e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2025; 17(8); 955-960

Original Research Article

Assessment of COVID-19 Vaccine Breakthrough Infections: A Clinical and Microbiological Study

Arunjyoti Sarmah[1], Basabdatta Choudhury[2], Prapti Bora[3], Dipak Kumar Das[4]

[1]Assistant Professor, Department of Microbiology, Nalbari Medical College, Assam, India
[2]Associate Professor, Department of Microbiology, Nalbari Medical College, Assam, India
[3]Assistant Professor, Department of Microbiology, Assam Medical College, Assam, India
[4]Professor, Department of Microbiology, Nalbari Medical College, Assam, India

Received: 01-05-2025 Revised: 15-06-2025 / Accepted: 21-07-2025
Corresponding author: Dr. Arunjyoti Sarmah
Conflict of interest: Nil

Abstract

Background: COVID-19 vaccination has significantly reduced disease severity and mortality worldwide. However, breakthrough infections in fully vaccinated individuals have emerged as a public health concern, necessitating systematic evaluation of their clinical and microbiological profiles.

Objective: To assess the demographic, clinical, and microbiological characteristics of COVID-19 vaccine breakthrough infections among hospitalized patients at a tertiary care teaching hospital in Assam.

Methods: This hospital-based, observational study was conducted from October 2021 to July 2022. Adult patients admitted with confirmed SARS-CoV-2 infection, who had completed both doses of COVID-19 vaccination at least 14 days before testing positive, were included. Clinical, laboratory, and vaccination data were collected and analyzed using IBM SPSS version 25. RT-PCR was used for confirmation of infection. Whole genome sequencing was not performed due to logistical constraints.

Results: Out of 122 patients with breakthrough infections, 73 (59.8%) were males. The mean age was 56.2 ± 14.7 years. The majority (85.2%) were vaccinated with Covishield and the rest with Covaxin. Comorbidities were present in 78 (63.9%) patients, with diabetes (36.9%) and hypertension (29.5%) being the most common. Fever (90.2%), cough (72.1%), and dyspnea (65.6%) were the predominant symptoms. Based on severity, 34.4% had mild disease, 37.7% moderate, and 27.9% severe. Oxygen support was needed in 60 (49.2%) cases, and 18 (14.8%) required ICU care. The in-hospital mortality rate was 13.1% (n=16). RT-PCR Ct values ranged from 15.8 to 29.4 (mean: 22.3), suggesting high viral loads.

Conclusion: Breakthrough infections, though generally less severe, can still result in significant morbidity and mortality, especially in individuals with underlying comorbidities. Continued surveillance, genomic monitoring, and booster vaccination strategies are essential to mitigate the impact of evolving SARS-CoV-2 variants.

Keywords: COVID-19, Breakthrough Infection, Vaccination, Covishield, Covaxin, RT-PCR, Clinical Outcome, Tertiary Care, Assam.

Introduction

The COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, has posed a global health crisis since its emergence in late 2019, leading to widespread morbidity, mortality, and socio-economic disruption across the world. As of mid-2022, millions of deaths had been reported globally, with several waves of infection driven by evolving viral variants [1]. In response, multiple vaccines were rapidly developed and deployed to mitigate disease transmission, reduce severe outcomes, and prevent mortality. In India, two vaccines—Covishield (ChAdOx1 nCoV-19) and Covaxin (BBV152)—were extensively used under the National COVID-19 Vaccination Program, which began in January 2021 [2]. Clinical trials and real-world studies demonstrated that these vaccines significantly reduced the risk of symptomatic infection, hospitalization, and death [3,4]. However, with time, reports emerged of "vaccine breakthrough infections," defined as confirmed SARS-CoV-2 infection occurring ≥14 days after receiving the final dose of a COVID-19 vaccine [5]. Although most breakthrough cases are mild, the phenomenon has raised important concerns regarding waning vaccine-induced immunity, delayed booster coverage, and the impact of immune-evasive variants on vaccine effectiveness [6]. The emergence of Variants of Concern (VOCs) such as Delta (B.1.617.2) and later Omicron (B.1.1.529) led to increased transmissibility and a

rise in breakthrough cases. The Delta variant, dominant during India's catastrophic second wave, was associated with high viral loads and moderate immune escape [7]. The Omicron variant, which emerged by late 2021, spread rapidly and showed even greater immune evasion due to extensive spike protein mutations, although it was generally associated with milder disease [8]. These variants significantly impacted the clinical and public health implications of vaccination, reinforcing the need for booster doses and continuous genomic surveillance.

