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

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Short Report

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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.^{2,3}

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.^{4,5} 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 1st March to 10th 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 ≥ 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 2nd 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 2nd 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 doses of 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

statistically significant. 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%). Co-morbidities 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.^{10,11} Earlier studies have suggested that COVID-19 vaccines might protect occurrence of severe illness and might help in preventing infection.¹² A study on healthcare workers had found symptomatic breakthrough infections occurring in 15 persons (13.3%), out of which 1 required hospitalisation.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.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.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.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.

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Figures

Figure 1

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