

# Profile of COVID-19 breakthrough cases and its comparison with unvaccinated COVID-19 cases among healthcare workers in a tertiary care centre in North Kerala

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## ABSTRACT

**Background:** Healthcare workers (HCWs) were the most vulnerable group during COVID-19 pandemic and had faced many challenges including high rate of breakthrough infections. **Aims:** To study the incidence of reported breakthrough infections among HCWs in Government Medical College, Kozhikode and to compare profile of COVID-19 infection between fully vaccinated and unvaccinated COVID-19 positive HCWs. **Settings and Design:** The research was conducted as a prospective study for a duration of 78 weeks from 1<sup>st</sup> of March 2020 through 31<sup>st</sup> of August 2021 in Government Medical College, Kozhikode. **Methods and Material:** The study was conducted among HCWs in a COVID-19 tertiary care institute. Real-time data were collected from 401 breakthrough cases and 390 unvaccinated COVID-19 positive HCWs through telephonic interviews. **Statistical Analysis Used:** Univariate analysis was done using frequency for categorical variables and mean and standard deviation for quantitative variables. Chi-square test was used to find out statistical significance. **Results:** Incidence of breakthrough infection was found to be 5.62% with 43.3% being asymptomatic. Fever was the most predominant symptom (62.5%). None of the breakthrough cases developed complication requiring intensive care (ICU). There was a reduction in incidence of acute post-COVID-19 syndrome in vaccinated group (17.45%) compared to unvaccinated group (57.2%). **Conclusions:** COVID-19 vaccination plays a key role in preventing severity, complication, and ICU admissions in COVID-19 infection. Incidence of post-COVID-19 syndrome is also less among fully vaccinated compared to unvaccinated individuals.

**Keywords:** Breakthrough cases, COVID 19 vaccination, healthcare workers, post COVID 19 syndrome

## Introduction

The novel coronavirus disease-2019 (“COVID-19”) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which started at the end of 2019 in Wuhan, experienced an outbreak that killed more than eighteen hundred and infected

over seventy thousand individuals within the first 50 days of the epidemic.

The SARS-CoV-2 virus is genetically related to SARS-CoV which in late 2002 had caused the first pandemic threat of a novel and deadly coronavirus leading to an outbreak of SARS.<sup>[1]</sup> The SARS 2003 outbreak stopped in June 2003 resulting in 8098 reported cases globally with 774 deaths and a case fatality rate of 9.7%<sup>[2]</sup> whereas the novel SARS-CoV-2 that emerged in December 2019 rapidly spread as a global pandemic. This pandemic is a challenge

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to both developed and developing countries causing huge stress on the healthcare system. India stands second in global burden in COVID-19 cases with around 33.3 million cases and 444 thousand deaths by the middle of September 2021.<sup>[3]</sup>

In all the pandemics so far, the most affected were the healthcare system and healthcare workers (HCWs). They were standing in the frontlines of this global crisis with the substantial task of diagnosing and treating a growing number of acutely ill patients. WHO defines HCWs as “all people engaged in actions whose primary intent is to enhance health”.<sup>[4]</sup> This includes doctors, nurses, midwives, paramedical staff, hospital administrators and support staff, and community workers, all of whom face the occupational risk of becoming infected with COVID-19, and at worst even death. During the 2002 SARS outbreak, as per the WHO report out of 8098 confirmed cases, 1707 (21%) were HCWs.<sup>[5]</sup>

Vaccination against SARS-CoV-2 is a leading strategy to change the course of the COVID-19 pandemic worldwide. The rapidly growing infection rate of COVID-19 worldwide during 2020 stimulated international alliances and government efforts to urgently organise resources to make multiple vaccines on shortened timelines.<sup>[6]</sup> On 2<sup>nd</sup> December 2020, the United Kingdom’s Medicines and Healthcare products Regulatory Agency (MHRA) gave temporary regulatory approval for the Pfizer–BioNTech vaccine, becoming the first country to approve the vaccine and the first country in the Western world to approve the use of any COVID-19 vaccine.<sup>[7-9]</sup> Following the emergency use authorisation of the COVID-19 vaccinations at the international level, the Ministry of Health and Family Welfare in India launched a vaccination campaign to immunise Indian population with two types of COVID-19 vaccines approved in India which are Covishield manufactured by Serum Institute of India and Covaxin manufactured by Bharat Biotech in India. On January 16<sup>th</sup> 2021, Government of India started its first vaccination programme for HCWs on a priority basis. As of August 31<sup>st</sup> 2021, 6.512 million doses have been administered across the country.<sup>[10]</sup> Despite the high level of vaccine efficacy, a small percentage of fully vaccinated persons will develop symptomatic or asymptomatic infections with SARS-CoV-2 virus.<sup>[11-14]</sup> Trials have shown that Covishield

