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Clinical Characteristics, Breakthrough Infections, and Reinfections with SARS-CoV-2 among Healthcare Workers in the Omicron Wave

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ABSTRACT

Introduction: A global increase in infections was noted with the emergence of the Omicron variant, which exhibited immune evasion capabilities against previous infections or vaccinations. Healthcare workers (HCWs) faced increased risk from occupational exposure. This study aimed to investigate the clinical characteristics, reinfection rates, and breakthrough infections among HCWs during the Omicron wave. **Methods:** A total of 312 HCWs who tested positive for SARS-CoV-2 during the Omicron wave (January 1–February 22, 2022) were enrolled in the study after providing consent. Participating HCWs completed a questionnaire to provide details on demographics, symptoms at testing, comorbidities, vaccination status, and prior COVID-19 infection history. Clinical outcomes were also recorded. Cases of reinfection and breakthrough infection were identified. **Results**: The median age of HCWs in the study was 32.9 years. The frequency of infection was higher in females (56.7%) and among the professional categories, doctors (58.3%) accounted for the majority of cases. Symptomatic infection was prevalent in 89.7% of cases, with most being mild. Out of 312 healthcare workers, 265 (84.9%) received at least one dose of the Covishield vaccine. Of these, 206 (77.7%) received two doses, and 41 (15.5% of vaccinated HCWs) also received a booster dose. 153 (49.1%) had a history of prior SARS-CoV-2 infection. Hospitalization was required for three unvaccinated HCWs with comorbidities, while no vaccinated HCWs required hospitalization; no deaths occurred. **Conclusions**: The study found that 312 healthcare workers were infected during the Omicron wave. Vaccination and prior infection did not provide complete protection against the Omicron variant. Consequently, breakthrough infections and reinfections were observed with notable frequency during this period.

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has continuously evolved throughout the pandemic, giving rise to variants such as Alpha, Beta, Delta, and Omicron, which have been implicated in subsequent infection waves [1, 2]. These variants often exhibit altered characteristics, including increased transmissibility, immune evasion capabilities, and potentially varying clinical manifestations. The Omicron variant, first identified in November 2021, rapidly spread globally, with its sublineages becoming dominant. The Omicron surge was initially driven by sublineages including BA.1 (including BA.1.1), and BA.2. The Omicron variant exhibits mutations, such as R203K and G204R in the nucleocapsid protein and H655Y, N679K, and P681H in the spike protein, contributing to increased transmissibility and immune evasion. The Omicron variant drove a third pandemic wave in India, beginning around January/February 2022, resulting in a surge of reported cases. This highly transmissible variant is known to cause breakthrough infections and reinfections due to its ability to evade the neutralizing antibodies generated by vaccination or previous infection [3-7].

In India, the SARS-CoV-2 vaccination campaign began on January 16, 2021, prioritizing healthcare workers. The campaign utilized two indigenous vaccines: Covishield (the Oxford/AstraZeneca viral vector vaccine manufactured in India) and Covaxin (an inactivated whole-virion vaccine). Initially, these vaccines were administered to high-priority groups, including healthcare workers [8]. Studies have shown that vaccine effectiveness against SARS-CoV-2

infection, severity, and transmission varies by vaccine type, circulating variant, and time since vaccination. Studies indicate that while vaccines like Covishield and Covaxin reduced severe disease, their short-term effectiveness against Omicron infection waned over time. This varied by vaccine type and interval since vaccination [9-10]. Vaccine effectiveness against Omicron subvariants varied by time since vaccination [11].

Understanding the clinical characteristics, risk factors, and outcomes associated with SARS-CoV-2 among healthcare workers is of utmost importance to mitigate viral spread within the hospital environment and to guide effective screening and infection control measures, particularly in high-prevalence, resource-limited settings. Understanding these clinical characteristics and outcomes is crucial for guiding effective screening and infection control measures, particularly in high-prevalence, resource-limited settings.

The primary objective of this study was to assess the clinical characteristics of healthcare workers at Government Medical College, Srinagar, and its associated hospitals, infected with SARS-CoV-2 during the Omicron-driven pandemic wave. Additionally, the study aimed to investigate the rates of reinfection and breakthrough infections in healthcare workers during the Omicron wave.

MATERIAL AND METHODS

Study design. This cross-sectional study was conducted in the Department of Microbiology, Government Medical College (GMC), Srinagar, Jammu and Kashmir, India.

