

Breakthrough COVID-19 Infection among Health Care Workers after Booster Dose during Third Wave, in a Teaching Hospital, India

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Background and study aim: Very few studies have demonstrated the effects of a booster dose, and almost none after the emergence of the Omicron sub-lineage variants. The policy of giving a booster dose to healthcare workers started with the eminent third wave. The aim was to calculate the breakthrough infection rate among healthcare workers after receiving a booster dose during the third wave of the pandemic in India.

Patients and Methods: The authors conducted the study in a teaching hospital in India. The study defined breakthrough infection as a positive report on day seven or later. The study collected the list of healthcare workers who took booster doses from 10 January to 15 February 2022 and tested symptomatic for SARS-CoV-2. From 16 January 2022, we telephonically contacted all positive persons and obtained their history. Similarly, the authors collected daily information about positive healthcare

workers from all wards and outpatient departments.

Results: Forty-eight healthcare workers had a breakthrough infection among 803 who took booster doses; however, 43 telephonically responded. The mean interval between booster dose and positivity was 13.93 (S.D.=6.10) days. The breakthrough infection rate was 194.51/per 100,000 person-days. The most affected profession was doctors (66.44%). The participants perceived that a history of contact (apart from their COVID-19 ward duty) was the commonest reason for contracting the infection. About one-fourth of them had some comorbidity. The commonest comorbidity was hypertension. All had mild symptoms.

Conclusion: Among healthcare workers, breakthrough infections were low during peak transmission.

INTRODUCTION

A few vaccines against SARS-CoV-2 were developed about a year after the first outbreak. For most vaccines, primary immunization consists of two doses. Many studies have been conducted to assess the efficacy of vaccines, particularly after primary vaccination [1–4]. Among these, some were supported by the pharmaceutical industries. Prolongation of the COVID-19 pandemic resulted in the recommendation of booster dose vaccination. In India, the Recombinant ChAdOx1 nCoV-19 Corona Virus Vaccine is predominantly used, as it is

produced in large quantities compared to other vaccines. Before the third wave, India reported the lowest COVID-19 cases (5,326) on 20 December 2021. Then, the third wave started, drastically increasing the number of cases. It reached the highest number of 3,47,256 in one month, i.e., on 20 January. The number also declined at a similar pace, 5,476 cases on 5 March 2022. India also devised a booster dose policy considering the rising number of patients globally. The booster dose administration started on January 10, 2022, for health care workers, frontline workers, and senior citizens with comorbidities. The

recommended guidelines for booster included a minimum interval of 39 weeks after the second dose and the use of the same vaccine for the booster dose. The government of India recommended the dose for a person diagnosed with COVID-19 after 12 weeks [5]. There have been reports of vaccine breakthrough infections after two doses [6–9]. But very few have been reported after a booster dose [10–12]. In India, with a population of 1.21 billion in the last census of 2011 [13], no study estimates the breakthrough infection rate of COVID-19 infection after booster during the third wave. Breakthrough infection studies have not been published even one and a half years after the present study. The booster dose administration started almost coincident with the onset of the third wave. Hence, it was an opportunity to calculate the breakthrough infection rate among health care workers in a medical college hospital during the third wave after receiving a booster dose. The second objective was to estimate the duration between the booster dose and positive results .

METHODS

Study design: It was an observational, short follow-up study

Setting: The authors conducted the study in a medical college hospital with 851 beds, with all broad specialties and most super-specialties. After a contract with the Pune Municipal Corporation, our teaching hospital functioned as a designated COVID-19 hospital. The hospital is certified by the National Accreditation Board for Hospitals & Healthcare Providers (NABH), and the laboratories are accredited by the National Accreditation Board for Testing and Calibration Laboratories (NABL). Pune is India's ninth most populous city, located in western Maharashtra. The study team collected the data on daily booster doses administered to health care workers from 10th January 2022. A research assistant compiled patients' data who tested positive on RT-PCR or Antigen test for COVID-19 from 16 January 2022 to 15 February 2022 .