has an efficacy of around 70% while Covaxin reportedly has shown an interim efficacy of around 81% in its Phase 3 trials.<sup>[15,16]</sup> That means none of these vaccines give 100% protection against COVID-19 disease and breakthrough COVID-19 infections are expected in a small number of people after vaccination which is defined by CDC as “A person who has SARS-CoV-2 RNA or antigen detected on a respiratory specimen collected ≥14 days after completing the primary series of a U.S. Food and Drug Administration (FDA)-authorized COVID-19 vaccine”.<sup>[17]</sup>

Indian Council of Medical Research studies showed that among 100.3 million people who had taken only the first dose of Covishield, 17,145 had got infected, which translates into a 0.02% prevalence.<sup>[18]</sup> Among the 15.7 million people who received the second dose of Covishield as well, 5,014 or about 0.03% had got infected later. Nearly 0.04% of people who had taken the second dose of Covaxin have tested positive for COVID-19.<sup>[18]</sup>

HCWs in the state of Kerala were immunised with either of the vaccines namely, Covishield or Covaxin. Surveillance data had shown few cases of breakthrough infection among HCWs all over the state. Therefore, the present study aimed to look into the incidence and profile of reported breakthrough infections among HCWs in Government Medical College, Kozhikode which is the largest public tertiary care centre in North Kerala. The study also did a comparison between COVID positive HCWs before and after the introduction of COVID vaccination. Knowledge regarding factors associated with breakthrough infections will help to identify high risk health workers, which is necessary for the effective functioning of health system.

### Subjects and Methods

The study was conducted in Government Medical College, Kozhikode, in North Kerala catering more than 8500 HCWs including employees and students. The institution had made arrangements to make free vaccination accessible to every HCWs within the hospital. The institution also offered free SARS-CoV-2 reverse-transcriptase–polymerase-chain-reaction (RT-PCR) testing and antigen-detecting rapid diagnostic testing (Ag-RDT) to symptomatic as well as asymptomatic HCWs.