Participant selection. Healthcare workers (HCWs) from GMC and its associated hospitals who tested positive for SARS-CoV-2 between January 1, 2022, and February 22, 2022, were eligible for the study. HCWs were considered infected if they tested positive by real-time RT-PCR or rapid antigen test (RAT). These HCWs were approached for their consent to participate in the study. HCWs who declined to participate were excluded from the study. No other exclusion criteria were applied. Healthcare workers were categorized into three groups: (i) Fully vaccinated (completed two doses of a vaccine), (ii) Partially vaccinated (received one dose), and (iii) Unvaccinated (received no doses). These groups were evaluated for disease severity, breakthrough infections, and outcomes such as hospitalization, Intensive care unit (ICU) admission, or death. Breakthrough infections were defined as SARS-CoV-2 infections in fully vaccinated HCWs (two doses), and reinfections as infections >90 days after a prior confirmed infection, adapted from CDC guidelines and consistent with recent HCW studies [12-14].

Testing procedure. During this period, healthcare workers who were symptomatic or identified as close contacts of a confirmed SARS-CoV-2 case were tested for SARS-CoV-2. Testing was performed using real-time RT-PCR or a rapid antigen test. For real-time RT-PCR, nasopharyngeal samples collected in viral transport medium were tested using a commercially available multiplex PCR kit (Meril one-step RT-PCR kit). The rapid antigen testing was carried out using the SD Biosensor kit.

Data collection. A structured questionnaire, adapted from the WHO/2019-nCoV/HCW Surveillance Protocol/2020, was distributed electronically via Google Forms to HCWs who consented to participate in the study. This questionnaire was adapted from the WHO/2019-nCoV/HCW Surveillance Protocol/2020 and modified to reflect the current epidemiological context [15]. The questionnaire collected data on demographics, symptoms at the time of testing, presence of comorbidities, vaccination status, history of COVID-19 infection, and clinical outcomes. Clinical outcomes were assessed based on whether the participant recovered fully, required hospitalization, or necessitated intensive care unit (ICU) admission. As part of routine SARS-CoV-2 genomic surveillance, samples from a subset of HCWs were submitted for whole genome sequencing. Sample submission adhered to the guidelines established by the Indian SARS-CoV-2 Genomics Consortium (INSACOG). A subset of 20 positive samples from HCWs with a cycle threshold (Ct) value below 30 was randomly selected for whole genome sequencing.

Statistical analysis. Data collected from healthcare workers were exported to a spreadsheet. Statistical analyses were performed using OpenEpi, version 3.01. Continuous variables were summarized as mean, while categorical variables were presented as counts and percentages. Comparisons between subgroups of healthcare workers were conducted using Pearson's chi-squared test or Fisher's exact test, depending on expected cell counts. A P-value of < 0.05 was considered statistically significant.

Ethical clearance: The study protocol was approved by the Institutional Review Board (IRB), Government Medical College, Srinagar (approval number IRBGMC/C5-26).

RESULTS

Demographics. A total of 312 healthcare workers (HCWs) who tested positive for SARS-CoV-2 during the third pandemic wave in Kashmir participated in this study. Of the participants, 50.0% (156/312) were aged 18–35 years, 37.5% (117/312) were aged 36–49 years, and 12.5% (39/312) were aged ≥50 years. The median age was 32.9 years (range, 18-60 years). The majority of participants (177/312; 56.7%) were female. The largest represented professional group was doctors (182/312; 58.3%), followed by nurses (47/312; 15.1%), and technicians (53/312; 17.0%).

Clinical presentation. Of the 312 participating HCWs, 247 (79.2%) were tested by RT-PCR, and 65 (20.8%) were tested using a rapid antigen test (RAT). Among the HCWs

who tested positive, 280 (89.7%) were symptomatic, with symptoms not requiring hospitalization. The most common symptom was fever (259/280; 92.5%), followed by cough (215/280; 76.8%), myalgia (197/280; 70.4%), sore throat (195/280; 69.6%), and fatigue (192/280; 68.6%) (See Table 1). Most symptomatic HCWs experienced multiple symptoms.

