield. The median age for breakthrough infection among referred cases was 47.0 years (IQR: 28.0) with a significantly older age group among Covishield recipients (Table 1). Around 43\% of the Covaxin recipients with breakthrough infection and reported to the facility were health care workers whereas it was around 10\% in Covishield recipients and the difference was statistically significant. The duration between the 2\textsuperscript{nd} dose and confirmed SARS-CoV-2 infection by RT-PCR was higher in Covishield (45 days; IQR-36) than Covaxin (33 days; IQR-42) recipients but was statistically insignificant. About 83.2\% of individuals were found to be symptomatic in nature and which was almost similar in both the vaccine groups. Around 9.9\% of the individuals were hospitalised with no significant difference between Covaxin and Covishield recipient groups. Only one individual (Covishield recipient) died.
post infection during the study period. The median duration of hospitalisation among the reported cases was 11.0 days (IQR: 6.0) with a single person still hospitalised to date. The median cycle threshold (ct) value of the individuals who tested positive in RT-PCR was 21.2 (IQR: 7.0) with no significant differences in both the groups.

Table 1: Demographic and medical characteristics of breakthrough cases receiving both the dos Covaxin and Covishield

| Variable                               | Total (n=274) | Covaxin (n= 35) | Covishield (n= 239) | p-Value |
|----------------------------------------|--------------|----------------|---------------------|---------|
| Age (Median, IQR)                      | 47.0 (28.0)  | 31.0 (20.0)    | 48.0 (25)           | 0.000*  |
| Sex                                    |              |                |                     |         |
| Male                                   | 186 (67.9%)  | 20 (57.1%)     | 166 (69.5%)         | 0.145   |
| Female                                 | 88 (32.1%)   | 15 (42.9%)     | 73 (30.5%)          |         |
| Occupation                             |              |                |                     |         |
| HWCs                                   | 40 (14.6%)   | 15 (42.9%)     | 25 (10.5%)          | 0.000*  |
| Non-HWCs                               | 234 (85.4%)  | 20 (57.1%)     | 214 (89.5%)         |         |
| Duration of Vaccination and RTPCR Positivity (Median, IQR) | 44.5 (36.0) | 33.0 (42.0) | 45.0 (36.0) | 0.318 |
| Symptomatic                            |              |                |                     |         |
| Yes                                    | 228 (83.2%)  | 29 (82.9%)     | 199 (83.3%)         | 0.952   |
| No                                     | 46 (16.8%)   | 6 (17.1%)      | 40 (16.7%)          |         |
| Hospitalisation                        |              |                |                     |         |
| Yes                                    | 27 (9.9%)    | 3 (8.6%)       | 24 (10.0%)          | 0.537   |
| No                                     | 247 (90.1%)  | 32 (91.4%)     | 215 (90.0%)         |         |
| Duration of Hospitalization (Median, IQR) | 11.0 (6.0) | 12.0 (--)      | 10.5 (7.0)          | 0.533   |
| Ct value (Median, IQR)                 | 21.2 (7.0)   | 21.0 (6.0)     | 22.0 (7.0)          | 0.812   |
| Antibody Positive against S protein    |              |                |                     |         |
| Yes                                    | 258 (94.2%)  | 27 (77.1%)     | 231 (96.7)          | 0.000*  |
| No                                     | 16 (5.8%)    | 8 (22.9%)      | 8 (3.3%)            |         |
| Antibody Titre (Median, IQR)           | 564.4 (1516.4) | 213.5 (537.5) | 647.5 (1645.1)     | 0.000*  |
| Comorbidities                          |              |                |                     |         |
| Yes                                    | 64 (23.4%)   | 5 (14.3%)      | 59 (24.7%)          | 0.174   |
| No                                     | 210 (76.6%)  | 30 (85.7%)     | 180 (75.3%)         |         |

HWCs-Healthcare workers, *p-value significant at <0.05

A total of 258 (94.2%) individuals were found to be positive for SARS-CoV-2 IgG antibodies against spike protein. There were significant differences in seropositivity between Covaxin (77.1%) and Covishield (96.7%). Recipients of Covishield showed higher median titre values than Covaxin among the reported cases which were
The median antibody titre values for Covaxin and Covishield were 213.5 AU/ml (IQR: 537.5) and 647.5 AU/ml (IQR: 1645.1) respectively. The titre values ranged from 4.0 AU/ml to 19835.2 AU/ml in Covaxin whereas it ranged from 0.4 AU/ml to 40000.0 AU/ml in case of Covishield recipients. The median antibody titre among hospitalised individuals (344.0 AU/ml) was lower than individuals advised for home isolation (593.4 AU/ml) (Figure 1). There was a marginal increase in the median titre values of symptomatic patients (564.4 AU/ml) than asymptomatic (527.9 AU/ml) individual. There was no significant difference between the antibody titres in terms of gender, occupation, hospitalisation, and symptom status. The most common symptoms found was fever (88.5%) followed by cough (77.6%) and sore throat (59.6%). Comorbidities such as diabetes, hypertension, hypothyroidism and asthma were present in about 64 (23.3%) individuals.