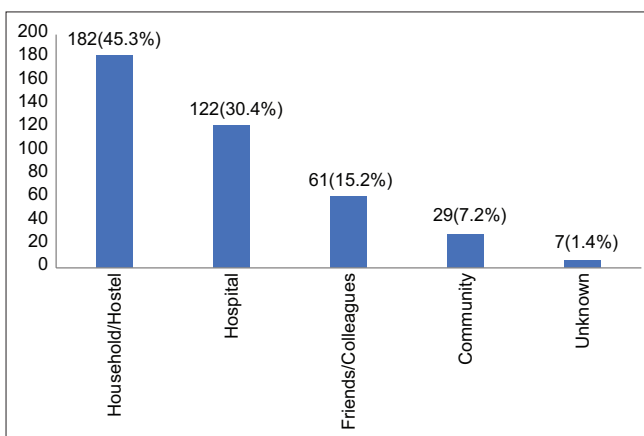


Figure 1: Sources of infection of breakthrough cases

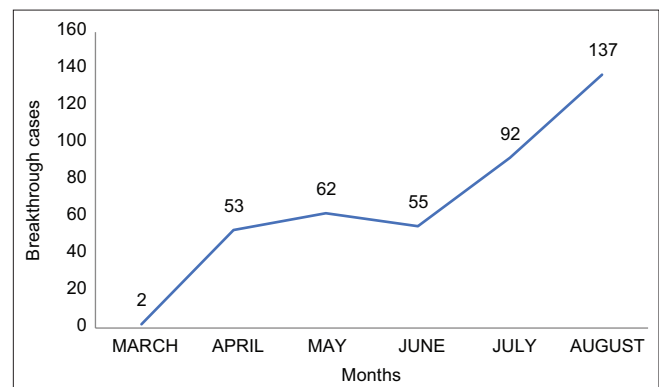


Figure 2: Month wise trend in breakthrough cases

## Study design

The research was conducted as a prospective study for a duration of 78 weeks from 1<sup>st</sup> of March 2020 through 31<sup>st</sup> of August 2021 in Government Medical College, Kozhikode. Study participants included HCWs who had turned COVID positive during the study period. COVID-19 vaccines were introduced in India from 16<sup>th</sup> January 2020, and the vaccine coverage for 2 doses among healthcare personnel in the institution reached around 98% during the study period. All staff and students who had received COVID vaccination were kept under surveillance for COVID-19 infection from the date of starting vaccination program.

Testing for the presence of SARS-CoV-2 by means of RT-PCR assay and/or Ag-RDT was available for fully vaccinated staff members and students who were symptomatic or had been exposed to an infected person, regardless of symptoms.

## Ethics

The study protocol was reviewed by the institutional review board and institutional ethics committee at Government Medical College, Kozhikode, and research was initiated only after getting approval from both. All procedures followed were in accordance with the ethical standards of the responsible committee and with the Helsinki Declaration. Written informed consent was obtained from study participants prior to the study. The protection of the privacy of research participants was ensured. The authors vouch for the accuracy and completeness of the data reported and for the fidelity of the study to the protocol.

## Outcome

The primary objective of this study was to find out the incidence and profile of breakthrough infections among HCWs in Government Medical College, Kozhikode. All HCWs who had become RT-PCR or Ag-RDT positive for COVID 19 after 14 days following 2<sup>nd</sup> dose of COVID vaccination were considered as a case of breakthrough infection. The secondary objective was to make a comparison between fully vaccinated HCWs who had received two doses of COVID vaccination and unvaccinated HCWs in the institution.

The data regarding sociodemographic details, potential source of infection, vaccination details, duration between vaccination date and postvaccination COVID-19 infection, symptomatology, persistence of COVID 19 symptoms, and potential primary contacts were collected as variables in this study through a telephonic interview. A pretested semi-structured questionnaire was utilised for collecting data.

## Statistical analysis

Data collected using a semi structured questionnaire were entered in an Excel sheet and checked for data completeness. No missing data have been found. Univariate analysis was done using frequency and proportions for categorical variables and means and standard deviation in case of quantitative variables. The

**Table 1: Profile of total COVID-19 positive HCWs in the institution**

	Frequency	Percentage
Number of unvaccinated HCWs turned COVID positive (n=557)		
Before starting COVID Vaccination	379	35.4%
After starting COVID Vaccination	178	16.6%
HCWs turned COVID positive after receiving COVID vaccination (n=513)		
Single dose alone	94	8.7%
Within 2 weeks of 2 <sup>nd</sup> dose	18	1.6%
2 weeks after 2 <sup>nd</sup> dose	401	37.5%
Total	1070	100%

\*HCWs, health care workers

**Table 2: Sociodemographic characteristics of COVID-19 positive HCWs**

	n=401, n (%)
Age group (years)	
<20	69 (17.2)
20-29	244 (60.8)
30-39	42 (10.5)
40-49	30 (7.5)
50-60	16 (4)
Gender	
Females	252 (62.8)
Males	149 (37.2)
Designation of HCWs	
Physicians	150 (37.4)
Nurses	56 (13.9)
Nursing Attenders/Cleaning staff	26 (6.5)
Laboratory technicians	13 (3.24)
Office staff	4 (0.9)
Students	141 (35.1)
Others	11 (2.7)