Participants: All the health care workers who took booster doses of the Recombinant ChAdOx1 nCoV-19 Corona Virus Vaccine were eligible. The health care workers included doctors, nurses, technicians, sanitation workers, security, medico-social workers, dieticians/nutritionists, and administrative staff. The names of those who received boosters were

collected from the vaccination registration section.

Data collection: The study monitored breakthrough infections among health care workers by two methods. Trained technicians collected nasopharyngeal swabs from all healthcare workers developing symptoms and subjected them to RT-PCR/RAT testing. The hospital infection committee also collected daily information about positive health care workers from all the departments, wards, etc. A research assistant retrieved the list of all patients who tested positive (RT-PCR or rapid antigen test) from the laboratory daily and contacted these patients telephonically. The research assistant confirmed the date of taking the booster dose. The research assistant also inquired about the exact profession of the health care worker, clinical severity of the current illness, history of probable exposure, and presence of comorbidities, if any.

Variables: A symptomatic person positive by RT-PCR or Rapid Antigen test in our laboratory or any other laboratory. The study defined a breakthrough infection as 'COVID-19 positivity on day seven or later' after taking a booster dose [12]. The authors classified the severity of the breakthrough infection as mild, moderate, or severe, as per government guidelines.

Data sources and measurements: The research assistant obtained the list of health care workers who took the booster dose from the vaccination registration section. The research assistant collected all positive persons' names and contact numbers from the microbiology laboratory daily. The infection control nurses collected daily information about positive health care workers from various wards/outpatient departments.

Sample size, sampling, and data analysis: We did not calculate the sample size. All eligible were included.

The research assistant entered the data in Excel. The statistician analyzed the data. We calculated the person-days follow-up from the date of taking the booster to the end of the study period or the date of positivity (those who turned positive).

RESULTS

From 10 January to 15 February 2022, 803 health care workers took the booster dose, and

76.96% (618/803) had taken the booster within the first six days. All had received two doses earlier. After starting the compilation of positive health care workers, 66 health workers were detected positive, including five antigens positive. Out of them, 48 were positive on the seventh day or later. About 10% of health care workers tested positive for antigens in laboratories. Figure 1 gives the details. Within 16 days from 17 January 2022 to 1 February 2022, 89.56% (43/48) were positive. Figure 2 shows daily positivity. The interval between taking booster and positivity had a normal distribution. Kolmogorov-Smirnov test statistic [D] is 0.161; $p=0.195$. The mean duration between booster and positivity was 13.93 days (S.D.=6.10). The incidence of breakthrough infection was 194.51/per 100,000 person-days followed .

The research assistant interviewed 43 health care workers. Table 1 gives the age and sex details of positive persons. The mean age of the patients

was 39 years (S.D.=13.40) the minimum age was 21, and the maximum was 65 years.

Among the detected positive persons, the doctors, including teaching faculty and residents undergoing post-graduate training, were maximum of 67.44% (29/43), followed by nurses, 20.93% (9/43), then laboratory technicians, 4.65% (2/43). The affected clerk, dietician, and nutritionist were 2.33% each (1/43). Table 2 gives the perception of health care workers about the probable reason for contracting the infection (history of contact with a COVID-19-positive person other than COVID ward duty).

