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Effectiveness of COVID-19 Vaccine in Prevention of Mortality among Moderate-Severe Cases: Case Control Study

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Abstract

Introduction: The present study was conducted for vaccine effectiveness in the prevention of mortality among moderate to severe COVID-19 cases. **Methods:** The study was conducted in a dedicated COVID-19 hospital in Northern India from April 2021 to June 2021. Only moderate and severe COVID-19 cases were admitted to the hospital. All patients with the outcome (recovery or mortality) till 30 June 2021 constitute the study population for the study. The study is designed as a case-control study. The outcome was mortality due to COVID-19. The control group was cases who have recovered. The exposure was vaccination status. The data about the age, sex, and vaccination status including the type of vaccine was collected from the case sheets. **Results:** A total of 735 participants were recruited, out of which 409 patients survived and 326 patients died due to COVID-19 in the hospital. The mean age was 52.80 years (SD = 14.1 years) in the cases group and 60.92 years (SD = 14.97 years) in control group (P = 0.001). 137 (33.50%) were female and 272 (66.50%) were male in the control group while in cases 134 (41.10%) were female and 192 (58.90%) were male (P = 0.03). A total of 473 (64.35%) patients were unvaccinated, 199 (27.07%) were partially vaccinated, and 63 (8.57%) were fully vaccinated. Among the patients who survived, 101 (24.69%) were partially vaccinated and 28 (6.85%) were fully vaccinated; in the cases group, 98 (30.06%) people were partially vaccinated and 35 (10.74%) were fully vaccinated. On multiple regression analysis, there was no association between vaccination status and mortality among moderate and severe cases. **Conclusion:** The present study brought out that there is no association between vaccination and mortality among moderate to severe COVID-19 cases admitted to the makeshift hospital in Delhi.

Keywords: *COVID-19 vaccine, mortality, vaccine effectiveness*

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Introduction

On December 31, 2019, Wuhan Municipal Health Commission, China reported a cluster of cases of Pneumonia, later identified to be caused due to SARS-CoV-2 virus and the disease was named COVID-19.[1] On January 30, 2020, COVID-19 was declared a Public Health Emergency of International Concern[2] and was subsequently declared a pandemic on 11th March 2020.[3] In India, the first wave of the pandemic peaked in September 2020. Nearly 6 months thereafter, the cases started to rise again from the first week of March 2021. In the second wave, the dominant strain has been the B.1.617 strain of SARS-CoV-2 which has resulted in a rapid rise in cases and mortality due to COVID-19.[4]

To put a deterrent to the rise in the number of cases, various measures were adopted by the center and the states including lockdowns, compulsory RT PCR

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testing before traveling to certain states, and authorizing vaccinations under Emergency Use Authorization (EUA) for Health care workers and Front line workers initially, followed by the general population of various age groups in a phased manner.[5-7] As of the date 23 Jan 2021 more than 1600 million doses have been given in the country.[8]

Of the two vaccines approved, Covaxin is an indigenous vaccine developed by Bharat Biotec, while Covishield is a version of the Oxford University-AstraZeneca vaccine. Both the vaccines have been proven efficacious in the prevention of severity and mortality among the COVID-19 cases.[5]

However, since these vaccines were of EUA, many aspects of the vaccine were not studied. World Health Organization has taken out guidelines for studying vaccine effectiveness in Low and Middle-Income countries through various observational study designs including case-control study.[6] The guidelines and various researchers have highlighted the role of Case-Control studies for evidence gathering on the effectiveness of the vaccine.[7] Hence, the present study was conducted for vaccine effectiveness in the prevention of mortality among moderate to severe COVID-19 cases.

Methods and Materials

The study was conducted in a dedicated COVID-19 hospital in Northern India from April 2021 to June 2021. The patients were admitted to the hospital after positive molecular testing (RT-PCR or RAT) for COVID-19. Only moderate and severe COVID-19 cases were admitted to the hospital.

