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Breakthrough infection after Covishield COVID-19 vaccine among health care workers at Patan Academy of Health Sciences, Nepal

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Abstract

Introduction: Coronavirus Disease 2019 (COVID-19) vaccines have an important role in the control and prevention of the pandemic. However, infection after vaccination, though uncommon, has been reported after partial or complete immunization. This study aims to find out vaccine breakthrough infection after the administration of the Covishield COVID-19 vaccine.

Method: This cross-sectional survey was conducted among the health care workers (HCWs) from May 2021 to July 2021 at Patan Hospital, Patan Academy of Health Sciences, Nepal who received the Covishield vaccine. The data were collected using Google form and a printed questionnaire on COVID 19 breakthrough infection ≥2w after vaccination. The rate of breakthrough infection, hospitalization, and its association with age, gender, and working departments of HCWs was analyzed using SPSS. Ethical approval was obtained.

Result: Out of 1462 HCWs approached, 880 completed the survey, among which 819(93.1%) had a completed vaccination status. Infection after the first and before the second dose was 164(18.7% of 880) and after two doses 131(16%). The breakthrough infection occurred in 83 (10.1% of 819). There was no statistically significant association of breakthrough infection with age, gender, and working department of HCWs. Total 74(8.4%) were managed by admission in hospital.

Conclusion: The findings of this study reveal a low breakthrough infection rate after Covishield vaccination among HCWs at Patan Academy of Health Sciences, Kathmandu, Nepal. Overall, COVID-19 infection rates decreased after the first and second dose of the vaccine.

Keywords: Breakthrough infection, Covishield COVID-19 vaccine, reinfection, Nepal

Introduction

There is a small percentage of re-infection of COVID-19 (caused by coronavirus SARS-CoV-2), and breakthrough infection after vaccination. COVID-19 vaccines help control the pandemic by preventing infection, decreasing its severity and hospitalization. 4

A breakthrough infection after vaccination is the detection of SARS-CoV-2 RNA or antigen in a respiratory specimen ≥14 d after vaccination.² Breakthrough infections are mild and occur in 0.03%-0.05%.⁵⁻⁷ Higher incidence of 13.3% (15 out of 107) among health care workers (HCWs) was reported in Fortis, India.⁸ Nepal began COVID-19 vaccination with Covishield first for health care workers on 27 Jan 2021.⁹ Effectiveness of a vaccine, and its equitable distribution is important to control COVID-19.¹⁰

This study aims to find out vaccine breakthrough infection among HCWs of Patan Academy of Health Sciences (PAHS), Nepal which will help in effective vaccine rollout and plans.

Method

This was a cross-sectional study conducted from May 2021 to Jul 2021 to find out breakthrough infection after the administration of Covishield (ChAdOx1 nCoV-19 Corona Virus Vaccine of AstraZeneca produced by Serum Institute of India) COVID-19 vaccine among HCWs at PAHS in Kathmandu, Nepal. All HCWs from the main teaching hospital (Patan Hospital) and 3schools (School of Medicine, Nursing and midwifery, Public Health) of PAHS were included. A list of HCWs who received Covishield was obtained from the vaccination record of PAHS. Head of Departments (HODs) provided the email addresses of their staff for the survey. The HCWs who were not familiar with email were requested to provide their phone numbers.

Data were collected via email (or social media account Viber) using Google form (LINK) which

included an information sheet for proforma and voluntary participation. Completion of the form was considered as consent. Data collection via print questionnaire was used for those participants who did not know how to use an electronic device to fill the Google form. The forms were distributed and collected within two days. For data collection, from the researchers among listed investigators (authors) were designated to cover the different departments of HCWs. Data collection required approximately 10 min of participants' time.

The study variables included HCWs demographics (gender, age, departments), number of vaccines (1st dose only or recommended two doses), COVID-19 infection after the vaccine, and the need for hospitalization.

For sampling purposes, the participants were grouped as per discipline, for example, HCWs medical (doctors, nurses, paramedical staff), non-medical (administrative staff, housekeeping staff, support staff, teaching faculties, and students). Teaching faculties involved in clinical work were grouped as medical; administrative staff included office workers except for medical, paramedical, support, teaching staff; support staff included housekeeping, security, driver, and other than paramedical, administrative, and teaching staff.

The breakthrough infection after COVID-19 vaccination was defined as Polymerase Chain Reaction (PCR) positive in a respiratory specimen ≥14 d after two doses of Covishield. Infection that occurred <14 d of vaccination was categorized as an early breakthrough. The PCR data were verified by one of the coinvestigators from the laboratory at Patan Hospital, PAHS.

