

Severe Acute Respiratory Syndrome Related Coronavirus 2 (SARS-Cov2) Infection Among Doctors and Nurses After Introduction of Vaccination - A Tertiary Care Experience from Mumbai

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ABSTRACT

Introduction: Acute Respiratory Syndrome related Coronavirus 2 (SARS-CoV2) is a novel Coronavirus causing the current pandemic. Among all the efforts to curtail the pandemic, vaccination is an important pillar towards halting transmission and reducing morbidity and mortality due to this disease. SARS-CoV2 has affected healthcare professionals (HCPs) globally. HCPs were a priority group that was vaccinated in the first phase in India. No vaccine is 100% effective. The effectiveness of the SARS-CoV2 vaccine in this high risk group needs to be studied.

Objective: This study was undertaken to understand the number of breakthrough infections among doctors and nurses, their clinical presentation and outcomes after SARS-CoV2 vaccination was started in January 2021.

Materials & Methods: This was a prospective study conducted in a 221 bed tertiary care hospital in Mumbai. Data regarding vaccination of doctors and nurses were collated from 16th Jan 2021 to 30th July 2021. The vaccines used were Covisheild (**ChAdOx1-S/nCoV-19**) and Covaxin (**BBV152**). A total of 638 HCWs were enrolled into the study comprising of 519 nurses and 119 doctors. Relative risk and chi-square test analysis was performed to determine if there was a significant difference between breakthrough infections among those fully vaccinated versus the partially or non vaccinated HCWs.

Results: 582/638 (84.3%) of our HCWs were vaccinated with atleast one dose of the vaccine as of 31st July 2021. 404/638 (63.3%) of the HCWs were vaccinated with both doses of the vaccines. 178/638 (27.9%) were vaccinated with only the first dose. 48/638 (7.52%) were not vaccinated till 31st July 2021. Breakthrough infections (BTIs) were seen in 5.2% (21/404) of HCWs. 22.9% (11/48) of unvaccinated HCWs had the infection in 2021 after vaccines were introduced. 17.4% (31/178) HCWs got infected after the first dose of vaccine. 13.5% (7/52) of infected HCWs got admitted but did not require any oxygen support indicating they all had mild disease. All HCWs recovered completely.

Conclusion: Our data clearly indicates that vaccination has a protective effect to SARS-CoV2 infection, with 22.9% infection among the unvaccinated HCWs and only 5% infection among HCWs who had taken two doses of the SARS-CoV2 vaccine. All infections post vaccination were mild in our study.

KEYWORDS: COVID vaccine, breakthrough infections, incidence, outcomes

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INTRODUCTION

Vaccination is considered as an important intervention in halting the transmission of the Severe Acute Respiratory Syndrome related –Coronavirus- 2 (SARS – CoV- 2) infection, a disease responsible for more than 240 million confirmed cases and > 4 million deaths since Dec 2019 (as of

19th October 2021). (1) On 16th January 2021, India began its first phase of COVID 19 vaccination with AZD 122 ChAdOx1-S/nCoV-19 (Covisheild) and BBV152 (Covaxin). (2)

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ChAdOx1-S/nCoV-19 is a recombinant vaccine containing a replication deficient Adenovirus vector that expresses the SARS-CoV-2 spike protein gene (3) It is manufactured by Serum Institute of India (SII, Pune) through a license from AstraZeneca – University of Oxford, UK. (3) BBV152 (Covaxin), is an indigenous vaccine developed by Bharat Biotech, Hyderabad in collaboration with the Indian Council of Medical Research (ICMR). The first phase of the vaccine roll out was planned to vaccinate , approximately 10 million healthcare workers , 20 million frontline workers and 260 million prioritized age groups (>50 years). (4) Vaccination for our healthcare workers at Breach Candy Hospital Trust, Mumbai also started on 16th January 2021.

No vaccine is 100% effective and the efficacy of the AZD 122 (ChAdOx1-S/nCoV-19) was found to be approximately 70% based on clinical trials and some real world studies. (5,6) Vaccine effectiveness needs to be determined from real world population studies. Hence post vaccination surveillance of infection is essential. As per the Centers for Disease Prevention and Control (CDC, USA), for the purpose of surveillance, a vaccine breakthrough infection (BTI) is defined as the detection of SARS-CoV-2 either RNA or antigen in a respiratory specimen collected from a person ≥ 14 days after they have completed all the recommended doses of an approved COVID-19 vaccine. (7) Data documenting BTIs among HCWs started being published from various parts of the world as well as India in the early 2021. There were no similar studies from Western India at the time. This study was under taken to determine the BTI rates among doctors and nurses at Breach Candy Hospital Trust, Mumbai since there was scarcity of literature from the Western part of India.