Table 1. Characteristics of healthcare workers

Characteristics	Number (No)	Percentage (%)
Age (years)		
18-35	156	50.0
36-49	117	37.5
>50	39	12.5
Sex		
male	135	43.3
female	177	56.7
Professional category		
Doctor	182	58.3
Nurse	47	15.1
Technician	53	17.0
Orderly	21	6.7
Administrative	9	2.9
Comorbidities		
Cardiovascular disease	18	5.8
Blood disorder	3	1.0
Metabolic disorder	38	12.2
Obesity (BMI ≥ 30 kg/m²)	3	1.0
Testing method		
RT-PCR	247	79.2
RAT	65	20.8
Clinical presentation		
symptomatic	280	89.7
asymptomatic	32	10.3
Symptoms (n=280)		
Fever	259	92.5
Cough	215	76.8
Nasal congestion	180	64.29
Chills	162	57.86
Headache	183	65.36
Myalgia	197	70.36
Sore throat	195	69.64
Arthralgia	83	29.29
Fatigue	192	68.57
Abdominal pain	29	10.36
Cutaneous rash	3	1.07
Diarrhea	35	12.5
Ocular pain	16	5.7
Anosmia	62	22.14
Shortness of breath	35	12.5
Other*	4	1.43
Vaccination status		
Fully vaccinated	206	66.0
Partially vaccinated	59	19.0
not vaccinated	47	15.0
Past SARS-CoV-2 infection		
Yes	153	49.0
No	159	51.0

*Other symptoms included dizziness, chest pain, nausea, vomiting, mood changes, and hair loss

Reinfections and breakthrough infections. Of the 312 HCWs who tested positive for SARS-CoV-2 during the Omicron period, reinfection (153/312) and breakthrough infections (265/312) were observed. Regarding vaccination status, 206 (66.0%) were fully vaccinated, 59 (19.0%) were partially vaccinated, and 47 (15.0%) were unvaccinated. Of those vaccinated, 41 (15.5%) had also received a booster dose. All HCWs had received the Covishield vaccine. A past history of SARS-CoV-2 infection was reported by 153 (49.0%) HCWs, indicating reinfection. Among these reinfected HCWs, 126 (82.0%) had been fully or partially vaccinated. As shown in Figure 1, which illustrates the relationship between symptom status, vaccination status, and prior SARS-CoV-2 infection (reinfection), no statistically significant association was observed between prior infection and symptom presentation ($P > 0.05$).

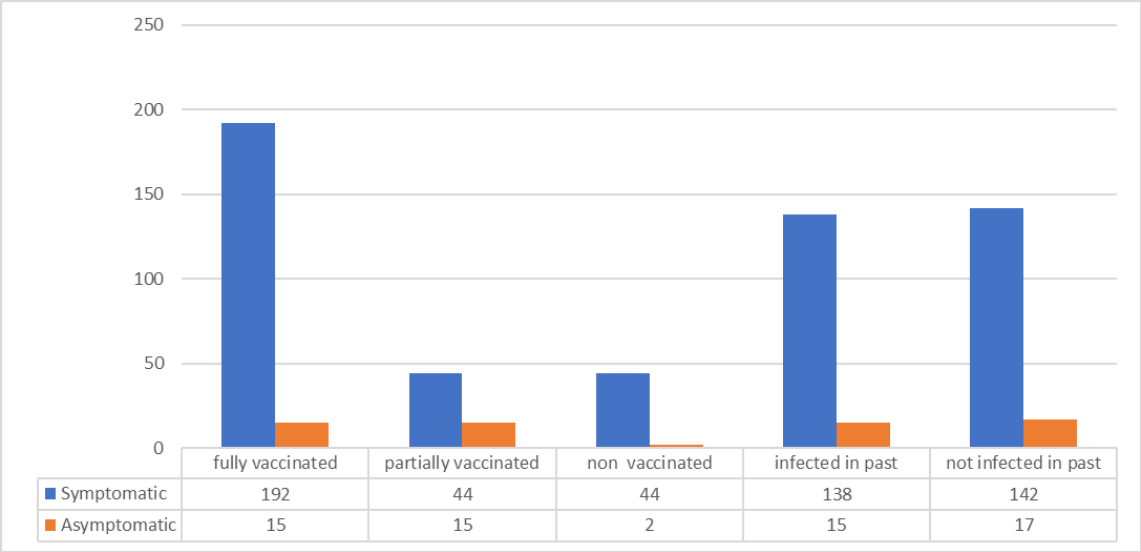

Fig. 1. Correlation between symptom status, vaccination status (breakthrough infections), and prior SARS-CoV-2 infection (reinfection)

The associations between breakthrough infections, reinfections, and demographic/clinical characteristics (age, gender, profession, and underlying disorders) were examined (Table 2). A statistically significant correlation was observed between comorbidities and breakthrough infections.

