ScienceDirect

Vaccine

Volume 48, 27 February 2025, 126722

Impact of SARS-CoV-2 inactivated vaccine on symptoms following omicron variant breakthrough infection

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https://doi.org/10.1016/j.vaccine.2025.126722 ↗

Highlights

- Inactivated vaccine induced considerable viral-specific immune responses.
- Inactivated vaccine influences the severity of symptoms following mild infection.
- Individuals with stronger vaccine-specific immunity experience milder symptoms.

Abstract

The SARS-CoV-2 Omicron variant and its sublineages continue to circulate widely. Clinical outcomes with this variant differ among individuals, primarily influenced by host immunity. Previous studies have explored the relationship between immune

responses and severe diseases in infected or convalescent patients. However, the impact of vaccine-induced immune responses on disease severity, especially in cases of mild infection following breakthrough infection, remains unclear. This is primarily due to the lack of assessment of immune status in vaccinated individuals before infection. In this study, we aimed to elucidate the causality between virus-specific cellular and humoral immune responses and the severity of symptoms in breakthrough infected patients from a long-term follow-up post-vaccination cohort. A questionnaire survey was conducted to collect general symptoms upon breakthrough infection with the Omicron variants. Plasma levels of specific antibodies (neutralizing antibodies, anti-S IgG, and anti-N IgG) and T cell responses induced by inactivated SARS-CoV-2 vaccine were evaluated. The findings revealed that individuals with milder symptoms, particularly lower peak fever temperatures, exhibited higher antibody levels and enhanced T cell activation and responses prior to infection. This suggests that cellular and humoral immunity induced by inactivated vaccines may provide protection against severe clinical symptoms following breakthrough infection.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in 2019, significantly impacting global health with over 700 million infections and 7 million deaths [1]. Vaccines based on the original strain of SARS-CoV-2 provide limited efficacy against variant strains, ultimately resulting in breakthrough infection [2]. The Centers for Disease Control and Prevention (CDC) defines “breakthrough infections” as the detection of SARS-CoV-2 RNA or antigen in respiratory specimens collected from individuals 14days or more after they have received all doses of a COVID-19 vaccine [3]. While vaccination may not prevent infection, it still provides protection against symptomatic illness following SARS-CoV-2 infection [[4], [5], [6], [7], [8]]. Real-world evidence has suggested the effectiveness of vaccination in reducing severe disease [5,6]. Both mRNA and inactivated SARS-CoV-2 vaccines have significantly lowered the risk of emergency hospital admissions and death. A Hong Kong prospective cohort study also confirmed the effectiveness of vaccines to protect against asymptomatic infection [7]. Currently, healthy individuals who are protected by vaccination and immune memory from previous infection are susceptible to mild infection when exposed to SARS-CoV-2 Omicron variants [[9], [10], [11]]. However, patients with mild infection who have not been hospitalized are often overlooked in clinical settings [8]. Particular attention should be given to the differences in symptoms among these patients, such as fever temperature, and the correlation between these symptoms and vaccine-induced immunity. Understanding this association in mild and moderate COVID-19, which are more common in the general population, is crucial for informing vaccination recommendations and policy development during the pandemic.

Additionally, most studies on vaccination protection against symptomatic illness emphasize epidemiological statistics in convalescent patients rather than examining actual differences in host immunity [[12], [13], [14]]. However, compared to post-infection immune activation, specific pre-infection immune responses are likely more crucial in determining disease severity. The lack of data about immune responses pre-infection hampers many studies in clearly establishing pre-infection baselines, thus limiting the in-depth exploration of pre-infection immune factors influencing breakthrough infection.

In this study, college students with uniform immunization and mild breakthrough infection symptoms were included. Samples were collected from volunteers at various time points after receiving booster doses of the inactivated COVID-19 vaccine and followed them longitudinally until the outbreak of Omicron variants. This enabled us to evaluate the baseline of specific immune responses and to associate them with the general symptoms of Omicron variant breakthrough infection in young adults.

Section snippets

Study participants

The study was conducted among university students at Peking University in China. Inclusion criteria included: 1) aged 16–36 years; 2) absence of underlying diseases such as diabetes, immune dysfunction, or cancer, and exclusion of smokers, alcoholics, or obese individuals; 3) receipt of three-dose inactivated COVID-19 vaccine (Sinovac CoronaVac), which is targeted against the original SARS-CoV-2 strain. Peripheral blood was collected 4 months after the second dose, as well as at 4, 10, 14, 21, …

Basic information of the cohort

Volunteers who experienced breakthrough infection despite receiving three doses of inactivated vaccine targeting the original SARS-CoV-2 strain were enrolled. All infection occurred at least 18 months post-vaccination. Sampling, detection, and analysis began with SARS-CoV-2 vaccination in April 2021 and continued until the Omicron variant

outbreak in May 2023. Basic information of the questionnaire respondents was presented in Table 1 and Supplementary Table 1. 94.7% of participants aged from …

Discussion

The SARS-CoV-2 Omicron variant, with numerous mutations in the S region, exhibits strong immune evasion and can cause breakthrough infections within six months of vaccination. Therefore, studies on breakthrough infection often involve strains antigenically similar to the original vaccine strains. Notably, this study examines breakthrough infection of the Omicron variant, which is genetically distant and highly mutated compared to the original vaccine strain, occurring in individuals who were …

Conclusion

Young volunteers experiencing Omicron breakthrough infection after receiving three doses of inactivated vaccine exhibited a brief infection duration, with most clearing the virus within 1–2weeks. Fever, cough, and sore throat emerged as the primary symptoms of Omicron infection, with fever presenting heterogeneously and cough often being persistent. The booster injection notably enhanced humoral immunity and S-specific and N-specific T cell responses against original SARS-CoV-2. Volunteers …

Ethics approval statement

The study was approved by the Peking University Institutional Review Board (PUIRB) (Ethical Approval Number: IRB00001052–22030) and was conducted in strict accordance with the Good Clinical Practice guidelines and the ethical principles outlined in the Declaration of Helsinki. …

Funding statement

This work was supported by grants from the National Natural Science Foundation of China (82072277) and Natural Science Foundation of Beijing Municipality (M21021). …

CRediT authorship contribution statement

Yuqi Zhang: Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Conceptualization. **Xinjie Li:** Writing – review & editing, Visualization, Validation, Methodology, Investigation. **Yingxiang Yang:** Writing – review & editing, Validation, Supervision, Resources, Project administration, Investigation. **Yue**

Yin: Writing – review & editing, Methodology, Investigation. **Yan Zhong:** Writing – review & editing, Investigation. **Qiang Xu:** Writing – review & editing, …

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. …

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