The Google form data were interpreted in Excel and analyzed by SPSS for frequencies and percentages, and the Chi-square test was used for an association between age, gender, working departments, and COVID-19 infection.

Data were collected after obtaining ethical approval from the Institutional Review Committee of PAHS (Ref: drs2105281528). Confidentiality was maintained by not sharing the data for any purpose other than this research. Data were saved in a password-protected file on a personal computer of the

researcher during data processing and thereafter deposited with the institution as required by the ethical committee/institution for storage of at least 5 y, accessible to the ethical committee and/or executive committee when required.

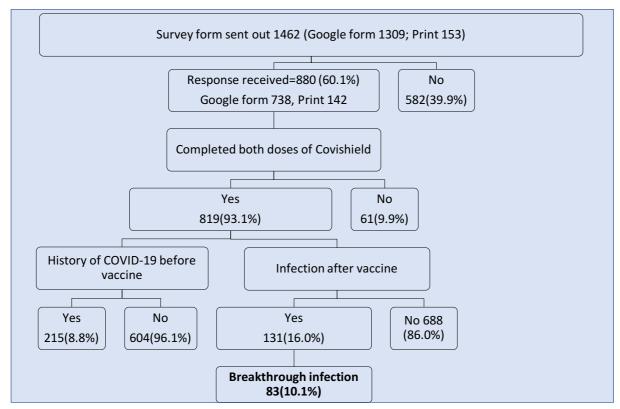


Figure 1. Flowchart of Covishield COVID-19 vaccine breakthrough infection survey among HCWs at PAHS, Nepal

Result

There were 880 participants (738 google forms, 142 print forms) who completed the survey, a response rate of 60.2% (880 out of 1462 approached). Google form response rate was 56.4%(738 replied of 1309), and print forms response was 92.8% (142 of 153).

Males were 194(22%). The majority of participants 606(68.9%) were in the age group 20-40 y. Medical HCWs (doctors, nurses, paramedics) were 464(52.7%), non-medical (administrative, teaching, support staff, and students) 416(47.3%), Table 1.

Out of 880 HCWs, 819(93.1%) completed the recommended two doses of Covishield. Infection after the 1st dose and before the 2nd

dose was 164(18.7% of 880); whereas after both doses was 131(16.0% of 819), Table 2.

Demographic variables had no statistically significant association with breakthrough infections, Table 3. Out of 819 HCWs who completed vaccination, 241(27.3%) had a history of COVID-19 infection before the vaccine, and out of these 215(89.2%) completed both doses of Covishield. Out of 639 who did not have COVID-19 infection prior to vaccination 604(94.5%) completed both doses of vaccine. Out of 215 who had infection prior to vaccine 24(11.1%) had a breakthrough infection while out of 604 who did not have infection prior to vaccine 58(9.6%) had a breakthrough infection, the difference was statistically significant, Table 4. None required ventilator support and mortality was nil.

Table 1. Demography HCWs at PAHS in Covishield COVID-19 vaccine breakthrough infection survey, N=880 Variable % Ν 43 Age in y <20 4.9 20-40 606 68.9 41-60 24.4 215 >60 16 1.8 Gender Male 194 22.0 Female 686 78.0 **HCWs Medical** 49 5.6 Dr. Nurse 350 39.8 **Paramedics** 65 7.4 **HCWs Non-medical** Administration 32 3.6 **Teaching** 35 4.0 Support 198 22.5 Student 151 17.2

HCWs- health care workers (all the staff and students of PAHS/Patan Hospital, Nepal), PAHS- Patan Academy of Health Sciences, Covishield- ChAdOx1 nCoV-19 Corona Virus Vaccine of AstraZeneca produced by Serum Institute of India

Table 2. COVID-19 infection after Covishield COVID-19 vaccine among HCWs at PAHS, Nepal						
Infection after vaccination	N	%				
After 1st dose* and before 2nd dose i.e. out of 880	164	18.7				
After two doses, i.e. out of 819	131	16.0				
Early breakthrough after complete vaccination <14 d	48	5.9				
Breakthrough inf. after complete vaccination ≥14 d	83	10.1				

^{*}Took the first dose of the vaccine only 61, and 11 had an infection.