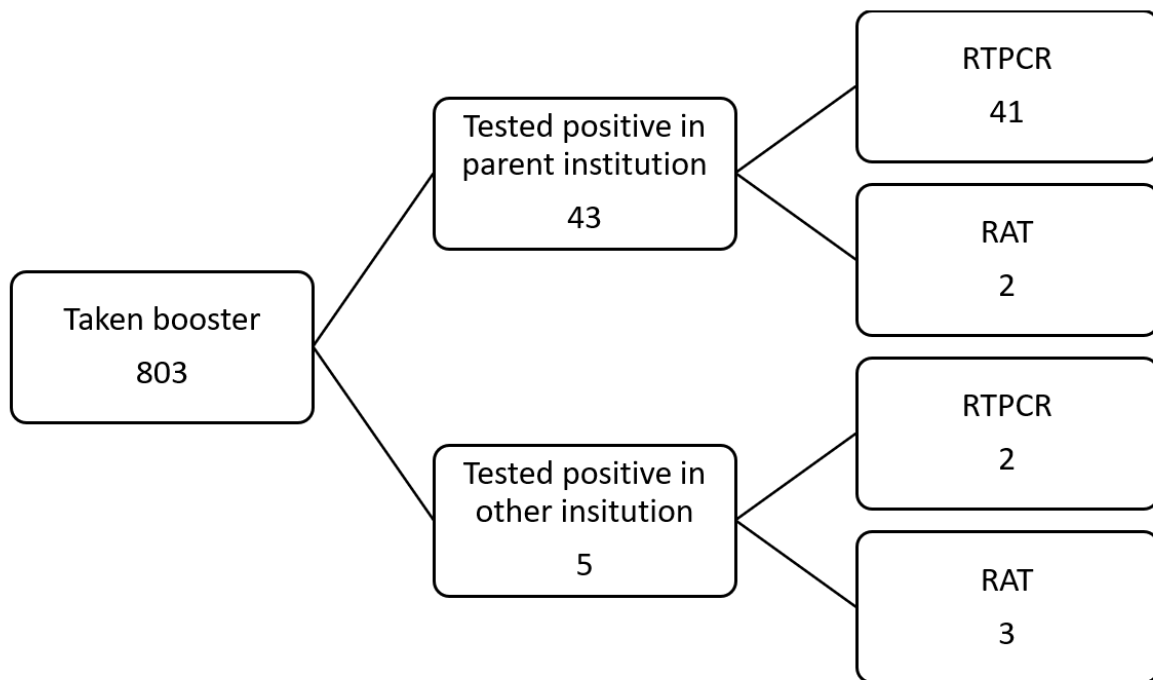
Comorbidities were present in 23.26% (10/43) of patients. Four patients had hypertension; two had hypertension plus diabetes. We had one person with diabetes, one with diabetes plus asthma, one with hypothyroidism, and one with obesity. The symptoms in all the patients were mild; thus, there was no need for hospitalization.

Table (1): Demographic characteristics of patients, Pune, India, 2022

Age groups in years	Sex		Total
	Female	Male	
20-29	13	3	16
30-39	8	2	10
40-49	5	0	5
50-59	6	2	8
60-69	1	3	4
Total	32	11	43

Table (2): Probable way of contracting infection, Pune, India, 2022

Perceived ways of infection	Frequency
History of contact with positive person	21 (48.84)
Crowded workplace	10 (23.26)
COVID ward duty	2 (4.65)
Attended crowd/gathering	3 (4.65)
Travel	4 (4.65)
Can't say	6 (13.95)
Total	43 (100.00)

**Figure 1.** Test and positivity among health care workers in a teaching hospital after receiving booster vaccine Pune, India, 2022.