MATERIALS & METHODS

This was a prospective study undertaken between 16th January 2021 to 31st July 2021 at a 221 bed tertiary care hospital managing COVID 19 patients in Mumbai. Prior to the roll out of vaccination, the local Municipal authorities had asked all healthcare facilities to send data of HCWs eligible for vaccination. HCWs were encouraged to take the one of the two vaccines available as mentioned above. A central data registry was maintained to track adverse events and records of vaccination. Only doctors and nurses were included in the study. Other HCWs categories were excluded from the study . All symptomatic HCWs were directed to a triage OPD for examination and testing. A Polymerase chain reaction (PCR) for SARS-CoV2 was performed for all symptomatic HCWs. The PCR detected 3 genes per assay namely E gene, S gene, RdRP gene and ORF 1AB or N gene as recommended by Indian Council of Medical Research (ICMR) (8)

Relative risk and chi-square test analysis was performed to determine if there was a significant difference between breakthrough infections among those fully vaccinated versus the partially or non vaccinated HCWs . Ethical clearance was

received for the study by Breach Candy Medical Research Center (BCMRC).

RESULTS

A total of 638 HCWs were enrolled into the study, 519 nurses and 119 doctors. The doctors included full time resident doctors and trainee post graduate doctors in various fields of Medicine. 562/638 (88%) HCWs were females & 76 (12%) were males.

All HCWs included in the study were vaccinated with ChAdOx1-S/nCoV-19 (Covisheild) only. 582/638 (84.3%) of these HCWs were vaccinated with at least one dose of the vaccine by 31st July 2021. (Fig 1). 178/638 HCWs(27.9%) were vaccinated with only the first dose (partially vaccinated) and 48/638(7.52%) were not vaccinated until 31st July 2021. (Fig 1) 8 nurses were lost to follow up. 404/638 (63.3%) of the HCWs were vaccinated with both doses of the vaccines (fully vaccinated) and were included in the assessment for determining breakthrough infections (BTIs).

Breakthrough infections (BTIs) were seen in 5.2% (21/404) of HCWs (Fig 2) . 19 females and 2 males were affected by breakthrough infections with median and mean Cycle threshold value (Ct) of 20 (range 12 – 29.56) . The median duration for BTI among the HCWs was 39.38 days (14 days to 112 days) from the second dose of the vaccine. 17.4% (31/178) HCWs got infected after the first dose of vaccine (Fig 2) and the median Ct value for this group was 18 (range 11- 30). The relative risk (RR) of infection in partially vaccinated HCWs was 3.0 (95% CI = 1.7693 to 5.0928 , p value <0.0001) when compared with the fully vaccinated HCWs . Among the HCWs who were not vaccinated, 22.9% (11/48) had SARS-CoV2 infection in 2021 after vaccines were introduced (Fig 2) with a median Ct value of 21.62 (range 12 - 28). The relative risk (RR) of infection in unvaccinated HCWs was 3.77 (95% CI = 1.9178 to 7.4238, p <0.001) when compared with the fully vaccinated HCWs . The Chi square test for partially vaccinated and unvaccinated HCWs was significant ($\chi^2_{(2)} = 9.52$, p <0.05) further indicating that full vaccination had a protective effect. (Table 1)

The most common complaints were fever, headache, body ache and sore throat experienced by the HCWs. 13.5 % (7/52) of infected HCWs got admitted but did not require any oxygen support indicating they had mild disease. None of the HCWs who experienced a BTI were admitted. All HCWs recovered completely. We did not document any secondary transmissions in our cohort.