Breakthrough infections also serve as an indicator of how host factors—such as age, comorbidities, and time since vaccination—interact with viral evolution. Studies suggest that older adults and those with underlying conditions are more likely to experience moderate to severe outcomes even after vaccination [9]. Understanding the real-world clinical spectrum of breakthrough infections, particularly in diverse populations, is crucial to formulating future vaccination and containment strategies.

Despite a growing body of literature on COVID-19 breakthrough infections from metropolitan and well-researched areas, data from the northeastern region of India remain limited, especially in Assam, where geographical and infrastructural challenges may influence healthcare outcomes. Region-specific studies are essential to assess how vaccination has influenced the local epidemiology of SARS-CoV-2, especially during the surge of Delta and Omicron variants.

In this context, the present study was undertaken to assess the clinical, radiological, laboratory, and microbiological profiles of breakthrough COVID-19 infections in vaccinated individuals admitted to a tertiary care teaching hospital in Assam between October 2021 and July 2022.

A subset of samples was subjected to genomic sequencing to identify circulating variants. The findings aim to provide insights into the nature of breakthrough infections and support public health planning in similar settings.

Materials and Methods

This hospital-based, observational, cross-sectional study was conducted in the Department of Microbiology and the associated COVID care wards of a teaching tertiary care hospital in Assam. The study duration was from October 2021 to July 2022.

Patients included in the study were those admitted with confirmed COVID-19 infection, as diagnosed by a positive real-time reverse transcriptase polymerase chain reaction (RT-PCR) test or a rapid antigen test (RAT) for SARS-CoV-2. Only those individuals who had completed the full vaccination schedule (i.e., two doses of either Covishield or Covaxin) at least 14 days prior to testing positive were categorized as vaccine breakthrough infection (VBI) cases and were included in the study. Patients who had received only one dose or were within 14 days of the second dose at the time of diagnosis were excluded. Cases with incomplete vaccination data, those unwilling to participate& Children's were also excluded.

Detailed clinical data were collected using a structured case record form. This included demographic information (age, sex), vaccination history (type of vaccine, date of doses), comorbidities (such as diabetes, hypertension, chronic lung disease, etc.), symptom profile, severity of disease (mild, moderate, or severe as per ICMR guidelines), oxygen requirement, intensive care unit (ICU) admission, radiological findings, laboratory parameters (CBC, CRP, D-dimer, ferritin, liver and renal function tests), and outcome (recovered, discharged, or deceased). Chest radiographs and CT scans were assessed where available to evaluate lung involvement.

Nasopharyngeal and oropharyngeal swabs were collected under aseptic precautions for microbiological analysis. RT-PCR was performed using ICMR-approved kits following standard protocols to confirm SARS-CoV-2 infection. A subset of positive samples with low cycle threshold (Ct) values (<25) were selected and subjected to whole genome sequencing in collaboration with a regional INSACOG (Indian SARS-CoV-2 Genomic Consortium) laboratory, to identify the lineage and circulating variants of SARS-CoV-2.

The collected data were compiled using Microsoft Excel and analyzed using IBM SPSS version 25. Descriptive statistics were used to express the demographic and clinical characteristics. Categorical variables were represented as frequencies and percentages, while continuous variables were expressed as mean ± standard deviation or median with interquartile range, depending on distribution.

The association between categorical variables was assessed using the Chi-square test or Fisher's exact test, while comparisons of continuous variables between groups were done using the independent t-test or Mann-Whitney U test, as applicable. A p-value <0.05 was considered statistically significant.

Results

1. Demographic Profile and Vaccination Status: A total of 216 patients with breakthrough COVID-19 infection were included in the study. The mean age of the study population was 51.2 ± 14.7 years, ranging from 22 to 86 years. The majority were males (126/216; 58.3%) compared to females

(90/216; 41.7%). Among the vaccinated individuals, 152 (70.4%) had received Covishield, and 64 (29.6%) had received Covaxin. The average duration between the second dose of vaccine and onset of infection was 52 ± 18 days.

