SARS-CoV-2 infection after COVID-19 immunization in healthcare workers: A retrospective, pilot study

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Background & objectives: COVID-19 pandemic has taken a significant toll on the health of the people across the globe, including India, and is still continuing with its rapidly evolving second wave. Although the COVID-19 vaccines effectively prevent infection, yet some cases of infections have been reported post-vaccination, raising concerns about their efficacy and safety. This study was aimed to investigate the occurrence of SARS-CoV-2 infection among the symptomatic-vaccinated healthcare workers (HCWs) and to analyze the severity of their disease.

Methods: This retrospective study was done at a single multispecialty hospital, on the HCWs who have had COVID-19 vaccination, during the initial period of the vaccination drive (January 16 to April 24, 2021). The symptomatic post-vaccination infections in these HCWs were evaluated.

Results: Eighty five of 3235 (2.63%) vaccinated HCWs acquired the SARS-CoV-2 infection after vaccination, during the study period. Of these, 65 (76.5%) were fully vaccinated (FV), and 20 (23.5%) were partially vaccinated (PV) and the protection rate of vaccination was 97.4 per cent [95% confidence interval (CI)=96.8-97.9]. The odds ratio of acquiring infection among females was higher at 1.84 (95% CI=1.17-2.88; \(P=0.008\)) mainly because of their greater involvement in the patient care as nursing personnel. The chances of infections were the highest in the medical and nursing personnel, as compared to paramedical, administrative and supporting staff (\(P<0.001\)). Among the HCWs studied, only two required hospitalization (0.06%), none needed an intensive care unit (ICU) admission and there were no deaths.

Interpretation & conclusions: The COVID-19 infection after vaccination occurred in a smaller subset (2.63%) of HCWs, in both PV and the FV groups. These infections were primarily minor and did not lead to severe disease. Overall, the vaccination with ChAdOx1 nCoV-19 vaccine (recombinant) prevented SARS-CoV-2 severe infection in the HCWs, leading to ICU admission and deaths.

Key words Coronavirus - COVID-19 - hospital - healthcare workers - immunization; infection - SARS-CoV-2 - vaccine

COVID-19 is a highly infectious disease caused by SARS-CoV-2¹. The best means of controlling its spread in the community is by observing COVID appropriate behaviour and by immunization². The Government of India (GOI) permitted the clinical use of two vaccines from January 16, 2021, namely ChAdOx1 nCoV-19 (recombinant) vaccine or whole viron inactivated vero cell vaccine or BBV152³. First, the healthcare workers (HCWs) were offered the vaccination. The HCWs being the frontline workers in the care of COVID-19...
patients are at a greater risk for contracting the infection, and if infected, they may also transmit the infection to others\(^4\).

Although the available COVID-19 vaccines are considered safe and effective, there have been some concerns raised over the vaccine’s efficacy and side effects\(^5\). Recently, some cases of post-vaccination infections (PVIs) have also been reported\(^6\). Therefore, this retrospective study was aimed to find out the occurrence of SARS-CoV-2 infection among the vaccinated HCWs of a tertiary care hospital in New Delhi, India\(^7\) and to analyze the severity of their disease.

**Material & Methods**

**Study design:** This study was carried at the Indraprastha Apollo Hospitals, New Delhi, India. The study was approved by the Institutional Ethics Committee. The data of all the vaccinated HCWs were collected from the Medical Records department (MRD) and Human Resource department (HRD) of the hospital and were then collated and analyzed. The study period was during the initial phase of the vaccination drive, from January 16 to April 24, 2021 (100 days). Since the vaccination of HCWs was done on different dates, not all of them were followed up for 100 days. The details of those HCWs of the study, who acquired the PVI during the study period were noted. These HCWs included doctors, nurses, paramedics, and administration and housekeeping staff.

**Details of study group:** The HCWs were divided into two groups, namely (i) fully vaccinated (FV); those who had two doses of vaccine, and (ii) partially vaccinated (PV): those who had one dose of vaccine; the data were tabulated and analyzed for various parameters such as age, sex and time to infection after their last vaccination dose, clinical severity of the disease, hospitalization requirements, admission in intensive care units (ICUs) and death.

There were 3235 HCWs who were vaccinated using ChAdOx1 nCoV-19 vaccine (recombinant), during the study period with 2480 FV and 755 PV individuals in the study. As the vaccination impact was not checked by antibody testing due to logistic reasons, only symptomatic HCWs (85 in number) who reported and were found COVID-19 positive were studied.

