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ORIGINAL ARTICLE

Effect of Covishieldtm (AZD1222) Vaccination on Incidences and Severity of Covid-19 among Health-Care Workers

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ABSTRACT

Introduction: Limited information is available regarding effect of vaccination on protection against Covid-19 infections and their severity as well. Objectives: In the present study, we assessed the effect of Covid-19 vaccination on incidences and severity of break through Covid-19 infections. **Method:** This retrospective study was conducted at a tertiary care center in Northern India during one calendar year, 1st August 2021 to 31st July 2022. The study population included Health-care workers (HCWs) who were treated for Covid 19 infection and had already received at least 1 dose of Covishield TM (AZD1222) Covid-19 vaccine. **Results:** Out of 1868 health care workers enrolled for the study, 513 contracted Covid-19 infections. Amongst infected HCWs, number of single and double doses of CovishieldTM (AZD1222) recipients were 112 and 401 respectively. Out of the 513 covid positive HCWs, 459 (89.4%) had mild disease, whereas 54 (10.6%) had moderate disease. None of the HCWs developed severe disease and no mortality was noted in either group. **Conclusion:** In this study, we found that immunization with two doses of CovishieldTM (AZD1222) vaccine was associated with decline in number of cases with moderate or severe Covid-19. Moreover, immunization with even single dose of CovishieldTM (AZD1222) vaccine prevented development of severe disease. Henceforth, it is concluded that although, immunization with CovishieldTM (AZD1222) could not protect all recipients from SARS-Cov-2 infection, it did prevent the progress of disease to severe grades.

Keywords: ABO blood group, coronavirus infection, Covid-19, critical care, intubation, mortality, severity

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INTRODUCTION

Over a period of three years, the Coronavirus and its variants caused global havoc, killing millions of people. Based on available scientific data, about 300 vaccines were developed, with some of these vaccines being approved for emergency uses (Forni and Mantovani, 2021). Many of these vaccines were used in mass vaccination campaigns. There were grossly four types of vaccines based on components/parts of the virus like, inactivated SARS CoV-2 viruses, SARS-CoV-2 proteins, naked viral DNA, and virus mRNA (Forni and Mantovani, 2021). Covid-19 vaccines have been shown to attenuate the severity of SARS-CoV-2 infection, although incomplete vaccination is associated with greater incidence of infection compared to complete vaccination (Ben Fredj *et al*., 2022). Such breakthrough infections affect the capacity of essential workforce across all sectors, including health services as well as pose a risk for transmission (Uschner *et al*., 2022).

Limited information is available regarding effect of vaccination on Covid-19 breakthrough infection as well as disease severity in India. In a recent study on the symptom profile and breakthrough infections among health care workers (HCWs)

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in Northern India, it was found that vaccination with two doses was significantly protective against acquiring infection (odds ratio 0.27), however, the disease severity was not compared (Malhotra *et al*., 2022). Another study compared disease severity between hospitalized and non-hospitalized patients in a center in Southern India and concluded that breakthrough infections among vaccinated HCWs occurred commonly, though they were usually mild or asymptomatic (Mohith and Chandrashekhar, 2022). However, it is not well understood how each dose of vaccine affects the disease severity and breakthrough infections. In the present study, we aimed to assess the break through Covid-19 infections among vaccine recipients and the effect of vaccination on the disease severity.

METHODS

Study Setting and Design

This was a retrospective study conducted at a tertiary care center in Northern India between 1st August 2021 to 31st July 2022. The study population included HCWs who were treated for Covid 19 infection and had already received at least 1 dose of CovishieldTM (AZD1222) Covid-19 vaccine. Comparisons were done between the single and double dose vaccinated HCWs to understand the effect of complete vaccination on disease severity and breakthrough infection in HCWs. The HCWs data was also compared with that of the patients admitted to the hospital and were either unvaccinated or received one or two doses of Covid-19 vaccine. The information regarding vaccination status for HCWs was collected on case report form by the investigator/co-investigators, while details regarding the patients admitted to dedicated COVID care facility within the hospital were collected from hospital records and telephonic enquiry. The study was approved by the institute's ethics committee (IEC-2021-185-IP-EXP-41).