**Table 3: Clinical features of COVID and post-COVID symptoms in breakthrough cases**

COVID-19 symptoms	n (%)	Post-COVID-19 symptoms	n (%)
	total=227		total=70
Fever	142 (62.5)	Fatigue	21 (30)
Headache	104 (45.8)	Dyspnoea on exertion	15 (21.4)
Sore throat	62 (27.3)	Headache	12 (17.1)
Cough	61 (26.8)	Myalgia	6 (8.5)
Myalgia	50 (22)	Cough	5 (7.1)
Rhinitis	48 (21.1)	Giddiness	4 (5.7)
Fatigue	21 (9.3)	Chest discomfort	2 (2.8)
Anosmia	26 (11.5)	Hair fall	2 (2.8)
Ageusia	12 (5.3)	Sleep disturbances	2 (2.8)
Vomiting/loose stools	9 (3.9)		

\*Multiple responses were counted in this table

significance of the difference between proportions was assessed using the Chi-square test. A *P* value < 0.05 was considered statistically significant. The statistical analysis was conducted using the statistical package SPSS for Windows version 16 (SPSS Inc, Chicago, IL).

## Results

Overall, 8665 HCWs in Government Medical College, Kozhikode had received at least one dose of COVID-19 vaccine by the end of 6 months following introduction of COVID vaccination in India on 16<sup>th</sup> January 2021. Among them only 7125 were fully vaccinated with 2 doses, whereas 1508 were partially vaccinated with the first dose of COVID vaccine. The rest remained unvaccinated as they were ineligible for COVID vaccination due to various contraindications as per the national guidelines existed during that time.

### Profile of COVID positive HCWs till August 2021

By the end of August 2021, a total of 1070 HCWs in the institution were confirmed to be COVID-19 positive either using RT-PCR assay or Ag-RDT. Out of total COVID-19 positive HCWs, 35.42% (n = 379) became positive before the COVID vaccination programme was introduced in the institution on January 16<sup>th</sup> 2021 and 47.9% (n = 513) became positive after receiving at least one dose of vaccine [Table 1].

### Breakthrough infection among HCWs

Four hundred and one HCWs turned positive for SARS-CoV-2 virus on RT-PCR assay or Ag-RDT after 14 or more days following receipt of a second dose of COVID vaccine making the incidence of breakthrough infection among HCWs in Government Medical College, Kozhikode as 5.62%.

Majority of breakthrough cases were between the age of 20–29 years (60.8%) with a mean age of 27.18 years (SD 8.87) and median of 24 years [Table 2]. Minimum age was 18 years and maximum age was 59 years. Breakthrough cases were predominant in female health workers (63%) than male health workers. First case of breakthrough infection was in a Physician on March 25<sup>th</sup> 2021 following which a general trend of monthly increase in cases was observed with maximum cases reported in August 2021 [Figures 1 and 2]. Minimum duration between second dose and COVID test positivity was found to be 19 days and maximum was 179 days with a mean duration of 97 days (SD = 40 days) and median 98 days (inter quartile range [IQR] = 57–124). Mean duration between first and second dose of COVID vaccination was 36 days with minimum duration being 28 days and maximum being 122 days. Majority of HCWs were diagnosed using rapid antigen test (86.3%, n = 346) followed by RT-PCR (12.5%, n = 50). Only 1.2% (n = 5) had undergone TruNAAT for diagnosing COVID. Most affected category in this study was physicians (37.4%).

### Clinical features of COVID-19 and post COVID-19 among breakthrough cases

43.3% (n = 174) of breakthrough cases were asymptomatic [Table 3]. Among symptomatics, majority presented with multiple symptoms (87%). The most common symptom was fever in 62.5%. Category B patients with moderate symptoms

constituted 53.6% (n = 215), and 46.4% (n = 196) were Category A patients having mild symptoms alone or even asymptomatic. None of the breakthrough cases developed severe symptoms of Category C having complications which required intensive care (ICU) admission. Out of all breakthrough cases 30.9% were in home isolation whereas 60.1% had to get admitted in hospital at some point during their course of illness.

### Post COVID-19 symptoms in breakthrough cases

The guideline published by the National Institute for Health and Care Excellence (NICE), the Scottish Intercollegiate Guidelines Network, and the Royal College of General Practitioners has defined post-COVID as “signs and symptoms developed during or following a disease consistent with COVID-19 and which continue for more than four weeks but they are not explained by alternative diagnoses”.<sup>[9]</sup>

Incidence of post-COVID symptoms among breakthrough cases was 17.45% (n = 70) with fatigue being the predominant symptom.