Table 2. Associations of demographic and clinical characteristics with breakthrough infections and prior SARS-CoV-2 infection among healthcare workers

Characteristic	Breakthrough infection	Unvaccinated	*P*-value	Past SARS-CoV-2 infection	No past SARS-CoV-2 infection	*P*-value (prior infection)
Age						
18-35	127	29		79	77	
35-50	105	12	0.16	59	58	0.36
>50	33	6		15	24	
Gender						
Male	113	22	0.59	76	59	0.02
Female	152	25		77	100	
Profession						
Doctor	165	17		94	88	
Nurse	35	12		18	29	
Technician	41	12	0.003	29	24	0.33
Orderly	15	6		9	12	
Administrative	9	0		3	6	
Comorbidities						
Cardiovascular disease	18	0		6	12	
Blood disorder	3	0	<0.001	3	0	0.07
Metabolic disorder	38	0		21	17	
Obesity (BMI ≥ 30 kg/m²)	3	0		0	3	

The association between the timing of vaccination and breakthrough infections is illustrated in Figure 2. As the time since vaccination increases, the probability of a breakthrough infection increases.

Co-morbidities and outcomes. In this study, 241 (77.4%) cases did not have any underlying co-morbidity. The most reported comorbidities were diabetes mellitus (a metabolic disorder) and hypertension (a cardiovascular disease), observed in 38 and 18 HCWs respectively. Of the 241 HCWs without comorbidities, 238 (98.8%) recovered without requiring hospitalization. Exceptions included three HCWs with comorbidities: One HCW had diabetes and hypertension and was treated with steroids, another HCW had obesity and required high-flow oxygen support, and the third HCW with chronic lung disease necessitated ICU admission. These three unvaccinated individuals experienced severe outcomes, but no mortality was reported.

Of 20 randomly selected samples with Ct <30 that were sequenced, 18 (90%) were identified as Omicron BA.2 and 2 (10%) as BA.1.

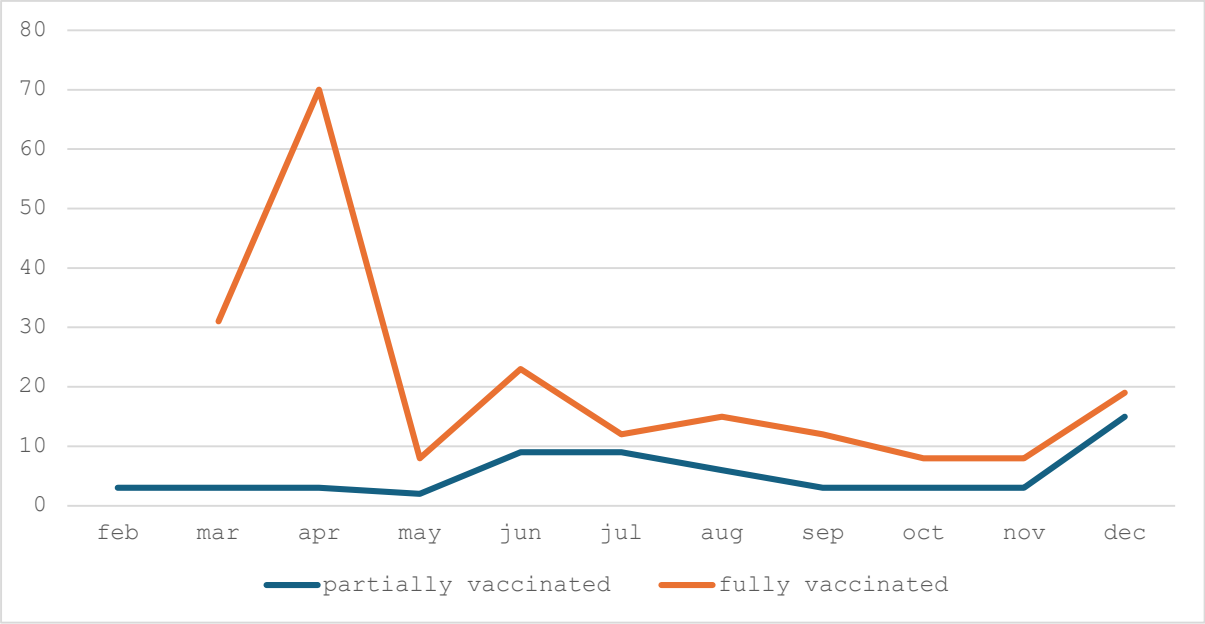

Fig. 2. Correlation between the elapsed time since vaccination and the incidence of breakthrough infections among healthcare workers.

