ORIGINAL PAPER

Incidence and severity of COVID-19 infection post-vaccination: a survey among Indian doctors

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Abstract

Purpose The rollout of COVID-19 vaccines began in India in January 2021, with healthcare professionals being the first to receive vaccination. The purpose of this research was to study the incidence and severity of COVID-19 infections among Indian doctors, following vaccination with ChAdOx1 nCoV-19 or BBV152.

Methods We conducted an online voluntary survey among Indian doctors who received one or two doses of ChAdOx1 nCoV-19 or BBV152. Questions pertaining to the incidence and severity of COVID-19 infection following vaccination were asked. Data thus obtained were analysed.

Results 9146 doctors were included in this study. 8301 of these received ChAdOx1 nCoV-19, while 845 received BBV152. 2842 (31.07%) respondents reported having a COVID-19 infection following vaccination. Presence of pre-existing medical comorbidities was associated with a higher incidence, while prior COVID-19 infection and two doses of either vaccine were associated with a lower incidence of COVID-19 infection post-vaccination. Exposure to COVID-19 patients on a daily basis did not increase the incidence of COVID-19 infection among doctors who were vaccinated. Increasing age, male gender, presence of pre-existing medical comorbidities, and daily exposure to COVID-19 patients were associated with increased severity of COVID-19 infection after vaccination. Two doses of either vaccine resulted in less severity of disease compared to one dose.

Conclusion ChAdOx1 nCoV-19 and BBV152 confer immunity against severe forms of COVID-19 infections. COVID-19 infections prior to vaccination result in a lower incidence of breakthrough infection. Presence of pre-existing medical comorbidities is associated with increased incidence and severity of breakthrough infections.

Keywords COVID-19 · Vaccine breakthrough infection · ChAdOx1 nCoV-19 · BBV152 · SARS-CoV-2 · Healthcare professionals

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Introduction

The goals of vaccination are: [a] to reduce, if not altogether eliminate the risk of infection, and [b] to reduce the severity and transmission of disease [1]. Though vaccines against COVID-19 have been shown to be effective, there still exists the possibility of infection despite vaccination [2]. This risk could potentially be higher among healthcare professionals, due to the higher rates of exposure to the SARS-CoV-2 virus at work.

The rollout of vaccines against COVID-19 in India began in January 2021, with healthcare providers being the first to receive two doses of a vaccine, 4 weeks apart. Two vaccines were approved for emergency use in India, they were ChAdOx1 nCov-19 (Covishield ™, Serum Institute of India, Pune, India) and BBV152 (Covaxin®, Bharat Biotech, Hyderabad, India). The safety and efficacy of both these vaccines are reported in the literature [3–13]. However, there is scarce literature regarding the incidence and severity of COVID-19 infection post-vaccination [14–19]. The reasons and risk factors for vaccine breakthrough infections are still under investigation [19].

The aims of our study were: [a] to assess the incidence of COVID-19 infection following vaccination with either ChAdOx1 nCoV-19 or BBV152, among Indian doctors, and [b] to assess the severity of the disease among those who developed infection with COVID-19 after vaccination. We chose doctors for the study since the vaccine rollout in India began with doctors, and doctors are better able to provide reliable and relevant information required for this survey.

Methods

Following presentation of our research protocol to the Institutional Ethics Committee, a waiver for Institutional Review Board (IRB) was obtained. We conducted an online survey, starting 100 days following the administration of the first vaccines in India. The survey (hosted on surveyplanet.com) comprised 12 questions (Table 1). An online messenger app (WhatsApp Messenger, from Facebook) was used for communication with potential participants, since correspondence using postal services could not be undertaken during the pandemic. Participation and disclosure of any personal information were voluntary. Results thus obtained, in the time interval between 26th April 2021 and 18th May 2021 were retrieved from the password-protected online database and exported to a Microsoft Excel sheet.