### Comparison between fully vaccinated and unvaccinated COVID-19 cases among HCWs in the institution

The most commonly affected age group in both vaccinated and unvaccinated was 20–29 years which corresponded to the vast majority of interns and post-graduates who were caring for COVID positive patients. Before vaccination was started, HCWs of age <20 years were spared but once vaccination was in place, fully vaccinated undergraduate students were allowed to see patients which resulted in 17.2% of breakthrough cases in age group less than 20 years which was statistically significant [Table 4]. Students were significantly affected around three times more in post-vaccination than in pre-vaccination phase [Table 4]. As students were accommodated in hostels, it became the major source of infection after the vaccination (45.3%) [Table 5] whereas community acquired COVID-19 cases reduced in the post-vaccination phase (7.2%) [Table 6]. There was a reduction in incidence of post-COVID-19 syndrome in vaccinated group (17.45%) compared to unvaccinated group of HCWs (57.2%). The most common symptom was fatigue in both groups [Tables 7 and 8].

**Table 4: Comparison between various age groups of COVID-19 positive HCWs**

Age Category	Unvaccinated n (%)	Fully vaccinated with 2 doses n (%)	P
<20 years	0	69 (17.2%)	0.001
20-29 years	196 (50.3)	244 (60.8)	
30-39 years	102 (26.2)	42 (10.5)	
40-49 years	45 (11.5)	30 (7.5)	
50-59 years	41 (10.5)	16 (4)	
60-69 years	6 (1.5)	0	
Total	390	401	



**Table 5: Comparison of sources of infection between vaccinated and unvaccinated HCWs**

Sources of infection	Unvaccinated n (%)	Fully vaccinated n (%)	P
Hospital	113 (28.9)	112 (30.5)	0.0001
Hostel/household	59 (15.1)	182 (45.3)	
Friends/colleagues	63 (16.1)	61 (15.2)	
Community	107 (27.5)	29 (7.2)	
Unknown	48 (12.3)	7 (1.4)	
Total	390	401	

**Table 6: Comparison of various categories of COVID-19 positive cases between vaccinated and unvaccinated HCWs**

Category of HCWs	Unvaccinated n (%)	Fully vaccinated n (%)	P
Doctors	129 (33)	150 (37.4)	0.012
Nurses	76 (19.5)	56 (13.9)	
Nursing attenders	54 (13.8)	26 (6.5)	
Technicians	30 (7.7)	13 (3.24)	
Office staff	20 (5.1)	4 (0.9)	
Students	51 (13.1)	141 (35.1)	
Pharmacists	6 (1.5)	0	
Security personnel	11 (2.8)	0	
Others	13 (3.3)	11 (2.7)	
Total	390	401	

**Table 7: Comparison of major clinical features between vaccinated and unvaccinated HCWs**

Symptoms	Unvaccinated (n=261) n (%)	Fully vaccinated (n=227) n (%)	P
Fever	123 (32.8)	142 (29.7)	0.0001
Myalgia	61 (16.3)	50 (10.5)	
Sore throat	40 (10.7)	62 (13)	
Cough	24 (6.4)	61 (12.8)	
Fatigue	25 (6.7)	21 (43.9)	
Headache	54 (14.3)	104 (21.7)	
Anosmia	24 (6.4)	26 (54.3)	
Ageusia	23 (6.2)	12 (2.5)	