Operational Definitions

Unvaccinated individuals were defined as those who had either not received first dose or less than two weeks had elapsed since the administration of first dose and the onset of symptoms. Partially vaccinated individuals were those who had received the first dose of vaccine more than two weeks ago from the onset of symptoms or had symptom onset at less than four weeks of second dose administration. Fully vaccinated individuals were those who received second dose of vaccine at least four weeks prior to the onset of symptoms. Severity was graded into three categories, Mild, Moderate and Severe based on O_2 requirements. Patients who did not require O_2 administration anytime during the course of disease was placed in Mild disease category. Anyone who was given O_2 therapy with either Nasal Prongs, Hudson's mask or Non-Rebreathing Mask (NRBM) was placed in moderate disease category. Severe disease category included patients who required Bi-PAP, Mechanical Ventilation or High Frequency Nasal Cannula (HFNC) support.

Data Sources and Study Variables

The data of the study participants included their basic demography (age and gender), comorbidities (Diabetes Mellitus, Hypertension, other comorbidities included any other pre-existing illness), date of the first vaccine dose and second vaccine dose (if taken) were extracted. These participants were contacted to know whether they developed COVID-19 infection or not, and if positive, the date of the Covid-19 positive test. Individuals with positive Covid-19 test prior to the study period were excluded. HCWs who were unvaccinated were also excluded from the study.

Sample Size Calculation

In single and double dose vaccinated HCWs, for 10% difference in individuals with moderate disease between single and double dose vaccinated groups (where expected moderate disease was assumed to be 8% and 18% respectively), it was estimated that 109 and 327 patients in the respective groups would be required (at assumed 1:3 ratio) for two-sided 95% confidence interval and 80% power of the study. Sample size was estimated using Power Analysis and Sample Size version-16 [PASS-16, NCSS, LLC, Utah, USA].

Statistical Analysis

Continuous variables (age in years, duration between vaccinated to covid positive in days) were presented in median (interquartile range 'IQR') and Mean ± SD, whereas categorical variables were expressed in number (%). Mann Whitney U test was used to compare the medians whereas Chi-square test was used to compare the proportion between groups. Classification and regression trees (CART)

analysis was used to present the distribution of the disease severity with vaccination status at the time of positive and presence of any comorbidity. P value <0.05 was considered statistically significant.

Table 1. Distribution of the Characteristics and Comorbidity between Covid Positive and Negative Study Participants (N=1868)

Variable	COVID Positive (n=513)	COVID Negative (n=1355)	p value
Age (Years), mean±SD	40.76±11.10	39.30±11.31	0.012
[Median, IQR]	[39, 31-52]	[37, 30-50]	
Sex			
Male	327 (27%)	886 (73%)	
Female	186 (28.4%)	469 (71.6%)	0.506
Diabetes	32(6.2%)	30(4.3%)	0.160
Hypertension	24(4.7%)	25(3.7%)	0.389
Other Comorbidity	19(3.7%)	18(2.6%)	0.275
Anyone comorbidity	66(12.9%)	63(9.2%)	
No comorbidity	447(87.1%)	625(90.8%)	0.024

Means compared using independent samples t test. Proportions compared using Chi-square test. P<0.05 significant

Statistical package for social sciences, version-23 [SPSS-23, IBM, Chicago, USA) used for data analysis.

RESULTS

During the study period, there were 1868 HCWs who were not COVID-19 positive on or before date of the first dose of the vaccination. Their mean and median age were 39.7 and 38 years respectively (range: 18-65 years), with majority being males (n=1213, 64.9%). Of these, 513 (27.5%) became COVID-19 positive and among them, 112 and 401 received single and double doses of CovishieldTM (AZD1222) Covid-19 vaccine respectively.

There was no significant difference in distribution of gender, presence of hypertension, diabetes and other comorbidity between COVID-19 positive and negative study participants (each p>0.05) whereas age of the participants was higher and presence of at least one comorbidity was noted in the COVID-19 positive group (p<0.05 each) [Table 1].