A total of 9767 doctors responded to the survey. 9336 among these were practising in India. 132 participants had not received any vaccination for COVID-19, and were excluded. 58 participants who received vaccines other than ChAdOx1 nCoV-19 or BBV152 were also excluded. This finally left us with 9146 subjects, whose results were analysed. Association of the following variables with the incidence of COVID-19 infection following vaccination was assessed: age, gender, presence of medical comorbidities, exposure to COVID-19 patients on a daily basis, COVID-19 infection prior to vaccination, and number of doses of either vaccine. Association of these variables with the severity of COVID-19 infection following vaccination was then assessed, by analysing the need for hospitalisation,

Table 1 Survey questionnaire

Q1. Age	Q7. Did you experience any adverse effects after vaccination? No Yes (please specify)
Q2. Sex Male Female	Q8. Have you been infected with COVID-19 prior to vaccination? No Yes
Q3. Comorbidities No Yes (please specify)	Q9. Have you been infected with COVID-19 after vaccination? No Yes
Q4. Are you involved in the treatment of COVID-19 patients Daily Occasionally No	Q10. If you developed COVID-19 infection after vaccination, after how many doses were you diagnosed with COVID-19? One dose Two doses
Q5. City/town, state and country where you practice	Q11. If you developed COVID-19 infection after vaccination, how many weeks after the vaccine were you diagnosed with COVID-19?
Q6. Status of vaccination (select one option) Not vaccinated Covaxin—one dose Covishield—one dose Covaxin—two doses Covishield—two doses Other vaccine (specify name and number of doses)	Q12. After vaccination, if you were infected with COVID-19, what was the severity of the disease? (you can select multiple options) Home quarantine Required hospitalisation Required Remdesivir Required steroid Required ventilatory support

Remdesivir, steroid therapy and ventilatory support as surrogate markers.

Statistical analysis was done using the SPSS® software (version 13.0). Mean with standard deviation (SD) was calculated for quantitative variables, while frequency was used for assessment of nominal or ordinal data. Association between categorical variables was assessed using Pearson's chi-square test. The independent T-test was used for comparison of means of numerical variables between independent populations.

Results

8301 out of the 9146 participants received the ChAdOx1 nCoV-19 vaccine- 7712 among these received 2 doses while 589 received only 1 dose. 845 participants received the BBV152 vaccine—686 received 2 doses, while 159 received only 1 dose. Overall, 2842 doctors (31·07%) among these developed COVID-19 infection post-vaccination. 2208 of these infections occurred after 2 weeks from the second dose of the respective vaccine.

Among the 2842 participants who reported developing COVID-19 infection despite vaccination, 244 required hospitalisation, 218 required administration of Remdesivir, 461 required administration of steroid, and 6 required some form of ventilatory support.

Age

The mean age (SD) of all the participants was 44.77 (10.78) years. The mean age (SD) of those who developed COVID-19 infection post vaccination was 44.39 (10.79) years, while it was 44.93 (10.77) years for those who did not. This difference, though statistically significant ($p = 0.025$), was not clinically relevant. The mean age (SD) of doctors treating COVID-19 patients on a daily basis was 42.52 (10.64) years, while that of doctors not treating COVID-19 patients on a daily basis was 45.50 (10.72) years ($p < 0.001$).

Among participants who developed COVID-19 infection despite vaccination, the mean (SD) age of participants who did and did not require hospitalisation, Remdesivir, steroid and ventilatory support is summarised in Table 2. A statistically significant positive association was observed between increasing age and severity of the disease, as assessed by all four parameters.

Gender

5466 men and 3680 women participated in the survey. Among the 5466 men, 1724 (31.54%) developed COVID-19 infection despite vaccination, while this number was 1118 (30.38%) among the 3680 women. This difference in the incidence was not statistically significant ($p = 0.24$). 1516 men (27.74%) and 751 women (20.41%) were treating COVID-19 patients on a daily basis ($p < 0.001$).

Among the 1724 men and 1118 women who developed COVID-19 infection despite vaccination, the frequency of requirement of hospitalisation, Remdesivir, steroid or ventilatory support is summarised in Table 3. A significantly higher percentage of men with COVID-19 infection following vaccination required hospitalisation, Remdesivir, and steroid, when compared to women. There was however, no significant association of the male gender with requirement of ventilatory support.