Table 3: Association of demographic variables for breakthrough infection (N=83) \geqslant 14 d after Covishield among HCWs at PAHS, Nepal

Variables	Breakthrough infection, N=83	X² value	p value
Age ≤40y	60(72.3%)	0.086	0.770
Age >40y	23(27.7%)		
Male	24(28.9%)	2.517	0.113
Female	59(71.8%)		
Medical	44(53.0%)	0.000	0.991
Non-medical	39(47.0%)		

Table 4. Comparison of reinfection in those who had COVID-19 infection before vaccination (Group A: N=215) with those who did not (Group B: N=604) at PAHS, Nepal

Infection after vaccine		Group A, prior infection before vaccine (N=215), N, %		Group B, No prior infection before vaccine (N=604), N, %	
After 1 st dose	<14 d	58	26.9	22	3.6
	≥14 d	39	18.1	33	5.5
After 2 nd dose	<14 d	23	10.7	23	3.8
	≥14 d*	24	11.1	58	9.6

^{*}breakthrough infection following complete vaccine, Chi Square statistics is 78.8, p value = <0.00001

74

295

8.4

33.5

Hospitalized

PCR confirmation, i.e., PCR positive

Discussion

Our survey among HCWs at PAHS, Nepal following the Covishield COVID-19 vaccine revealed a breakthrough infection (≥14 d of complete vaccination) of 83(10.1%) confirmed by a PCR test. We did not find a statistically significant difference in breakthrough infections among medical and non-medical HCWs. The breakthrough infection rate is higher than the generally reported of 0.03% to $0.05\%^{5,6,7,11}$ and lower than 13.3%(15/107)from Fortis, India.8 The Fortis report was after completion of vaccination (1/3rd received Covaxin and 2/3rd Covishield) among HCWs (doctors, nurses, paramedical workers, and other staff). Such a high rate of breakthrough infection could be due to virus variants, and the lack of further analysis separately for and Covishield. Breakthrough infection among HCWs was 0.97% to 1.19% in California USA.⁵ The breakthrough infection in the real world scenario during mass vaccination has been higher than (0.05%) reported during the clinical trials.^{5,12}

Our data show that only 74(25%) out of 295(164 after 1st dose and before 2nd dose plus 131 after two vaccine doses) were hospitalized, for isolation or treatment. The hospital data show none required ventilator support and mortality was nil. The hospital policy has been revised to admit only those who require oxygen support and further treatment otherwise home isolation for 2w. Most of the studies report breakthrough infections are mild. The Indian Council of Medical Research (ICMR) reports 9.8% of infections required hospitalization, and fatality of 0.4%. 13 Another Indian study reports only 5.5%(6 of 108) breakthrough infections hospitalization for mild to moderate symptoms, none required oxygen or ICU care and mortality was nil.³ Similar studies among HCWs from India found breakthrough infections were 11%(36 infections out of 326 HCWs) and the majority (94.4%) were mild, not requiring oxygen therapy. 4 Literature and our findings on breakthrough infections following vaccines are reassuring that vaccine rollout is effective in the control and prevention of COVID-19.

We found 241(27.4%) HCWs had an infection before vaccine rollout. The reinfection and breakthrough were higher in those who had infection prior to the vaccination and the breakthrough rate was also higher. One of the studies has expressed COVID-19 infection to confer greater immunity than vaccine¹⁴, yet another study has reported that with prior natural infection of COVID-19, they were 4.5 times less likely to experience re-infection even after partial vaccination.4 This was however not seen in our study as we did not monitor antibody levels in those who reported being infected prior to vaccination, and we did not evaluate the period of infection before vaccination. It has been observed that IgG antibody peaks approximately after 25 days of infection and remains detectable for at least 120 days of infection. 15 In our study, the rate of decreased with subsequent vaccination, conferring the development of herd immunity. The development of herd immunity has been demonstrated in several studies, even in cases of mild infection 16,17 and a decreased rate of severe infection¹⁶, but there is still a possibility of a small percentage of mild to moderate infection after the vaccine.

In our study, both with or without prior infection before vaccines, the reinfection and/or breakthrough infections were mild to moderate without severe or critical cases, none required ICU care or ventilator support. We found breakthrough infections (≥14 d) in 83(10.1% of 819), and early breakthrough, i.e., <14d in 48 (5.9% of 819) after a complete vaccine of two doses. Infection after the incomplete vaccine, i.e., after 1st and before 2nd dose was higher occurring in 164 (18.9%). Thus, until full immunity is developed after vaccination, common measures of nonpharmaceutical interventions (NPI) should be observed. In a similar study of 326 HCWs, 65 (19.9%) breakthrough infections occurred after at least one dose vaccine and before 2nd dose or <14 d of 2nd dose.⁴ Longitudinal studies on mRNA vaccines ha reported total infections after the vaccine occurred in 189(0.8% of 22,729 HCWs), out of which only 26 (13.8% of 189) occurred in \ge 14 d of 2^{nd} dose. This emphasizes the role of NPIs until full immunity is achieved after the vaccine. 18