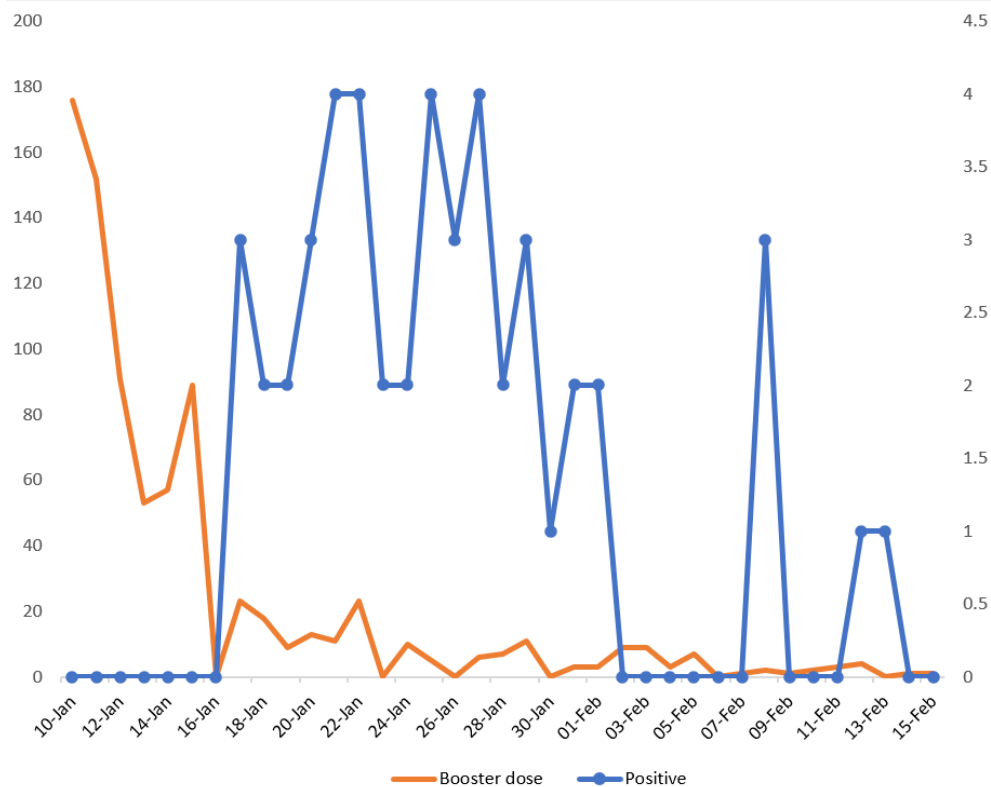


Figure 2: Daily booster doses and positivity among health care workers in a teaching hospital, Pune, India, 2022.

DISCUSSION

The effectiveness of a booster or third dose is established [14,15]. The present study is probably the first in India to measure the incidence of breakthrough COVID-19 infection after a booster dose. Within one week of taking the booster, we recorded 18 symptomatic and positive health care workers, which implied that they might be in the incubation period at the time of taking the booster. We had to stop the study as the number of positive persons in our institution daily almost reduced to zero after one month. The third wave in the country was almost over by 15th February 2022; the number of cases decreased to only 30,615 (91.83% reduction against 20th January number of 3,47,256). It indicated that the peak transmission period was only one month. It is known that adequate antibodies develop within a week after booster dose administration [10]. Breakthrough infection after booster is confirmed if infection occurs > 7 days after receiving the booster [12]. The study adopted this criterion to confirm the breakthrough infection. After one week, the odds ratio of getting positive results among received boosters drastically reduces compared to

receiving two doses [16]. In the present study, the mean period between booster and positivity was 14 days. The occurrence of breakthrough infection during the peak transmission was 194.51/per 100,000 person-days followed. The most probable reason for contracting the disease perceived by the health care workers was a history of contact with a positive person (apart from ward duties). The reasons for breakthrough infection can be grouped into four categories: vaccine parameters, viral properties, host determinants, and immunity characteristics [17]. In the present study, the last two are more relevant. We had an intermediate risk of breakthrough infection compared to other studies among health care workers.

One of the reasons for the comparatively small number of breakthrough cases or intermediate risk in our study could be strict compliance to the optimal interval of 39 weeks between the second and booster doses, concordant with a small study that observed the best effect after a 35-week gap between the second and booster doses [6]. Many studies have calculated breakthrough infection after two doses. Breakthrough infections are certainly less after booster than receipt of two doses [7]. The booster dose offers protection

even for very senior citizens [18]. After the booster, the vaccine efficacy may be as high as 97% for two months; then, it may decline [19]. The best protective property lies between half to one month. [6] In the present study, the mean follow-up period was only 15 days, implying that a longer follow-up could have detected a few more cases. In another small study, the breakthrough infections occurred 22 to 59 days after the booster [11]. However, a more extended follow-up period of about two months may not have added any additional cases: or the increase in the actual number of patients may have been minimal. The number of positive patients drastically declined across the city, state, and country when the present study was on. India reported the maximum number of cases on 20 January 2022, then the number reduced drastically [20]. There might be some asymptomatic cases among health care workers who could have gone undiagnosed. However, it has minimal clinical significance.