DISCUSSION

In India, emergency use authorization approval was received for the use of ChAdOx1-S/nCoV-19 (Covisheild) and BBV152 (Covaxin) during the first phase roll out. Sharma et al reported 11.3 % BTIs in their cohort of 325 HCWs from a

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medical college and hospital complex in Delhi in June 2021. (9) Another study from The Institute of Liver & Biliary Sciences, New Delhi documented 11.79% BTIs from 1858 HCWs that were enrolled into the study. (10) A study from Uttar Pradesh, India, enrolled both HCWs and non HCWs and reported 17.2% laboratory confirmed BTIs (247/1435). (11) A large tertiary care center from South India reported 9.6% BTI among their 7080 fully vaccinated HCWs. (12) Ghosh et al reported a BTI rate of 0.19% (2512 /1312938) in fully vaccinated healthcare workers and frontline workers of the Indian Armed Forces. (13) We reported 5.2% BTI infections in our cohort of HCWs who had taken ChAdOx1 nCoV-19 vaccine which was lower than other hospital based studies from North & South India. As is seen from various Indian studies, the BTI rate of infection seems to vary from 0.19% to 17.2%. Jung et al reported 4 BTIs among 8678 (0.04%) among HCWs from Asan Medical Center in Seoul South Korea. All of them had received the ChAdOx1 nCoV-19 vaccine (Oxford–AstraZeneca) vaccine. (14) Lange et al described BTI in 4 (0.35%) HCWs in a fully vaccinated cohort of 1137 who were vaccinated with BNT162b2 (Pfizer–BioNTech) from University Medical Center Mannheim in Germany. (15) Mosa et al from Qatar also reported 0.7% of BTIs among 22,247 HCWs who had taken the Pfizer-BNT162b2 or Moderna-mRNA1273 vaccines (16) Bergweck et reported 2.6% BTIs from a study conducted on 1497 HCWs in the largest medical center in Israel following vaccination with the BNT162b2 messenger RNA vaccine. (17) From the above studies, it is observed that globally BTI rates among HCWs are lesser than those reported in India. (Table 2)

The sudden increases in India's daily positivity rate from 1.62% on 1st March 2021 to 20% on 13th May 2021 marked the second wave of the COVID 19 pandemic in India. (18) Mumbai recorded 7,24,710 cases and 9,440 deaths (till 12th May) during the second wave. (19) Genomic analysis during the second wave suggested a predominance of the Delta variant, B.1.617.2, which had mutations in the spike protein gene. (20) This was also reflected in our study with approximately 73% of infections among our HCWs being due to variants with the Spike gene being absent in the PCR result. The Delta variant was also common in other studies from India (10, 20). Lange et al reported, Variant of concern (VOC) B.1.1.7 (Alpha) in the 4 HCWs with breakthrough infection at their center in Germany (15) Bergweck et al also reported B.1.1.7 variant in 85% of the breakthrough infections reported from their center in Israel and observed that this was similar to its prevalence in the community. (17) Rovida et al from Italy also reported the alpha variant to predominate in their cohort of HCWs with BTIs (21)

In our study, the median duration of BTI from the second dose was 39.38 days. Other Indian studies have reported 39 days (11), 47 days (9,12) and 50 days (10) as the median duration

for a BTI to occur. Studies from other countries report the median time for BTI after the second dose to be 37 days from South Korea (14), 39 days from Israel (17) and 61.5 days from Germany (15). The reason for this shorter median duration in our study is likely to be the coincidental second wave that Mumbai experienced during the period of the study. The median Ct value for fully vaccinated and partially vaccinated HCWs in our study was 20 and 18 respectively which indicates high viral loads. Kale et al also reported median Ct values of 23.24 and 21.13 in fully vaccinated and partially vaccinated HCWs in their study cohort from New Delhi. (10) Other HCWs based breakthrough infection studies from Germany and South Korea reported median Ct value of 22.5 and 13.1 respectively. (14,15) In the study conducted by Bergweck et al in Israel, 74% of infected HCWs had a Ct value of <30. (17) All the studies thereby indicate that despite high viral loads, most patients with infections after vaccination have had mild illness due to the protective effects of the COVID 19 vaccines.

In our study, the relative risk (RR) of infection in unvaccinated HCWs to the fully vaccinated HCWs was 3.77 (95% CI = 1.9178 to 7.4238, p value <0.001). Victor et al also documented the protective effect of vaccine among HCWs who were fully vaccinated versus the unvaccinated HCWs. (12)

To the best of our knowledge this is the first study from Western India describing the impact of vaccination among HCWs who were at the forefront of managing COVID 19 cases. A limitation of our study was the absence of genomic analysis of the SARS-CoV2 strains infecting this cohort.