Table 2 Association of age with the various surrogate markers for severity of disease; mean (SD) age of participants in years, among the various sub-groups is tabulated

	Hospitalisation	Remdesivir	Steroid	Ventilatory support
Required	47.18 (11.62) years	49.06 (10.33) years	47.99 (10.74) years	54.17 (10.53) years
Did not require	44.13 (10.68) years	44.00 (10.74) years	43.69 (10.67) years	44.37 (10.79) years
p value	$p < 0.001$	$p < 0.001$	$p < 0.001$)	$p = 0.026$

Table 3 Association of gender with the various surrogate markers for severity of disease; frequency of requirement of hospitalisation, Remdesivir, steroid and ventilatory support among the 1724 men and 1118 women who developed COVID-19 infection despite vaccination is summarised

	Hospitalisation	Remdesivir	Steorid	Ventilatory support
Male (1724)	184 (10.67%)	174 (10.09%)	320 (18.56%)	4 (0.23%)
Female (1118)	60 (5.37%)	44 (3.94%)	141 (12.61%)	2 (0.18%)
p value	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p = 0.76$

Pre-existing medical comorbidities

2498 participants had pre-existing medical comorbidities, while 6648 did not. Among these, 827 (33.11%) doctors with medical comorbidities and 2015 (30.31%) without pre-existing comorbidities developed COVID-19 infection despite vaccination, respectively. Pre-existence of medical comorbidities was thus associated with a significantly higher risk of developing vaccine breakthrough COVID-19 infection ($p = 0.01$).

The association of pre-existing medical comorbidities with need for hospitalisation, Remdesivir, steroid and ventilatory support is summarised in Table 4. There was a significant positive correlation between presence of comorbidities and severity of disease in terms of requirement of hospitalisation, Remdesivir and steroid, but not ventilatory support.

Exposure to COVID-19 patients on a daily basis

2267 participants were exposed to COVID-19 patients on a daily basis, while the remaining 6879 were not. Among these, 719 (31.72%) and 2123 (30.86%) respectively reported developing a COVID-19 infection despite vaccination. This difference in incidence was not statistically significant ($p = 0.45$).

The association between daily exposure to COVID-19 patients, and severity of COVID-19 infection following vaccination is summarised in Table 5. There was a significant positive association between daily exposure to COVID-19 patients, and severity of infection in terms of need for hospitalisation and Remdesivir, but not with need for steroid or ventilatory support.

COVID-19 infection prior to vaccination

1427 participants were infected with COVID-19 prior to vaccination, while the remaining 7719 were not. Among these, 188 (13.17%) and 2654 (34.38%) respectively reported developing COVID-19 infection despite vaccination. This difference in incidence was statistically significant ($p < 0.001$).

The association between COVID-19 infection prior to vaccination, and severity of COVID-19 infection following vaccination is summarised in Table 6. There was no

Table 4 Association of pre-existing medical comorbidities with the various surrogate markers for severity of disease; frequency of requirement of hospitalisation, Remdesivir, steroid and ventilatory support among the 827 participants with and 2015 participants without comorbidities who developed COVID-19 infection despite vaccination is summarised

	Hospitalisation	Remdesivir	Steroid	Ventilatory support
With Pre-existing medical comorbidities (827)	93 (11.25%)	101 (12.21%)	197 (23.82%)	2 (0.24%)
Without comorbidities (2015)	151 (7.49%)	117 (5.81%)	264 (13.10%)	4 (0.20%)
p value	$p = 0.001$	$p < 0.001$	$p < 0.001$	$p = 0.82$

Table 5 Association of daily exposure to COVID-19 patients with the various surrogate markers for severity of disease; frequency of requirement of hospitalisation, Remdesivir, steroid and ventilatory support among the 719 participants with and 2123 participants without daily exposure, who developed COVID-19 infection despite vaccination is summarised

	Hospitalisation	Remdesivir	Steroid	Ventilatory support
Daily exposure to COVID-19 patients (719)	75 (10.43%)	68 (9.46%)	120 (16.69%)	0 (0.00%)
Not exposed to COVID-19 patients on an everyday basis (2123)	169 (7.96%)	150 (7.07%)	341 (16.06%)	6 (0.28%)
p value	$p = 0.041$	$p = 0.037$	$p = 0.69$	$p = 0.15$

Table 6 Association between COVID-19 infection prior to vaccination, and the various surrogate markers for severity of disease; frequency of requirement of hospitalisation, Remdesivir, steroid and ventilatory support among the 188 participants with and 2654 participants without prior infection, who developed COVID-19 infection despite vaccination is summarised

	Hospitalisation	Remdesivir	Steroid	Ventilatory support
Prior COVID-19 infection (188)	15 (7.98%)	10 (5.32%)	25 (13.30%)	1 (0.53%)
No prior COVID-19 infection (2654)	229 (8.63%)	208 (7.84%)	436 (16.43%)	5 (0.19%)
p value	$p = 0.76$	$p = 0.21$	$p = 0.26$	$p = 0.32$

significant association between COVID-19 infection prior to vaccination, and severity of infection following vaccination, in terms of need for hospitalisation, Remdesivir, steroid or ventilatory support.