Discussion

A total of 274 cases were found to be infected with the SARS-CoV-2 virus ≥14 days after receiving a second COVID-19 vaccine (Covaxin or Covishield) dose and were defined as breakthrough infections. Only 16.8% of individuals were asymptomatic with no difference in the ct values between the symptomatic and asymptomatic. Out of the 27 individuals with breakthrough infections and requiring hospitalizations, one died. Odisha has vaccinated 9 million citizens with at least a single dose of either BBV-152 or AZD1222 vaccine and among them, 1.9 million people got both the dosages (complete vaccination) as of mid-June. As COVID-19 vaccines do not provide 100 percent protection, post-vaccination breakthrough infection is possible but rare.\textsuperscript{10,11} Earlier studies have suggested that COVID-19 vaccines might protect occurrence of severe illness and might help in preventing infection.\textsuperscript{12} A study on healthcare workers had found symptomatic breakthrough infections occurring in 15 persons (13.3%), out of which 1 required hospitalisation.\textsuperscript{13} The study on the variants of the breakthrough cases would help in further enlighten knowledge towards various mutations and its effect on the vaccine's capacity in preventing severe illness.\textsuperscript{14} The mean ct value of the infections in our study was in line with another study in Cleveland, which showed a mean ct value of 20 in about 5 (12%) fully vaccinated individuals detected positive post vaccination.\textsuperscript{15}

The study has two limitations, firstly, the number of documented COVID-19 vaccination breakthrough cases may be a significantly underestimated of all SARS-CoV-2 infections among fully vaccinated persons and secondly the data is based on passive and voluntary reporting of individual, and might not be complete representation of breakthrough cases as most asymptomatic individual or with mild illness post vaccination might have not got tested. It is anticipated that even with administration of effective authorized vaccines, breakthrough cases are expected to happen, till the immunity reaches sufficient levels among the population to further decrease transmission.\textsuperscript{9}

The importance of the ongoing battle between immunisation and natural selection of potential viral escape mutants is highlighted by our research. SARS-CoV-2 variants will likely be evolved continuously, driven by selection for increased transmissibility and evasion of the host immune response. The results reported here highlight the importance of national surveillance to identify the breakthrough infection and detect the circulating viruses which will help to monitor the emergence of vaccine escape variants if any. This study urges the need for a larger study which would help to define correlates of protection to determine whether there is a
need to produce modified vaccines, or doses and to development of monoclonal antibodies targeting the conserved spike protein epitopes that are difficult to mutate.

**Declarations**

**Data availability**

All data and statistical code to reproduce the tables and figures in the manuscript are available on request to the corresponding author.

**Declaration of Competing Interest**

The authors have no competing interests in any form.

**Authors Contributions**

DB, JK & SP designed the study. GCD, SS, DP, SR, JS, UKR & RRN were involved in the testing and analysis of data. GCD, SK, HRC & MP were responsible for data collection and analysis. GCD, DP, DB & SS wrote the manuscript. All authors have read and approved the final manuscript.

**Acknowledgement**

The authors gratefully acknowledge all the healthcare workers for their tireless dedication at each level to fight COVID-19 and for voluntarily participating in this cohort study. The authors are thankful to the Indian Council of Medical Research, New Delhi and Dept. of Health & Family Welfare, Govt. of Odisha for providing financial support for the study.

**References**

1. Madiha, A. & Misbahud, D. The expected second wave of COVID-19. *Int J Clin Virol*. 4, 109–110 (2020).
2. WHO Coronavirus Disease (COVID-19) Dashboard. [https://covid19.who.int/](https://covid19.who.int/) (Accessed 12 April 2021).
3. Ministry of Health and Family Welfare, Government of India (COVID-19) Dashboard. [https://www.mohfw.gov.in/](https://www.mohfw.gov.in/) (Accessed 12 April 2021).
4. Gupta, R. et al. Guidelines of the Indian Society for Sleep Research (ISSR) for practice of sleep medicine during COVID-19. *Sleep Vigil*. 4, 1–12 (2020).
5. Bagcchi, S. The world's largest COVID-19 vaccination campaign. *The Lancet Infectious Diseases* 21, 323 (2021).
6. Vaccination Dashboard. MoHFW, Government of India. 2021. [https://dashboard.cowin.gov.in/](https://dashboard.cowin.gov.in/) (Accessed on 24th June 2021)
7. Fontanet, A. & Cauchemez, S. COVID-19 herd immunity: where are we? *Nat Rev Immunol*. 20, 583–584 (2020).
8. CDC COVID-19 Vaccine Breakthrough Case Investigations Team et al. COVID-19 Vaccine Breakthrough Infections Reported to CDC — United States, January 1–April 30, 2021. *MMWR Morb. Mortal. Wkly. Rep*. 70, 792–793 (2021).
9. COVID-19 Vaccine Effectiveness Research | CDC. https://www.cdc.gov/vaccines/covid-19/effectiveness-research/protocols.html (2021).

10. Baden, L. R. et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. *N Engl J Med.* **384**, 403–416 (2021).

11. Polack, F. P. et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *N Engl J Med* **383**, 2603–2615 (2020).

12. Bagchi, S. et al. Rates of COVID-19 Among Residents and Staff Members in Nursing Homes — United States, May 25–November 22, 2020. *MMWR Morb. Mortal. Wkly. Rep.* **70**, 52–55 (2021).

13. Tyagi, K. et al. Breakthrough COVID19 infections after vaccinations in healthcare and other workers in a chronic care medical facility in New Delhi, India. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews.* **15**, 1007–1008 (2021).

14. Hacisuleyman, E. et al. Vaccine Breakthrough Infections with SARS-CoV-2 Variants. *N Engl J Med.* **384**, 2212–2218 (2021).

15. Redmond SN, Jones LD, Sadri N, Schmotzer C, Navas ME, Zabarsky TF, Bhullar D, Donskey CJ. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in vaccinated and unvaccinated healthcare personnel in a Veterans Affairs healthcare system. *Infection Control & Hospital Epidemiology.* **27**, 1-6 (2021)

Figures
Figure 1

Median antibody titre values of demographic and medical characteristics of breakthrough cases