The breakthrough infection rate in the present study is higher than in a similar study among health care workers in Israel, which recorded an incidence of 12.8/100,000 person-days [12]. A smaller study in Italy among healthcare workers observed a higher incidence of 2.5 cases per 1000 person-days [21]. Therefore, we feel that our breakthrough infection rate was intermediate. The breakthrough incidence also depends on the previous infection, as hybrid immunity gives better protection [21]. In contrast to no hospitalization in the present study, data analysis from the United Kingdom recorded a low incidence of severe/hospitalization of 7.6 events per 1000 person-years [22]. But that study followed the persons for a more extended period. Theoretically, a longer follow-up in the present study may have resulted in a slight increase in the absolute number but decreased the rate of occurrence because of a substantial increase in the number of person-day follow-ups, i.e., the denominator. That might have been closer to the Israel study [12]. In the community, the incidence may be as low as 1.90 in the USA to 8.81/per 100,000 person-days in Israel [10,23]. The apparent reason for the higher incidence among health care workers than in the community is the greater exposure to the virus. In particular, the current study's comparatively high incidence may be due to a short follow-up period and a large proportion [about one-fourth] having some comorbidity. Proportionate to the

coverage of booster dose vaccination, the proportion of having received booster dose among positives decreases. Among those testing positive, the proportion of individuals receiving the booster dose has been reported at around 7% [19]. In concordance with the present study, it has been universally observed that the illness is usually mild among those who received booster doses, and usually hospitalization is not required [21]. Only about one to three percent may require hospitalization [6,10]. There may be different views about booster doses for infection prevention [24], but prevention of severe disease is sure [25].

One study reported seven cases after a booster dose. The isolates confirmed during the third wave were omicron (PANGO lineage B.1.1.529, Nextstrain clade 21K) [11]. We believe that most of our cases were omicron infections] 26 [.

There is some hesitancy in accepting the booster dose of the COVID-19 vaccine. India has covered only about 25% of the eligible population for the booster dose [27]. The usual reasons for hesitancy include fear of side effects, efficacy [particularly with changing strains] of vaccination, and the need. The need for increasing booster dose coverage continues as few cases are still being reported, indicating very low endemicity. A novel pictorial way of convincing people about the impact of a booster dose may be helpful [28]. The results of this study may help in promoting the booster dose.

CONCLUSION

The findings reiterate that a booster dose offers protection from the disease even to high-risk professionals like health care workers and prevents hospitalization during peak transmission. Naturally, the incidence of breakthrough infection in the community will be far less than observed in this study. Dissemination of these results should serve to encourage individuals to take booster doses.

Limitations: We did not study the genomic sequence of the isolated viruses, neutralizing antibody titer, or cell-mediated immunity. It was not a microbiological study; the only objective was to estimate the breakthrough infection rate after booster dose. We did not test asymptomatic individuals and did not ask for a history of COVID-19 infection. The follow-up period was short.

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Statement of Ethics: The Institutional Ethics Committee (DCGI Reg. No. ECR518/Inst/MH/2014/RR-17) approved this research proposal. The authors obtained verbal consent from all the participants.

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Author Contributions: We declare that all listed authors have made substantial contributions to all of the following three parts of the manuscript:

- Research design, or acquisition, analysis or interpretation of data[‡]
- drafting the paper or revising it critically[‡]
- approving the submitted version.

We also declare that no-one who qualifies for authorship has been excluded from the list of authors.

Research Highlights:

1. Covid 19 vaccine booster dose offers protection from the disease even to high-risk professionals like health care workers.
2. Among healthcare workers, breakthrough infections were low during peak transmission.

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