Number of doses of vaccine (ChAdOx1 nCoV-19 group)

8301 doctors received the ChAdOx1 nCoV-19 vaccine. 589 received one dose, while 7712 received 2 doses. Among these, 259 (43.97%) and 2294 (29.75%) respectively reported developing COVID-19 infection despite vaccination. This difference was statistically significant (p < 0.001).

The association between number of doses of the ChAdOx1 nCoV-19 vaccine, and severity of COVID-19 infection following vaccination is summarised in Table 7. Among the doctors who received two doses of the vaccine, there was significant lesser requirement of Remdesivir and steroid, but not hospitalisation and ventilatory support when compared to those who received only one dose of the vaccine.

Number of doses of vaccine (BBV152 group)

845 doctors received the BBV152 vaccine. 159 received 1 dose, while 686 received 2 doses. Among these, 65 (40.88%) and 224 (32.65%) respectively reported developing COVID-19 infection despite vaccination. This difference was statistically significant (p < 0.049).

The association between number of doses of the BBV152 vaccine, and severity of COVID-19 infection following

vaccination is summarised in Table 8. Among the doctors who received two doses of the vaccine, there was significant lesser requirement of hospitalisation, Remdesivir and steroid, but not of ventilatory support when compared to those who received only one dose of the vaccine.

Discussion

In our study, 31·07% of the respondents reported COVID-19 infection following vaccination. The efficacy of the Oxford/AstraZeneca vaccine against COVID-19 infections also has been reported to be around 70%, while the BBV152 vaccine efficacy against asymptomatic and symptomatic COVID-19 has been shown to be 63.6% and 77.8%, respectively [3, 10]. The mean age of doctors treating COVID-19 patients on a daily basis was lower than that of those who were not, by over 3 years. However, though the mean age of those who developed an infection post-vaccination when compared to those who did not, was lesser, the difference in the means was too little to be considered clinically relevant according to the authors (Table 2). These results are in concurrence with our finding that exposure to COVID-19 patients on a daily basis did not increase the incidence of COVID-19 infection among doctors who were vaccinated.

Male doctors were treating COVID-19 patients on a daily basis more frequently when compared to female doctors, however they were not more likely to develop COVID-19 infection post-vaccination when compared to female doctors. Vaccinated doctors with pre-existing medical comorbidities had a significantly higher incidence of

Table 7 Association between number of doses of ChAdOx1 nCoV-19 vaccine, and the various surrogate markers for severity of disease; frequency of requirement of hospitalisation, Remdesivir, steroid and ventilatory support among the participants who reported COVID-19 infection despite vaccination with ChAdOx1 nCoV-19 is summarised (259 participants received one dose, and 2294 participants received 2 doses)

	Hospitalisation	Remdesivir	Steroid	Ventilatory support
One dose ChAdOx1 nCoV-19 (259)	29 (11.20%)	30 (11.58%)	52 (20.08%)	1 (0.39%)
Two doses ChAdOx1 nCoV-19 (2294)	188 (8.20%)	159 (6.93%)	347 (15.13%)	4 (0.17%)
p value	p = 0.10	p = 0.007	0.038	p = 0.47

Table 8 Association between number of doses of BBV152 vaccine, and the various surrogate markers for severity of disease; frequency of requirement of hospitalisation, Remdesivir, steroid and ventilatory support among the participants who reported COVID-19 infection despite vaccination with BBV152 is summarised (65 participants received 1 dose, and 224 participants received 2 doses)

	Hospitalisation	Remdesivir	Steroid	Ventilatory support
One dose BBV152 (65)	14 (21.54%)	13 (20.00%)	22 (33.85%)	0 (0.00%)
Two doses BBV152 (224)	13 (5.80%)	16 (7.14%)	40 (17.86%)	1 (0.45%)
p value	p < 0.001	p = 0.002	p = 0.006	p = 0.59

COVID-19 infection post-vaccination. Recipients of two doses of either vaccine also had a significantly lower rate of COVID-19 infection post-vaccination compared to those who received only one dose of the corresponding vaccine.