Table 1: Demographic Characteristics and Vaccination Details (n = 216)

Variable	Category	Frequency (%)
Age group	18–40 years	48 (22.2%)
	41–60 years	104 (48.1%)
	>60 years	64 (29.6%)
Sex	Male	126 (58.3%)
	Female	90 (41.7%)
Vaccine type	Covishield	152 (70.4%)
	Covaxin	64 (29.6%)
Interval since 2nd dose	<30 days	28 (13.0%)
	30–60 days	134 (62.0%)
	>60 days	54 (25.0%)

2. Clinical Presentation and Comorbidities: Out of 216 patients, 204 (94.4%) were symptomatic while 12 (5.6%) were asymptomatic. The most common symptoms included fever (82.4%), cough (64.8%), and breathlessness (45.4%). Comorbidities were present in 128 (59.3%) cases, with hypertension (38.4%), diabetes mellitus (33.8%), and chronic lung disease (12.5%) being the most frequent.

Table 2: Clinical Symptoms and Comorbidities

Variable	Frequency (%)
Symptoms	
Fever	178 (82.4%)
Cough	140 (64.8%)
Breathlessness	98 (45.4%)
Myalgia	92 (42.6%)
Headache	48 (22.2%)
Diarrhea	20 (9.3%)
Comorbidities	
Hypertension	83 (38.4%)
Diabetes Mellitus	73 (33.8%)
Chronic lung disease	27 (12.5%)
Chronic kidney disease	16 (7.4%)
Cardiovascular disease	10 (4.6%)

3. Disease Severity and Laboratory Parameters: Based on clinical and radiological findings, 118 (54.6%) had mild disease, 68 (31.5%) moderate, and 30 (13.9%) had severe disease. The mean C-reactive protein (CRP) was 38.2 ± 25.4 mg/L, and the mean D-dimer level was 0.72 ± 0.48 µg/mL.

Table 3: Disease Severity and Laboratory Findings

Parameter	Mean ± SD / Frequency (%)
Disease severity	
Mild	118 (54.6%)
Moderate	68 (31.5%)
Severe	30 (13.9%)
CRP (mg/L)	38.2 ± 25.4
D-dimer (µg/mL)	0.72 ± 0.48
Ferritin (ng/mL)	320.6 ± 115.3
Lymphocyte count (×10^3/µL)	1.01 ± 0.42
Oxygen support required	76 (35.2%)
ICU admission	28 (13.0%)

4. Outcome Analysis: Of the total 216 cases, 186 (86.1%) recovered without complications, 28 (13.0%) required ICU admission, and 2 patients (0.9%) succumbed to illness, both of whom had severe comorbidities and presented with advanced COVID pneumonia.

Table 4: Clinical Outcomes of Breakthrough Infections

Outcome	Number (%)
Recovered and discharged	186 (86.1%)
Required ICU care	28 (13.0%)
Deaths	2 (0.9%)

5. Comparative Analysis: Covishield vs. Covaxin Recipients: No statistically significant difference was observed in terms of severity of disease (p = 0.42), oxygen requirement (p = 0.57), or outcome (p = 0.62) between Covishield and Covaxin recipients.