DISCUSSION

The present study describes the clinical course of SARS-CoV-2 infection during the Omicron-dominant transmission period. It also documents the reinfection and breakthrough infection cases during this time. The Omicron surge led to a marked increase in SARS-CoV-2 infections among HCWs. The increased infection rates were attributed to the Omicron sublineages' (such as BA.1 and BA.2) higher transmissibility and ability to evade vaccine-induced and natural immunity [3, 6].

The 18–35-year age group accounted for 50% of infections. This finding aligns with prior studies demonstrating that infection and reinfection occur primarily in younger populations, although a study by Malhotra *et al*. (2022) suggested that the age group above 35 years experienced fewer infections during the Omicron period due to their likely prior exposure to earlier, potentially more severe variants of SARS-CoV-2, leading to a degree of immune protection [8].

Our study observed a higher incidence of infection in females compared to males, consistent with sex differences highlighted in several studies. Doctors, laboratory technicians, and nurses had higher infection rates during the Omicron wave, as suggested by significant associations (P=0.003) likely due to greater occupational exposure to infected individuals or contaminated samples [16, 17].

Compared to earlier variant-driven waves, the Omicron wave was associated with milder symptoms and fewer hospitalizations. Common symptoms included fever, chills, myalgia, and easy fatigue. Sore throat was common (195/280; 69.6%), while anosmia occurred less frequently (62/280; 22.1%) compared to reports from the Delta wave [8, 18-20]. This trend was observed globally. Compared to previous waves, fewer hospitalizations and ICU admissions were recorded, with only three unvaccinated HCWs with comorbidities requiring hospitalization in our study. These individuals were unvaccinated, underscoring the protective benefit of vaccination against severe disease.

The Omicron period witnessed a surge in both reinfections and breakthrough infections. In this study, 84.9% (265/312) of HCWs were vaccinated and experienced breakthrough infections, and 49.0% (153/312) had prior infections and experienced reinfections. While vaccination and prior infection reduced severe disease (only unvaccinated HCWs required hospitalization), protection against Omicron infection was incomplete, with 265 of 312 HCWs (84.9%) experiencing breakthrough infections. This aligns with findings in immunocompromised populations, where Omicron posed ongoing risks despite vaccination [21]. This increase is attributed to several factors. Firstly, the Omicron variant's substantial genetic divergence, particularly with 26-32 mutations in its spike protein, which facilitates immune evasion and high transmissibility, diminished the protection conferred by previous infection. Secondly, studies have shown that protection from vaccination declines over time [19, 22-24]. Breakthrough infections were also observed in HCWs who had taken a booster dose. Although vaccine effectiveness against Omicron infection may wane over time, studies have consistently proven that protection against severe disease, hospitalization, and death remains substantial. A study by Hall *et al*. found evidence of

considerable waning of immunity over a period after vaccination, dropping to 22-66% after 6 months. Even the 41 boosted HCWs (15.5% of vaccinated HCWs) experienced mild breakthrough infections, consistent with waning vaccine-induced immunity over time [22]. Studies have reported that alternative prophylaxes, such as tixagevimab/cilgavimab, showed limited efficacy against newer Omicron variants [22, 25]. Our findings support this, as no cases of severe disease or death was observed in vaccinated HCWs. In our study, hospitalization was seen in three HCWs, all of whom were unvaccinated and had underlying comorbid illness.

First, as a single-center study, the findings may not be generalizable to other healthcare settings or populations. Second, the retrospective nature of the study introduces the possibility of recall bias. Third, some HCWs, whether symptomatic or asymptomatic, might not have been tested during the study period. To address these limitations, future research should involve multicenter studies with prospective data collection to reduce bias and provide reliable data for public health policies and infection control measures.

In conclusion, our study underscores a substantial proportion of HCWs infected during the Omicron phase. Breakthrough infections and reinfections were observed more frequently in comparison with previous pandemic waves. Vaccination and previous infection offered reduced protection compared to other variants. This suggests the need for updated vaccine strategies or additional preventive measures to better manage future variants.

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CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest associated with this manuscript.

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