There was a significantly lower incidence of COVID-19 infection following vaccination among participants who were infected with COVID-19 prior to the administration of the vaccine ($p < 0.001$), which could imply a certain level of natural immunity conferred upon persons who develop the infection once. This reiterates the findings of Letizia et al., wherein the risk of developing a subsequent COVID-19 infection among young adults who were seropositive for SARS-CoV-2 IgG, was found to be one-fifth that of those who were seronegative at the commencement of their study [20]. Moreover, a synergy resulting in "hybrid immunity" due to a combination of vaccination and natural immunity could contribute to this reduction in incidence of COVID-19 infections among this group of participants [21]. Prior studies have also reported that a single dose of mRNA vaccines could result in substantial enhancement of neutralizing antibody response against COVID-19 variants in the context of prior COVID-19 infection [22, 23].

According to our data, increasing age, male gender, presence of medical comorbidities, and daily exposure to COVID-19 patients are associated with an increased severity of COVID-19 infection even after vaccination. Two doses of either vaccine is associated with reduced severity of the infection after vaccination. This data would help in planning and deploying personnel in areas with high COVID-19 exposure.

Gender, pre-existing medical comorbidities, exposure to COVID-19 patients on a daily basis, COVID-19 infection prior to vaccination, and number of doses of the respective vaccine, had no significant association with the need for ventilatory support among doctors who developed COVID-19 infection following vaccination (Tables 3, 4, 5, 6, 7, 8). One probable reason for this lack of significant association, could be the low number of participants who required ventilatory assistance. Also, doctors who did require ventilatory support, but eventually died, cannot be included in an analysis based on survey results.

We chose doctors for our survey for certain reasons, the first being that they were the first to receive vaccination in India. Secondly, they would be better equipped to provide reliable and relevant information necessary for the research. Doctors have easy access to diagnostic and treatment facilities. They are on the frontline of COVID-19 management and are at a high risk of acquiring severe infections. Data on incidence and severity of COVID-19 infections among doctors could potentially give a better understanding of the actual efficacy of different vaccines, especially in the times of "lockdowns" and "work-from-home".

Our research has limitations inherent to its study model. Data provided by survey participants has limitations in terms of data accuracy, selection bias and the breadth and depth of information that can be collected. Our survey was posted on doctors' groups on WhatsApp messenger. While the accuracy of every answer to every question cannot be physically verified in a long-distance survey or interview, the fact that the respondents were themselves doctors would certainly alleviate concerns regarding the reliability of the data, to an extent. Moreover, most doctors are likely to have access to a source of internet, which would reduce, if not eliminate selection bias. Other limitations of our study are that long-term follow-up of the participants following vaccination, and an exhaustive analysis of all possible risk factors could not be undertaken. We did not enquire as to which diagnostic modality was used to confirm COVID-19 infection. Also, doctors who succumbed to COVID-19 infections could not have been included for assessment.

Despite these limitations however, our study has several strengths. While the safety and efficacy of ChAdOx1 nCoV-19 and BBV152 vaccines are well reported in the general population [3–13], there is scarce literature on the incidence and severity of vaccine breakthrough infections [14–19], especially among healthcare professionals, who are at a high risk of developing COVID-19 infections. To our knowledge and till date, this is the largest number of reported vaccine breakthrough COVID-19 infections. Our study was not funded by any vaccine company, and the authors have no conflicts of interest, which lends credibility to the study.

Conclusion

Two doses of ChAdOx1 nCoV-19 and BBV152 result in significantly reduced incidence and severity of COVID-19 infection compared to one dose. They also confer a certain level of immunity against severe forms of COVID-19 infections. Doctors who are vaccinated, despite being exposed to COVID-19 patients on a daily basis, do not have a significantly higher incidence of COVID-19 infection post-vaccination. Presence of pre-existing medical comorbidities is associated with increased incidence and severity of breakthrough infections. Further independent studies are required to validate the manufacturer-reported efficacy of COVID-19 vaccines, among both the general as well as high-risk populations.

writing—review and editing. MI, data curation, formal analysis, writing—original draft. HA, investigation, writing—original draft.

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