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POST-VACCINATION COVID-19 INFECTION AMONG HEALTH CARE WORKERS: DESCRIPTION, DETERMINANTS AND EVENT-HISTORY ANALYSIS

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Abstract

Background: Healthcare workers (HCWs) faced a heightened risk of exposure to COVID-19 during the pandemic. Vaccination is crucial in reducing infection rates among HCWs; however, no vaccine guarantees complete immunity. Socio-demographics, occupational, and personal characteristics may influence the trajectory and susceptibility to breakthrough infections. This study aims to evaluate the incidence, determinants, and time to infection post-vaccination among HCWs, offering insights into identifying vulnerable individuals and guiding resource allocation and policy formulation.

Keywords: COVID-19, Vaccination, Breakthrough Infection, Healthcare Workers, Incidence Density

Introduction: The healthcare sector has been at the front line during the entire course of the COVID-19 pandemic. With the trajectory of the pandemic, healthcare workers offered services in environments with a high probability of viral exposure.[1], [2] Governmental agencies issued the regulatory guidelines and took all the possible measures to prevent infections amongst HCWs. Still, the magnitude and duration of the pandemic were unprecedented.[3] This long-term occupational exposure, relative proximity to high viral settings in facility/community, the rapidness of case volumes, absence of definitive knowledge about preventive measures and lack of vaccine during the early phases of the pandemic were some of the reasons that made the HCWs as one of the highest risk of infection during this pandemic.

After the launching of vaccines through a nationwide drive, a significant number of cases among healthcare workers were averted, attributed to vaccine intake. However, the fundamental knowledge from vaccinology clearly states that no vaccine is 100% effective. [6] A small percentage of people may not be protected from a particular disease even after vaccination, and for a few others, this protection may wane over time. This differential immunity for the same vaccine may be attributed to the individualistic response of the immune system to the vaccine antigen. The strength of the response is rooted in genetic differences (HLA typing and cytokines productions), pre-existing or cross-reactive immunity status, individual demographic attributes, any disease like autoimmune/chronic disorders, stress, nutritional status, sleeping patterns and most importantly, the factors unknown to us.

Sporadically, some published studies have reported these breakthrough infections from the Indian subcontinent. The entire cohort of HCWs can be categorised as a susceptible population for post-vaccination COVID-19 infection with limited data on time to event. This detailed cohort analysis is crucial to determining and guaranteeing uninterrupted healthcare services in future pandemics. The empirical data on description, patterns, time since events and associated factors may throw light upon determining the most susceptible individuals, allocating resources, and developing policies and procedures.

Methodology: An ambi-directional cohort study was conducted among HCWs at a tertiary COVID-19 hospital in Bhopal, India, from September 2021 to July 2022. The follow-up period was set at six months post-second vaccine dose. Bivariate analysis was used to compare socio-demographic, occupational, and personal characteristics. Exploratory data analysis was followed by univariate and multivariate Cox regression models, with time-period adjustments, to evaluate risk factors.

This longitudinal study was conducted among the HCWs of a dedicated COVID-19 tertiary care teaching hospital in Bhopal, Madhya Pradesh. HCWs from this facility administered at least a single dose of any COVID-19 vaccine were included in the study and the data collection period lasted from September 2021 to July 2022.

We defined post-vaccination COVID-19 infection as a confirmed case of COVID-19 infection occurring at least 14 days after the first or second dose of COVID-19 vaccination.

Healthcare workers (HCWs) were categorized into two groups for questionnaire administration. Doctors, nurses, para-medical/administrative staff and students were contacted through Electronic Mail and Mobile Messaging Platforms, while security, housekeeping and other support staff were contacted through supervisor assistance. The responses were directly obtained through Computer-Assisted Data Collection Tools (CADCT) or transferred to these platforms after manually filling the forms.

The recruitment of HCWs occurred from October 1, 2021, to February 28, 2022, with simultaneous follow-up phone calls extending until July 2022. The follow-up endpoint was set at 6 months from the date of the second dose of COVID-19 vaccination. Data collection for HCWs was ambi-directional: HCWs recruited beyond 6

months from the second dose were retrospectively surveyed (n=443 HCWs), while others were prospectively followed up (n=250 HCWs)..

The data was prepared for analysis using standard data cleaning and data wrangling procedures using base R and the 'tidyverse' universe of packages. Categorical variables were summarised as frequency and percentage, while continuous variables were presented as mean and standard deviation for parametric and as median and interquartile range for non-parametric data. This was followed by comparing relevant socio-demographic, occupational, and personal characteristics amongst those with and without a history of breakthrough infections by bi-variate analysis. Appropriate statistical tests (chi-square/unpaired t-test) were applied. The incidence density of post-vaccination COVID-19 infection was computed by dividing the number of confirmed cases (by RTPCR method) among healthcare workers by the total person-days at risk, presented as 100 person-years. Person days were calculated from 14 days after the first vaccination to 6 months after the second dose. The outcome variable, post-vaccination COVID-19 infection, was delineated as a binary variable as either the presence or absence of an event. A bi-variate analysis followed it by comparing relevant socio-demographic, occupational, and personal characteristics amongst those with and without incident post-vaccination COVID-19 infection.

This exploratory data analysis was tailed by Cox regression analysis for selected variables from exploratory analysis grounded in statistical or clinical significance. All the HCWs did not take the vaccine at the same time after launching the nationwide vaccination campaign, and the force of the infection was different at different time periods. This fact is essential from the perspective that India witnessed the second wave of COVID-19 roughly corresponding from 15th March 2021 to 30th May 2021. We accounted for this clustering (Force of infection, more or less) by considering it as a correlated group of observations and have added a cluster term "Time Since Second Wave" indicating the time of the second vaccination dose before or after 30th May 2021. Hence, the standard errors of the CPH model's dependent variables are fitted after adjusting to account for period correlations.

The overall robustness of model was assessed by likelihood and Wald statistic. The regression coefficients with exponential transformations (point estimates & 95%CI) were estimated to obtain hazard ratios. The p-value of 0.05 was considered significant in all analyses.

A forest plot and adjusted survival curve with cumulative hazard function were drawn for the visualization of hazard ratios and cumulative survival probabilities. The assumption of constant risk of other dependent variables over time was checked with the plot of scaled Schoenfeld residuals. We further tested the null hypothesis that the gradient does not differ from the zero for each variable through the chi-square test.

All statistical analysis was performed using the statistical programming language R and associated packages "survival" and "survminer" that are available in the public domain were used for model building, visualizations, and running diagnostics.

Results: The incidence density of post-vaccination COVID-19 infection was 10.64 per 100 person-years (95% CI: 7.53–13.75). Doctors exhibited the highest incidence density (27.2 per 100 person-years), followed by nurses (15.7 per 100 person-years). The median time to infection was 76 days, with differences observed between partially and fully vaccinated individuals. Older age was associated with a lower risk (HR=0.35, 95% CI: 0.15–0.79), while longer working hours increased the risk (HR=1.28, 95% CI: 1.07–1.52). Immediate Care Provider status (doctors/nurses) showed a notable but statistically insignificant increased risk (HR=2.35, 95% CI: 0.95–5.97). All cases were mild, with no hospitalization reported.

Conclusion: Immediate Care Providers reported a higher incidence density of breakthrough infections. This study underscores the need for targeted preventive measures based on occupational risk while reaffirming the vaccine's efficacy in mitigating severe illness.

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