Out of the 513 covid positive HCWs, 459 (89.4%) had mild disease, whereas 54 (10.6%) had moderate disease. None of the HCWs developed severe disease and no mortality was noted in

Table 2. Distribution of the patient characteristics and comorbidity between disease severity in COVID-19 positive study participants (N=513)

Variable	Total (N=513)	Mild Infection (n=459)	Moderate Infection (n=54)	p value
Age (Years)	40.76±11.10 [39, 31-52]	40.89±11.14 [39, 31-52]	39.85±10.70 [39, 32-48]	0.517
Sex				
Male	327 (63.7%)	294(89.9%)	33(10.1%)	
Female	186 (36.3%)	165(88.7%)	21(11.3%)	
At least one Comorbidity	66(12.9%)	56(84.8%)	10(15.2%)	
No comorbidity	447(87.1%)	403(90.2%)	44(9.8%)	0.190
Diabetes	31(6.4%)	26(83.8%)	5(16.2%)	0.256
Hypertension	24(4.6%)	19(79.2%)	5(20.8%)	0.085
Others	19(3.7%)	18(94.7%)	1(5.3%)	0.515
COVID-19 Infection				
After single dose	112(21.7%)	91(81.3%)	21(18.7%)	
After double dose	401(77.7%)	368(91.8%)	33(8.2%)	0.005
Duration days				
After single dose (n=14)	68.57±21.60 [70, 63-80]	65.14±27.21 [71,64-77]	72.0±15.59 [67, 60-92]	0.574
After double dose (n=499)	80.41±13.75 [81,73-88]	80.73±13.54 [81,73-88]	77.34±15.46 [80, 70-85]	0.107

Means compared using independent samples t test. Proportions compared using Two proportional z test / Chi-square test. P<0.05 significant

either group. Age, sex, comorbidities, and days to development of infection since vaccination were comparable among the participants who had mild or moderate disease (p>0.05). Significantly lower proportion of the patients had moderate disease in the double dose vaccinated patients as compared to single dose (8.2% vs 18.7%, p=0.005) [Table 2]. Classification and regression trees analysis showed that vaccination with double dose and absence of comorbidity were significant preventive factors for disease severity (i.e., moderate disease) [Figure 1]. It depicts that double-dose vaccination prevented the severity of COVID-19, even in patients with comorbid illnesses. The percentage of moderate disease in double-dose recipients with comorbidities was 12.5% in comparison to 18.8% of single-dose recipients without any comorbid diseases.

DISCUSSION

In the present study, we assessed the incidence and severity of SARS-CoV-2 infection among the patients and HCWs with regards to vaccination using CovishieldTM (AZD1222) Covid-19 vaccine. By the time the HCWs had the infection, over 77% had received 2 doses of vaccine indicating rapidity of vaccination once the program came into effect in January 2021. Malhotra *et al*. in their study at a north-western Indian hospital during April-June 2021 noted that 53% of the HCWs who developed Covid-19 infection had received both doses of vaccine (Malhotra *et al*., 2022).

The mean age of the HCWs who got infected in our study was 40 years. Other authors have reported mean age of HCWs between 32-46 years (Malhotra *et al*., 2022; Contractor *et al*., 2022; Abhilash *et al*.,