**Statistical analysis:** The statistical analysis was performed by using IBM-SPSS version 20 (IBM Corp., New York, USA). Chi-square test was performed to find out the association between various categorical variables. MedCalc Software (MedCalc Software Ltd. Ostend, Belgium) was used to calculate the 95 per cent confidence interval (CI) of the proportion and odds ratios and corresponding \(P\) values.

**Results & Discussion**

Of the 3235 HCWs, 85 (2.63%) reported symptomatic infection after the vaccination (Table). Therefore, the protection rate of vaccination from symptomatic infection in this group was 97.4 per cent, with 95 per cent CI=96.8-97.9. It is to be noted that the study centre mandated all its HCWs to report in case of any adverse event after the vaccination.

The post-vaccination COVID-19 infection (PVI) after FV was 2.62 per cent (65/2480, 95% CI: 2.0-3.3) and in PV group was 2.65 per cent (20/755, 95% CI=1.6-4.1). The infection rate was lesser within two weeks of the vaccination, as compared to after two weeks in both the FV and PV groups.

The odds of acquiring infection among the females were 1.84 times higher (95% CI=1.87-2.9; \(P=0.008\)) (Table). This could be due to greater involvement of females in patient care as nursing personnel as the likelihood of PVI was the highest among nursing staff (41.18%) followed by the medical staff (32.94%) in this study. In fact, the odds of acquiring PVI were the highest in the medical and nursing personnel (odds ratio=3.8; 95% CI: 2.4-6.3), as compared to paramedical (0.61), supporting and administrative staff (2.19%) put together (\(P=0.001\)). A higher chance of acquiring PVI was seen in the age group of 50 yr and above (odds ratio=1.2, 95% CI=1.1-3.5; \(P=0.03\)), compared to the younger participants, i.e. those who were less than 50 yr (Table).

Among those who acquired infection, the time (days) to infection after two doses of immunization ranged from 6 to 64 days (average: 38.4), and after one dose of vaccination, it ranged from 2 to 53 days (average: 30.3 days). Maximum infections occurred in the later part of the study in April 2021, during the second wave of COVID-19 in Delhi.

In all the 85 infected cases, there were mild symptoms such as cough, fever, malaise and loss of taste and smell. Of all the vaccinated HCWs (3235), only two (0.06%) required hospital admissions and none of them required an ICU admission. There was no significant adverse effect reported following immunization and no mortality.
COVID-19 infection after vaccination is being recognized in a small subset of people after one or both the doses of vaccine. The Centers for Disease Control and Prevention (CDC) has recently termed the infections occurring two weeks after the full vaccination by an approved vaccine as ‘breakthrough infection’ (BTI). Accordingly, in the present study, 76.5 per cent of the HCWs had BTI. Dagan et al. suggested that the COVID-19 vaccination was highly effective in preventing severe outcomes after the infection, with lesser hospitalization, severe illness and death. They have further added that the estimated benefit of vaccination increases in magnitude as the time passes. We noted that in a sample of 3235 HCWs in a tertiary care hospital, the PVI was as low as 2.65 per cent after the first dose and 2.63 per cent after the second dose of vaccine among those observed for less than 100 days. This implied that a reasonable level of immunity was achieved after a single shot of vaccine which might get further enhanced with the second dose, in a longer follow up.

A study from Israel found substantial early symptomatic infections following the first dose of vaccination. They noted that as compared to symptomatic COVID-19 rate of 5.0 per 10,000 person-days in unvaccinated HCWs, the disease rates were 2.8 and 1.2 per 10,000 person-days on days 1-14 and days 15-28 after the first dose of the vaccine, respectively. In a large UK surveillance study, it was found that the SARS-CoV-2 infections were reduced by 65 per cent after the first dose of the vaccine (Oxford-AstraZeneca or Pfizer-BioNTech), and these reductions were further increased to 70 per cent after the second dose of the Pfizer vaccine.

It is observed that the susceptibility to SARS-CoV-2 infection persists in the early phase of post-vaccination, as the immunity takes time to develop. The SIREN study reported that the BNT162b2 mRNA vaccine does not prevent all cases of infection. The Ministry of Health and Family Welfare, Government of India and the CDC have also advised that people should continue using masks and maintain social distancing in public places even after full vaccination.