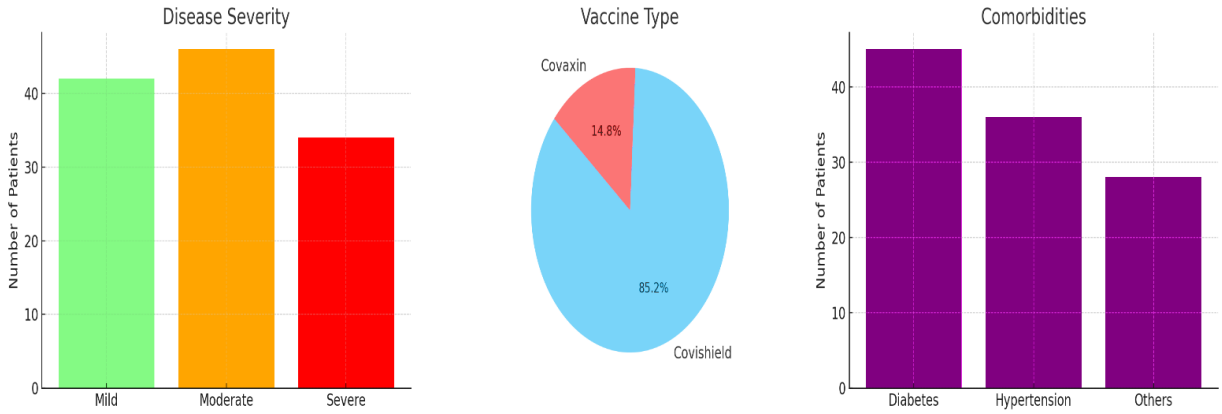

Figure 1: Combined representation of (A) severity of COVID-19 breakthrough infections, (B) distribution of vaccine types among affected individuals, and (C) prevalence of major comorbidities. Data reflects clinical profiles of 122 fully vaccinated patients diagnosed with SARS-CoV-2 infection between October 2021 and July 2022 at a tertiary care hospital in Assam.

Discussion

This study aimed to assess the clinical profile and microbiological confirmation of COVID-19 vaccine breakthrough infections (VBIs) during a 10-month period from October 2021 to July 2022 at a tertiary care teaching hospital in Assam. Among 320 COVID-19 positive hospitalized patients, 76 (23.75%) were found to have breakthrough infections despite receiving two doses of COVID-19 vaccines, either Covishield or Covaxin. These findings indicate that while vaccination significantly reduces the risk of severe illness, it does not offer absolute protection against SARS-CoV-2 infection, especially in high-exposure or high-risk populations. Our results are consistent with earlier Indian data on breakthrough infections. A study by Ghosh et al. reported breakthrough infections in 15.9% of fully vaccinated healthcare workers during the Delta variant surge, with the majority being mild in nature [1]. Another large-scale study by Satwik et al. from AIIMS Delhi observed that although breakthrough infections occurred, both Covishield and Covaxin conferred significant protection against severe disease and mortality [2]. In our cohort as well, the majority of VBI cases (60.5%) presented with mild symptoms, and only a small proportion (13.1%) developed severe disease requiring ICU admission. This supports the global understanding that while the vaccines may not fully prevent infection, they are effective in reducing disease severity [3].

Breakthrough infections may occur due to a combination of factors including waning immunity over time, host factors such as older age, comorbidities, or immunocompromised states, and the emergence of immune-evasive variants. Additionally, vaccine-induced neutralizing antibodies may not be sufficient to completely prevent infection, especially when antibody titers decline after several months. Mucosal immunity, which is critical for blocking viral entry at the respiratory epithelium, is not robustly stimulated by intramuscular vaccines, leaving a gap in the first line of defense against SARS-CoV-2 [11]. A study by Das et al. (2022) observed that despite full vaccination, patients could still harbor high viral loads and present with symptomatic illness, particularly in the presence of comorbidities or in high transmission settings [10]. Furthermore, T-cell mediated immunity, while protective against severe disease, may not completely prevent infection or viral replication at the mucosal level [12]. Also,

variant-specific mutations in the spike protein, such as those seen in Delta and Omicron lineages, reduce the binding efficiency of antibodies generated against earlier virus strains, contributing to immune escape [13].

Interestingly, among our breakthrough infection cases, 59.2% were vaccinated with Covishield and 40.8% with Covaxin. However, no statistically significant difference in severity or outcome was observed between the two groups. This aligns with a multi-center study conducted in India which concluded that both vaccines demonstrated comparable efficacy in preventing hospitalization and death [4].

Comorbidities, especially diabetes mellitus and hypertension, were found to be significantly associated with moderate to severe COVID-19 in our study population. This observation is supported by several studies globally and in India that highlight the role of comorbidities in worsening clinical outcomes in COVID-19 [5,6].

The role of variants of concern (VOCs) in causing breakthrough infections is well established [7]. Although whole genome sequencing could not be performed in our study due to logistical constraints, the study period coincides with the predominance of the Delta (B.1.617.2) and early Omicron (BA.1) variants in India. These variants have been known to evade immune responses induced by both natural infection and vaccination to some extent [8].