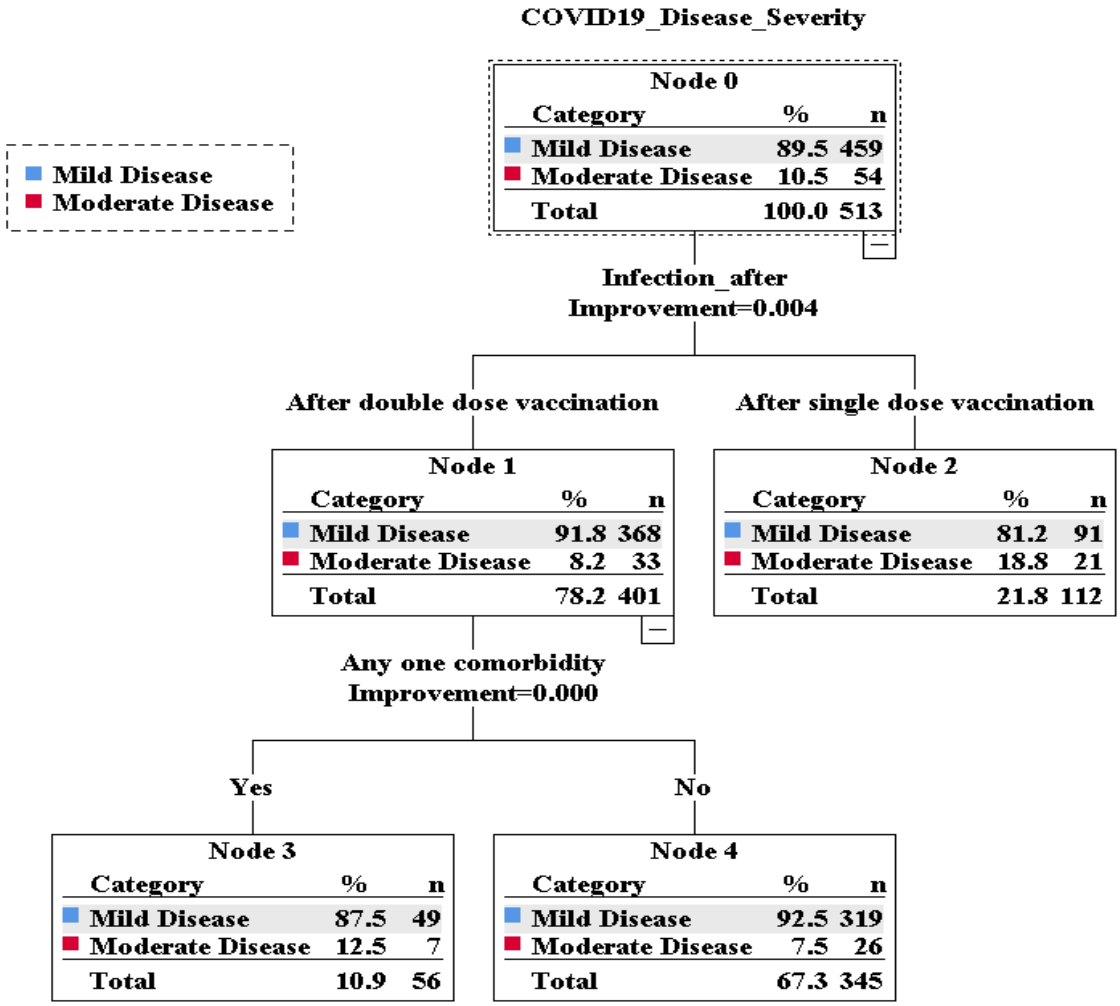

Figure 1. Classification and regression trees analysis showed the distribution of severity of the disease between patients, who were vaccinated at the time of COVID-19 infection

2022). The difference in mean age of participants can be attributed to the different age range of available study cohorts at different hospitals/study center. As private/corporate and government hospitals have different manpower pools. A multicenter study can alleviate this difference. Older age is an independent risk factor for severe infection regardless of vaccination status. Ben Fredj *et al*. (2022) Although studies have implicated the role of male gender in susceptibility to infection and more severe outcomes of Covid-19 infection, we did not notice such differences in our study population (Gebhard *et al*., 2020; Scully *et al*., 2020). As our study cohort included only healthcare workers with comparable working conditions and outdoor activities for males and females, no gender preponderance was observed for catching SARS-Cov 2 infection. No significant difference in disease severity between males and females in our study can be attributed to easy and quick accessibility to healthcare for HCWs. We also found that at least one comorbidity was associated with COVID-19-positive status. Frailty, comorbidity, and age predict the outcomes for patients with Covid-19 infection, including mortality (Lee *et al*., 2022). Frailty surpasses age in predicting adverse outcomes from Covid-19 (Lee *et al*., 2022). Associations between comorbidity and death also decrease with age. Zakaria *et al*. (2023) reported that between the ages 20 to 34 years, the likelihood of death is 19 times greater in patients with three or more comorbidities compared to patients with none, while for 80+-year-olds the likelihood of death is only two times greater for patients with six or more comorbidities compared to patients with none.