CONCLUSION

While additional research is needed to understand the efficiency of vaccination on the changing variants of SARS-CoV2. Our data clearly indicates that vaccination has a protective effect to SARS-CoV2 infection, with 22.9% infection among the unvaccinated HCWs and only 5% infection among HCWs who had taken two doses of the SARS-CoV2 vaccine. All infections post vaccination were mild in our study indicating the SARS-CoV2 has a protective effect towards severe infections.

Conflict of Interest

No conflict of interest

Author Contributions

All authors have contributed in the study, preparation and review of the manuscript

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Tables & Figures

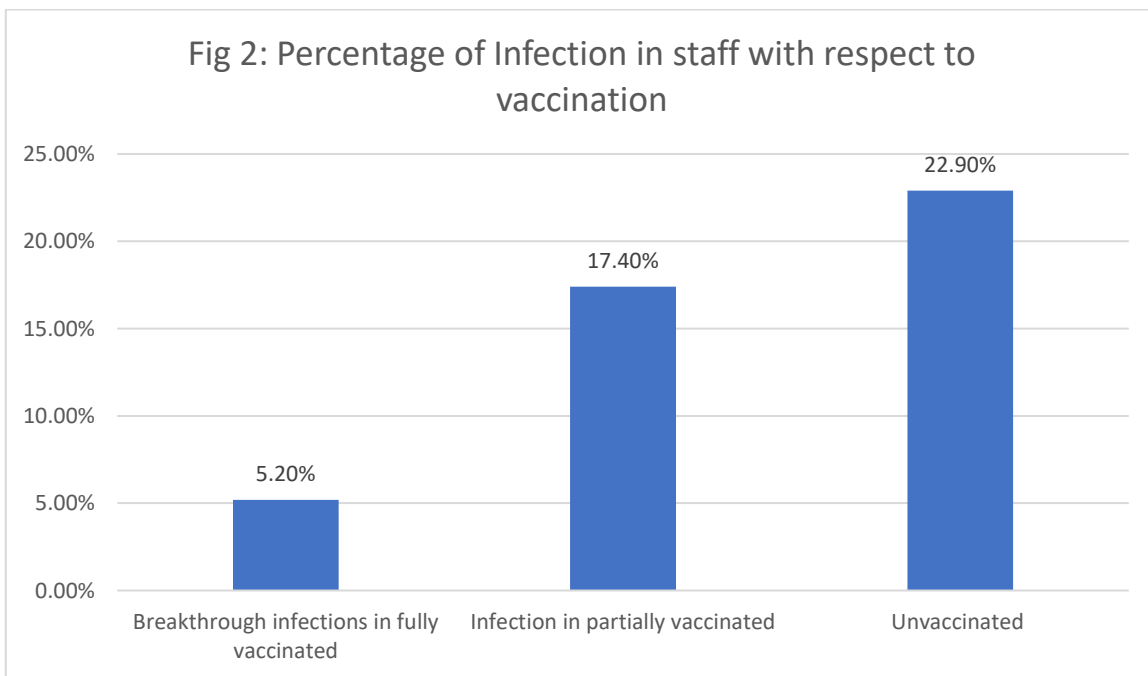
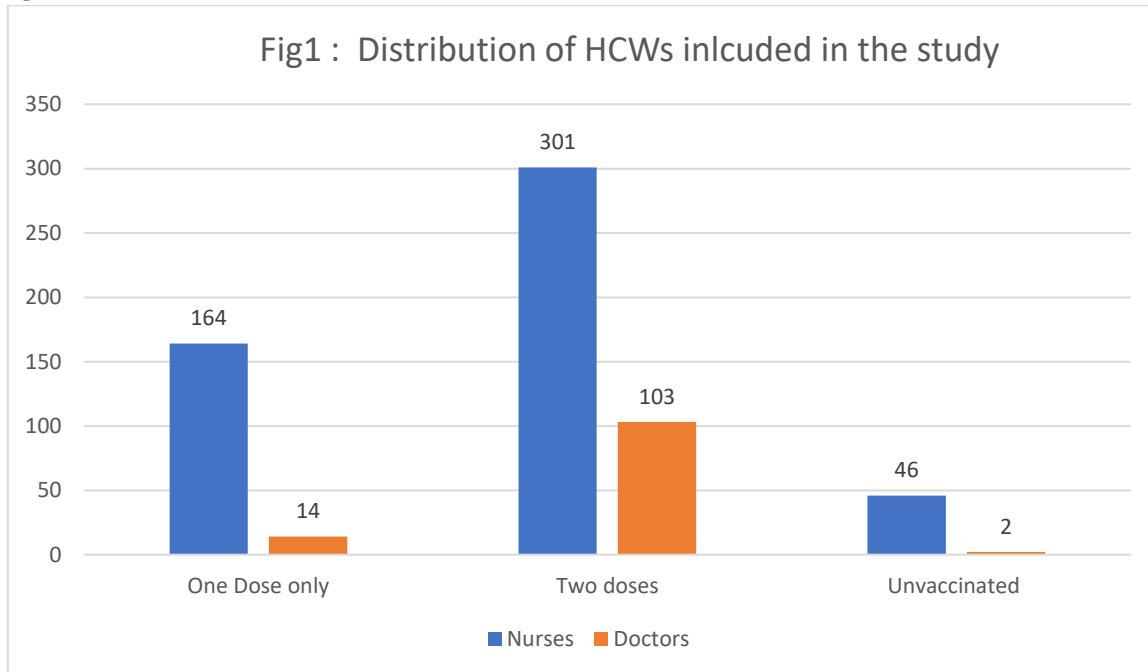