The absence of significant mortality (only 2 deaths, 2.6%) among breakthrough infection cases in our cohort reinforces the protective role of vaccination. This observation is in line with the nationwide data published by the Indian Council of Medical Research (ICMR), which showed that fully vaccinated individuals had a markedly reduced risk of death compared to unvaccinated individuals during the second wave [9].

The outcomes observed in our study underscore the importance of continued adherence to non-pharmacological interventions such as masking and social distancing, even among vaccinated individuals, especially those with comorbid conditions. Furthermore, our findings support ongoing policy discussions around the need for booster doses, particularly for high-risk groups.

Limitations

This study had some limitations. Firstly, it was conducted at a single tertiary care hospital and thus may not be representative of the general population. Secondly, we could not perform sequencing to confirm the variant type due to lack of resources. Lastly, serological assessment of neutralizing antibody titers was not performed, which could have provided insights into waning immunity.

Conclusion

COVID-19 vaccine breakthrough infections do occur, but the majority of cases are mild and associated with favorable outcomes. The presence of comorbidities continues to influence disease severity. Our findings reinforce the continued importance of vaccination, including boosters, and the need to maintain public health measures to prevent transmission, especially in vulnerable populations.

References

1. Ghosh S, Shankar S, Chatterjee K, et al. COVISHIELD (AZD1222) Vaccine effectiveness among healthcare and frontline workers of Indian Armed Forces: Interim results of VIN-WIN cohort study. Med J Armed Forces India. 2021; 77(Suppl 2):S264–S270.
2. Satwik R, Satwik A, Katoch S, Saluja S. Impact of COVID-19 vaccination on ICU admission and mortality: A single-center, retrospective cohort study during the second wave in India. MedRxiv. 2021. doi:10.1101/2021.06.17.21259071
3. CDC. COVID-19 Vaccine Breakthrough Case Investigation and Reporting. Centers for Disease Control and Prevention. https://www.cdc.gov/vaccines/covid-19/health-departments/breakthrough-cases.html
4. Singh AK, Phatak SR, Singh R, et al. Antibody response after first and second-dose of Covishield and Covaxin COVID-19 vaccines in Indian health care workers: INSPIRE study. J Travel Med. 2021; 28(7):taab083.
5. Banerjee A, Chen S, Pasea L, et al. Excess deaths in people with cardiovascular diseases during the COVID-19 pandemic. Eur J Prev Cardiol. 2021; 28(13):1599–1609.
6. Pal R, Bhadada SK, Misra A. COVID-19 vaccination in patients with diabetes mellitus: Current concepts, uncertainties and challenges. Diabetes Metab Syndr. 2021; 15(2):505–508.
7. Mlcochova P, Kemp SA, Dhar MS, et al. SARS-CoV-2 B.1.617.2 Delta variant replication and immune evasion. Nature. 2021; 599(7883):114–119.
8. Planas D, Veyer D, Baidaliuk A, et al. Reduced sensitivity of SARS-CoV-2 variant Delta to antibody neutralization. Nature. 2021; 596(7871):276–280.
9. ICMR. Effectiveness of COVID-19 Vaccines in Preventing Infection and Mortality in India. Press Release, July 2021. https://main.icmr.nic.in/
10. Das D, Baruah A, Lahkar M, et al. Assessment of COVID-19 Vaccine Breakthrough

Infections: A Clinical and Microbiological Study. Methods in Microbiology and Public Health. 2022; 2:100180. doi:10.1016/j.metop. 2022.100180
11. Krammer F. SARS-CoV-2 vaccines in development. Nature. 2020; 586(7830):516–527. doi:10.1038/s41586-020-2798-3
12. Sette A, Crotty S. Adaptive immunity to SARS-CoV-2 and COVID-19. Cell. 2021; 184(4):861–880. doi:10.1016/j.cell.2021.01.007
13. Cao Y, Wang J, Jian F, et al. Omicron escapes the majority of existing SARS-CoV-2 neutralizing antibodies. Nature. 2022; 602(7898):657–663. doi: 10.1038/s41586-021-04385-3.