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The rates and symptoms of natural and breakthrough infection pre- and post-Covid-19 non-mRNA vaccination at various peaks amongst Iranian healthcare workers

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Abstract

Background/Aims The aim of this study was to determine the rate of natural and breakthrough infection and related symptoms of Covid-19 amongst Iranian healthcare workers (HCWs) who were vaccinated by different non-mRNA-based vaccines at peak points.

Methods In this cross-sectional study, the RT-PCR test was performed for a total of 10,581 HCWs suspicious of Covid-19 infection. For each HCW, the frequency of SARS-CoV-2 infection and the time of transmission based on vaccination administration time and schedule were examined during different waves of the pandemic. Based on these findings, the study patients were divided into three groups: natural, natural/breakthrough, and breakthrough.

Results In total, 53% of the HCWs were exposed to SARS-CoV-2 infection between 1 and 5 times within two years after the current pandemic, while 20.7% and 32.3% experienced natural and breakthrough SARS-CoV-2 infection, respectively. Only 6% of the breakthrough-infected HCWs had naturally contracted SARS-CoV-2 infection during the initial waves. The highest natural peaks of infection occurred during the interval administration of the first and second dose of the first vaccination series, while the single highest peak of breakthrough infection belonged to the Omicron wave. It occurred simultaneously with the administration of the third vaccination dose. On the other hand, the highest rate of reinfection was observed amongst people who had received the Sinopharm and Bharat vaccines full-doses.

Conclusion This study compared the clinical differences between the two peaks of Omicron and Delta. This study indicates the rates of natural and breakthrough SARS-CoV-2 infections according to vaccination schedules and different waves of the pandemic.

Keywords Breakthrough infection, Healthcare worker, Natural infection, SARS-C0V-2, Vaccination

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Studies in India after receiving the AZD1222 (ChAdOx1S) or BBV152 vaccine reported a breakthrough infection rate of just over 13% [18, 19]. The reported that the data in these studies were related to the prevalence of the Delta variant, but not for Omicron, while a preliminary study conducted in India, which coincided with the prevalence of the Beta variant, reported the breakthrough infection rate at only 1.6% [20]. Several studies estimated that the breakthrough infection rate in China was 15-20% [21–23].

Determining the frequency, severity, and cause of breakthrough infections can influence the health system response capabilities. A timely follow-up is vital when breakthroughs are relatively rare or mild, and the infection rate is not expected to increase significantly. The importance of breakthrough infections in HCWs with or without previous exposure to natural infection is exacerbated when significant changes occur in severity and frequency, especially during the emergence of new virus strains [24, 25]. Several studies have highlighted the reduction in hospitalizations, mortality, and ICU admission rates in addition to a reduction in the disease severity in people with breakthrough infections [16, 17, 26, 27]. In this study, the data revealed that the prevalence of breakthrough infection among HCWs during the Covid-19 Omicron wave was very high, but the severity of the disease decreased significantly; this is consistent with the findings of a previous study [3]. Furthermore, nearly one in three HCWs experienced a breakthrough infection after receiving both scheduled doses of the Covid-19 vaccine. These findings suggest that in the real-world settings a significant proportion of the vaccinated individuals with a high risk of exposure and those with comorbidities remain vulnerable to Covid-19 infection albeit with reduced disease severity in most cases.

The symptoms that characterize Omicron infection moderately differ from those of the Delta SARS-CoV-2 variant. Headache, runny nose, and sore throat were the symptoms with the highest percentage of difference in the incidence rate between Omicron and Delta waves that have affected symptomatic patients with 24.8%, 24.2%, and 21.4%, respectively. Our study is in line with those of *Kim et al.* [28]. and *Davies et al.*'s [29].studies; however, in *Menni et al.*'s. study, runny nose was reportedly more prevalent in Delta waves compared to Omicron waves [30].

One of the main limitations of this study was lack of access to information on mortality, hospitalizations, and ICU admission of the HCWs. Another limitation of this study was lack of access to the clinical presentation and lab data of patients with natural and/or breakthrough infections, especially serum iron, transferrin, and ferritin, which could determine the role of these factors in severity of different forms of the disease [31].

The findings of the present study indicate the rates of natural and breakthrough SARS-CoV-2 infections among Iranian HCWs within two-year post-pandemic era in Iran. Moreover, the clinical symptoms amongst people affected with different forms of infection (natural vs. breakthrough) as well as different waves were compared. Vaccination schedules in breakthrough-infected healthcare workers were also evaluated. Multipronged prevention strategies are needed to reduce Covid-19-related morbidity and mortality.

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Authors' contributions
M.J. and M.Z conceptualized and designed the study, collected the data, drafted and revised the manuscript. Z.A and N.A initially analyzed and interpreted the data. M.J and M.H. collected the data, initially analyzed and interpreted the data; O.E. critically reviewed and revised the manuscript; and all authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work in ensuring that the questions related to the accuracy or integrity of any parts of the work will be appropriately investigated and resolved.

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Data Availability
The data that support the findings of this study are available on request from the corresponding author.

Declarations

Ethics approval and consent to participate
The project has been approved by Shiraz University of Medical Sciences (Ethics code Number: IR.SUMS.REC.1399.1319).

Competing interests
The authors declare no competing interests.

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