Table 1. Relative risk of SARS-CoV2 infection in unvaccinated or partially vaccinated HCWs

Type of HCW SARS-CoV2 infections	Relative risk	Confidence Interval (p value)
Partially vaccinated (n=31,17.4%)	3.0	95% CI = 1.7693 to 5.0928 (p <0.0001)
Not vaccinated (n=11)	3.77	95% CI = 1.9178 to 7.4238 (p <0.001)

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Table 2. BTI rates among global and Indian studies

Author name and year	Place of study	Vaccine type	Sample cohort considered	No. of subjects	BTI rate	Median duration of BTI	Conclusion	Ref. No
Sharma et al June 2021	Delhi	AZD 122 ChAdOx1-S/nCoV-19 (Covisheild) and BBV152 (Covaxin)	HCWs	325	11.5 %	47 days	1 in nine HCWs experienced a BTI	9
Kale P 2021	Delhi	AZD 122 ChAdOx1-S/nCoV-19 (Covisheild) and BBV152 (Covaxin)	HCWs	1858	8.62 %	50 days	1 in ten vaccinated HCWs got infected. Fully vaccinated are better protected	10
Kaur U et al 2021	Uttar Pradesh	AZD 122 ChAdOx1-S/nCoV-19 (Covisheild) and BBV152 (Covaxin)	HCWs	1650	17.2 %	39 days	There is difference in vaccine effectiveness and BTIs based on the timing of surveillance. BTIs can be high during a peak	11
Victor PJ et al 2021	Vellore	AZD 122 ChAdOx1-S/nCoV-19 (Covisheild) and BBV152 (Covaxin)	HCWs	9080	9.6%	47 days	Vaccination has a protective effect	12
Ghosh et al 2021	Pan India	AZD 122 ChAdOx1-S/nCoV-19 (Covisheild)	HCWs & FLWs of armed forces	1312938	0.19 %	Not mentioned	~93% reduction in COVID-19 breakthrough infections with Covisheild	13
Jung et al 2021	Seoul, South Korea	ChAdOx1 nCoV-19 vaccine (Oxford–AstraZeneca)	HCWs	8678	0.04 %	37 days	Transmission of SARS-CoV2 is possible between two vaccinated individuals	14
Lange et al 2021	Germany	BNT162b2 (Pfizer–BioNTech) or mRNA-1273 (Moderna) mRNA vaccine	HCWs	1137	0.35 %	62 days	variants of concern may not only be more transmissible than the original SARS-CoV-2 but may also escape vaccine protection more frequently	15

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Mosa et al 2021	Qatar	BNT162b2 (Pfizer–BioNTech) or mRNA-1273 (Moderna) mRNA vaccine	HCWs	22247	0.7%	Not mentioned	presence of symptoms and contact with a confirmed case are major risk factors for breakthrough SARS-CoV-2 infection after vaccination.	16
Bergweck et al	Israel	BNT162b2 (Pfizer–BioNTech)	HCWs	11453	13.7%	39 days	Most breakthrough infections were mild or asymptomatic	17
Present study	Mumbai	AZD 122 ChAdOx1-S/nCoV-19 (Covisheild) and BBV152 (Covaxin)	HCWs	404	5.2%	39.38 days	Vaccination had a protective effect . All BTIs were mild	