Overall, infection occurred about 68 days after a single dose and 80 days after a double dose of the vaccine. A shorter period between single dose and infection, around 31 days, whereas reported the same as 77 days (Malhotra *et al*., 2022; Victor *et al*., 2021). In our study, the median time to development of infection after single or double doses of vaccine were not significantly different between those HCWs who developed mild infection versus those who developed moderate infection. As the duration between the vaccination and contraction of infection is quite long (about 68 days after single dose and 80 days after double dose of vaccine) that is sufficient to bring immune responses to vaccination, the duration has no impact on severity of disease. If the second wave of Covid-19 infection had hit earlier after initiation of vaccination campaign, the scenario of disease severity could have different course and might be related with the duration of vaccination and contraction of infection

On comparing the data of HCWs who had Covid-19 infection with the patients who were admitted for treatment of Covid-19 infection at the hospital during the same period, we found that the disease severity was significantly lower for the HCWs who were also better vaccinated compared to the patients. Although the cohorts of HCWs and other patients admitted to our hospital were not comparable as it was beyond the scope of our study, it was observed to a great extent that vaccination of HCWs was protective for them compared to the general population. Previous studies to have reported that the majority of vaccinated HCWs developed mild symptoms only, without the need for ICU care, and with no mortality (Malhotra *et al*., 2022; Tyagi *et al*., 2021, Bouton *et al*., 2021). The frontline workers in India were among the first ones to receive the COVID-19 vaccine and played a pivotal role in delivering healthcare in one of the worst health crises ever seen. About 65% of the patients in our study who were admitted were unvaccinated. Abhilash *et al*. (2022) Concluded that among symptomatic COVID-19 patients, prior vaccination reduced mortality due to delta variant circulation, and more excellent protection was achieved with complete rather than partial vaccination.

Regarding the development of immunity, a study by Thachanun *et al*.(2023), demonstrated that the immune response to the ChAdOx1 vaccine in patients with comorbidity was significantly lower than in healthy controls after the first and second doses of vaccination. Verma *et al*. (2022), observed that Covishield® induces a higher antibody titre in those with pre-existing ASAb. The vaccine-induced antibody starts falling five months after vaccination. Goel *et al*., 2022 reported that Covishield® induces high titers of ASAb and NAb in cirrhosis. A higher titer is achieved if two doses are given at an interval of more than six weeks. Bhadauria DS *et al*. (2023) explored the immunity in patients of renal failure receiving hemodialysis. They observed that two doses of ChAdOx1 nCoV-19/AZD1222 (Covishield®) vaccine, given 12 weeks apart, achieved a high titer of ASAb and a high percentage of NAb in people on hemodialysis. Vaccination also brought in some side effects; interestingly, functional disorders were also reported, along with some organic complications (Sanjeev *et al*., 2022).

Our study has a few limitations. This study is not a typical efficacy study. Further, it reflects

the vaccination status and infection pattern in just one tertiary-level healthcare facility, where many patients were referred from the peripheral centers as they required high-level care, which can be seen by a high percentage of unvaccinated patients with severe symptoms. Another limitation is that we studied the results of only one vaccine (CovishieldTM) and hence, it is not possible to comment on its comparative efficacy against other vaccine types. However, despite these limitations, it gathers data from a large pool of HCWs and patients and provides important information on predictors of Covid-19 disease severity and its relation with vaccination status.

CONCLUSION

In this study, we found that immunization with two doses of CovishieldTM (AZD1222) vaccine was associated with decline in the number of cases with moderate or severe Covid-19 disease among the HCWs. Moreover, immunization with even single dose of CovishieldTM (AZD1222) vaccine prevented development of severe disease. Henceforth, it is concluded that, although immunization with CovishieldTM (AZD1222) vaccine could not protect the recipients from SARS-Cov-2 infection, it did prevent the progress of disease to severe grades.

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