In our survey, breakthrough infections among females were more common (71.1% out of 83) than males, but statistically not significant. A study from India reports 72 (66.7% out of 108) breakthrough infections occurred in females.³ In a large series by CDC America, 2/3rd (65%) of infections occurred in women, and among fatal COVID-19 vaccine breakthrough infection (of 1,949 out of 123 million) 980 (50%) were female.² The CDC argued that more breakthrough infections in females could have been due to the tendency of women to get tested more than men. The CDC America revealed that among 5,800 breakthrough infections among 77 million vaccinated persons, 1/3rd (29%) were asymptomatic, 396 (6.8%) required hospitalization, and 74 (1.3%) died from COVID-19. All ages were affected, but 40% occurred in >60 y, possibly more infection due to virus variants of concern (VOC) B.1.351 (SA variant).^{2,19} The VOCs are increasingly responsible for more infections recently. 10,18,20 The European Medicines Agency (EMA) and the European Centre for Disease Prevention and Control (ECDC) strongly recommend vaccination²¹, and also WHO because vaccination effectively prevents severe illness and death by VOCs.

In Nepal, VOCs have been confirmed. Among the 14 traveler mountaineers, six were symptomatic while three required hospitalizations and a 61-y with two-dose mRNA-1273 had a breakthrough infection by Delta variant B.1.617.2.²² We did not conduct genome sequencing due to lack of logistics. The ICMR found that >86% of the breakthrough infections were due to the Delta variant, 9.8% required hospitalization with a fatality of 0.4%. 13 The study also reported that the Alpha variant was predominant in north India, while Delta and Kappa in the rest of the country.

The Chinese Centre for Disease Control and Prevention (CCDC) in early Apr 2021 allowed mixing vaccines to boost immunity. Gao Fu, the head of the CCDC revealed that he got the 3rd dose of different COVID-19 vaccines and that a booster dose may protect against new variants. The ICMR found that a mixed

vaccination (among 18 UP residents who inadvertently received mixed doses of Covishield and Covaxin) was safe and possibly effective against VOCs.²⁵ In Nepal there is no policy of mixing vaccines as of yet.

Vaccine coverage of 70% is the minimum to control the ongoing pandemic, which also requires taking into consideration decreased immunity over time, transmission by children and adolescents (who are not included in mass vaccination), and inequitable access, delivery, and distribution of vaccine around the world. Priority supply to COVAX and not the bilateral (commercial or political) deal maintain the equitable vaccines for the global good. Vaccine coverage is the ultimate measure for control of ongoing pandemics and thus the countries with vaccine production capacity and resources need to consider that 'no country is safe until every country is safe'. 10,28

To maintain a functional environment in the ongoing COVID-19 pandemic, staged vaccination includes a priority for essential workforces like HCWs, law enforcement, security, nursing homes, social welfare institutes, community services, energy, food, and transportation sectors, and overseas workers/students; followed by older adults, individuals with underlying health conditions and pregnant women to reduce the severity, and lastly extension to adults without underlying health conditions and children to stop virus transmission.²⁹ Caution for the lifting of NPIs is necessary as shown by a data-driven model of COVID-19 from China for the need of NPIs for one year after the start of vaccination i.e. throughout 2021, to prevent the outbreaks and their escalation.³⁰

In Nepal, VOCs 'B.1.1.7', 'B.1.617.1' 'B.1.617.2' have been confirmed.³¹ Limitations of this study might be contributed by factors like missed asymptomatic individuals with breakthrough infection due to lack of policy to test all vaccine recipients, and the causative VOCs genome sequencing for possible VOCs due to lack of resources. However, the hospital data show that there was no severe breakthrough infection requiring ventilator

support, and there was no mortality. This shows that vaccination has benefits and effectively reduces severe infection and mortality. Larger studies, preferably in the community, with a diverse population and with comorbidities may provide further data on these aspects of vaccine breakthrough infection.

Conclusion

Breakthrough infection (≥14 d) after Covishield COVID-19 vaccination occurred with a low frequency (10.1%) among health care workers at Patan Academy of Health Sciences, Nepal. The vaccine was effective; as breakthroughs were mild, didn't require ventilator support, and mortality was nil as per hospital record.

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Conflict of Interest

None

Funding

None

Author Contribution

Concept and design: All; Data collection: PS, SD, SK; Data analysis: PS, AS, NP, JNS; Literature review, Draft manuscript: JNS; Revision of draft manuscript: PS, AS, NP, JNS; Final manuscript: ALL

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