## Discussion

This study was done to describe the characteristics of breakthrough cases among HCWs during the first 6 months after COVID-19 vaccination was introduced in Government Medical College, Kozhikode, and also to compare the profile of breakthrough cases with that of unvaccinated COVID-19 positive HCWs. Our study found a breakthrough infection incidence of 5.62% which was consistent with other studies<sup>[20,21]</sup> but high in comparison to findings by Moriah Bergwerk *et al.*<sup>[22]</sup> A study done in Delhi reported 6.1% non-breakthrough infections in the HCWs who were vaccinated with at least a single dose of a COVID-19 vaccine, or both doses, but prior to 14 days since the administration of the second dose.<sup>[21]</sup> But it was only 1.57% in the present study. The median interval

between the receipt of the second dose of vaccine and diagnosis was 37 days in a study<sup>[22]</sup> against a median of 98 days in the present study. Physicians constituted the majority of breakthrough cases in our study and same was found by Pragya Sharma *et al.*<sup>[21]</sup> Moza Alishaq *et al.*<sup>[23]</sup> revealed that nursing and midwifery job family were the largest group with breakthrough infection (41.5%), followed by allied health professionals and physicians, the main source of infection being house hold contacts followed by hospital contact. Asymptomatic were more in breakthrough cases in our study than that of unvaccinated HCWs. Similar was the scenario in a randomised trial of the mRNA-1273 vaccine (Moderna) vs. placebo where vaccinated participants were two-thirds less likely to be asymptomatic carriers than unvaccinated participants.<sup>[11]</sup> Most common symptom in our study among breakthrough cases was fever. But in many studies fever as a symptom was less in breakthrough cases.<sup>[22,24]</sup>

Hospitalisation among breakthrough cases was more in this study the reason being the hospital institutional policy of admitting junior doctors who were staying in campus hostels to avoid further spread of infection. But symptoms were less severe among breakthrough cases in line with other studies.<sup>[24-26]</sup> The study by Tenforde *et al.*<sup>[27]</sup> demonstrates that vaccines are associated with a lower likelihood of hospitalisation along with attenuation of the seriousness of illness during hospitalisation. This is also supported by Sun *et al.*<sup>[28]</sup> whose study established a decrease in disease severity and hospitalisations in vaccinated immunocompromised persons who had a breakthrough infection compared with immunocompromised persons who had a COVID-19 infection before vaccination. In contrary, Juthani *et al.*<sup>[29]</sup> found that 26% of breakthrough cases had severe or critical illness, the median age for severity being 80.5 years (IQR 76.5–85.0). A recent systematic review by Stephen Y Wang *et al.*<sup>[30]</sup> also found that 37% of severe or critically ill COVID-19 breakthrough cases had a mean age of 71.5 years. But our cohort included working age groups, the highest age being 60 years.

Rate of post-COVID-19 syndrome in our study was 17.45% among breakthrough cases and 57.2% among unvaccinated HCWs. Almost similar figures were arrived by Moriah Berghweg.<sup>[22]</sup> A cohort study by Reaz Mahmud *et al.*<sup>[31]</sup> in Bangladesh found that 46% of unvaccinated COVID cases had developed post-COVID-19 syndrome with post-viral fatigue being the most predominant symptom. Female gender was found to a significant risk factor.

## Summary and Conclusion

Vaccination against COVID-19 still remains the most important strategy in preventing COVID-19 cases. Though breakthrough cases are possible, vaccination prevents severity and complication and reduces ICU admissions and incidence of post-COVID-19 syndrome. Protecting HCWs is key to ensuring a functioning health system and a functioning society. So it is advisable to make it mandatory to be part of hospital policy to vaccinate HCWs

**Table 8: Comparison of major post-COVID symptoms between vaccinated and unvaccinated HCWs**

Symptoms	Unvaccinated (n=194) n (%)	Fully vaccinated (n=70) n (%)	P
Fatigue	103 (53.4)	21 (30)	0.18
Myalgia	34 (17.6)	6 (8.5)	
DOE	93 (48.1)	15 (21.4)	
Cough	21 (10.7)	5 (7.1)	
Headache	24 (12.2)	12 (17.1)	
Chest discomfort	17 (9)	2 (2.8)	
Sleep disturbances	8 (3.9)	2 (2.8)	

preferably free of cost with complete doses of COVID-19 vaccine.

**Limitation:** The details about vaccination status, date of vaccination, and symptomatology were collected through a telephonic interview which could have led to information bias.

**Future aspects of the study:** Further studies are needed to assess the long-term sequelae and duration of protection of COVID-19 vaccines.

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### Conflicts of interest

There are no conflicts of interest.

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