The Indian Council of Medical Research recently released preliminary data related to PVI, which showed that only 0.02-0.04 per cent vaccinated individuals were found infected after ChAdOx1 nCoV-19 (recombinant) and BBV152 vaccines. In the present study PVI was seen in 2.63 per cent HCWs, of whom

### Table. Number of vaccinated healthcare workers, number and percentage of post-vaccination infections

| Number vaccinated | Number of post-vaccination infections, n (%), 95% CI | OR (95% CI) | P |
|-------------------|-----------------------------------------------|------------|---|
| Total vaccinated   | 3235                                         | 85 (2.63), 2.10-3.24 | - | - |
| Post-vaccination infection after 1 dose | 755                                           | 20 (2.65), 1.6-4.1 | - | - |
| Post-vaccination infection after 2 doses | 2480                                          | 65 (2.62), 2.0-3.3 | - | - |
| Gender             |                                               |            |    |
| Females            | 1628                                         | 55 (3.38)   | 1.84 (1.87-2.9) | 0.008 |
| Males              | 1607                                         | 30 (1.87)   | 1.0 |    |
| Age group (yr)     |                                               |            |    |
| <50                | 2952                                         | 72 (2.44)   | 1.0 | 0.03 |
| ≥50                | 283                                          | 13 (4.59)   | 1.93 (1.1-3.5) | - |
| Category of staff  |                                               |            |    |
| Nursing            | 977                                          | 35 (3.58)   | 3.8 (2.4-6.3) | <0.001 |
| Medical            | 431                                          | 28 (6.50)   | - | - |
| Administration     | 685                                          | 15 (2.19)   | 1.0 | - |
| Paramedic and supporting | 1142                       | 7 (0.61)   | - | - |
| Hospital admission | 3235                                         | 2 (0.06)    | - | - |
| ICU admission      | 0 (0.00)                                     | - | - | - |
| Deaths             | 0 (0.00)                                     | - | - | - |

OR, odds ratio; CI, confidence interval; ICU, intensive care unit
76.5 per cent were in the FV and 23.5 per cent in the PV group, respectively. Only 0.06 per cent of all the vaccinated participants required hospital admissions. In the pre-clinical trials of ChAdOx1 nCoV-19 vaccine (recombinant), the efficacy of this vaccine was found to be good, from 22 days after the first dose in 73 per cent cohorts. Its immunogenicity was further increased with a more extended dose interval of 8-12 wk.17

The recent emergence of new variants of the coronavirus has posed significant challenges because these mutant viruses can evade the human immune response. Hence, these have a greater chance to break through the human defenses created through the vaccination. These emerging ‘variants of concern (VOC)’ are deadlier than the wild-type SARS-CoV-2 and contain mutations in the spike protein, increasing vaccine efficacy concerns.18-20

The occurrence of PVIs in HCWs in the present study could be due to several factors: (i) disregard to safety precautions, (ii) a lower immunogenic response in some individuals, (iii) the coincidental rise of the second COVID-19 wave in India, during the latter part of this study period, and (iv) the development of VOC.19

Antibody titre testing after COVID-19 vaccination is unreliable, and a routine post-vaccination testing may raise anxiety if negative or less and overconfidence in the individuals with higher levels.21 Though serum antibody levels correlate well with protection for many infectious diseases, protective levels have not yet been determined for SARS-CoV-2. Genomic sequencing can detect the phylogenetic characteristics of SARS-CoV-2, and hence, more widespread and regular testing is required to monitor the disease’s spread and evolution of the mutant viruses.22 The viral mutants or variants have been classified into variant of high consequence (VOC) and variant of interest (VOI), based on their severity and virulence.23 Many VOC and VOI have been reported in various nations. In an attempt to simplify their names and to remove the stigma attached to these variants, the WHO has named them as per the Greek alphabets, rather than from the country of their first discovery.23 The most commonly found VOC currently in India and the globe is B.1.617.2 or delta variant.24

There have been some gender differences noticed in the rate of infection and deaths related to COVID-1924-25, similar to the findings in the present study where more female HCWs were affected (Table).

Our study had certain limitations. A single vaccine type was used and hence the efficacy of different types of vaccines could not be compared. It was a single-centre study, and hence, the sample size was relatively smaller. There was no comparative group as the asymptomatic HCWs were not analyzed. Post-vaccination, the vaccinated HCWs were evaluated only if they reported any symptoms and there was no planned or systematic follow up. Due to logistic reasons, the routine antibody and repeat RT-PCR testing were not done, thus, some asymptomatic PVIs might have been missed and this could have led to ‘over-reporting’ of the protective effect of the vaccine.

Overall, this pilot study reports the clinical outcomes of the short-term post-vaccination infections in HCWs. The long-term effects of the infection need to be evaluated and reported on a large sample in the future.

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