All patients with the outcome (recovery or mortality) till 30 June 2021 constitute the study population for the study. The study is designed as a case-control study. The outcome was mortality due to COVID-19. The control group was cases who have recovered. The exposure was vaccination status. The data about the age, sex, and vaccination status including the type of vaccine was collected from the case sheets. The following co-morbidities are Hypertension, Diabetes Mellitus, Cardiac disease, Chronic Kidney disease, Chronic Obstructive Pulmonary Disease, Epilepsy, Hypothyroid, Parkinson's, Dementia, Obesity, Rheumatoid Arthritis, Malignancy, HIV, Dyslipidemia, Depression, or any other co-morbidity were noted from the case-sheet.

As per MOHFW, GOI, Moderate cases of COVID-19 are defined as patients with shortness of breath, difficulty in breathing, a respiratory rate of more than 24 but less than 30, SPo2 90-93% at room air. Severe cases of COVID-19 defines as patients with shortness of breath, difficulty in breathing, a respiratory rate of more than 30/min, and SPO_2 less than 90% on room air except in COPD patients.[9]

A full vaccinated person is defined as one who receives both doses of either Covishield or Covaxin Vaccine. In the analysis, patients who receive a single dose of vaccine and completed 14 days after vaccination were considered partially vaccinated patients and patients who received a 2nd dose of vaccination and completed 14 days were considered fully vaccinated.

The sample size was calculated assuming the probability of exposure in the control group as 40%, odds ratio of two, 90% power and 1% error. The calculated sample size was 251 for cases and control groups. However, we could finally enroll 326 and 409 in the cases and control group. These were enrolled using convenience sampling by recruiting first cases and control who agreed to participate in the study. The study was ethically approved by the institution's ethical committee vide their letter number Mar/2021 dated 13 March 2021.

The data was collated in an excel sheet. The continuous variables were described as mean and standard deviation. The categorical variables were described as numbers and percentages. The contingencies table was made. Bivariate and multiple Logistic regression analysis were done to find out the association among variables. The data was analyzed using StataCorp. 2019. *Stata Statistical Software: Release 16*. College Station, TX: StataCorp LLC. The *P* value of less than 0.05 was taken as statistically significant.

Results

A total of 1684 patients were admitted to the hospital, out of which 810 (48.1%) did not survive. In the present case-control study, 735 were recruited, out of which 409 patients survived and 326 patients died due to COVID-19 in the hospital.

Among the cases admitted to the makeshift hospital the mean age was 52.80 years (SD = 14.1 years) in the cases group and 60.92 years (SD = 14.97 years) in the control group (*P*-value = 0.001). 137 (33.50%) were female and 272 (66.50%) were male in the control group while in cases 134 (41.10%) were female and 192 (58.90%) were male (*P*-value = 0.03). The mean length of stay in the control group was 8.23 days (SD = 5.7) and 5.54 days (SD = 4.85) in the cases group (*P* value = 0.001).

A total of 473 (64.35%) patients were unvaccinated, 199 (27.07%) were partially vaccinated, and 63 (8.57%) were fully vaccinated. Among the patients who survived, 101 (24.69%) were partially vaccinated

and 28 (6.85%) were fully vaccinated; in the cases group, 98 (30.06%) people were partially vaccinated and 35 (10.74%) were fully vaccinated. Of all the vaccinated people, 118 (45.38%) received Covishield, 141 (54.23%) received Covaxin, and one person received Pfizer (0.38%).

A total of 131 (40.18%) in the cases group and 232 (56.72%) in the control group were not having any comorbidities, 86 (26.38%), 74 (22.70%), and 35 (10.74%) were having single, two, and three or more comorbidities, respectively, in cases group, 139 (33.99%), 33 (8.07%), and 5 (1.22%) were having single, two, and three or more comorbidities, respectively, in the control group [Table 1].

In bivariate logistic regression analysis, partial vaccination, full vaccination, increase age, female sex, shorter stay in the hospital, and co-morbidity were associated with mortality. However, on adjustment of variables, there was no association of vaccination (partial or complete) with mortality and sex of the patients. Increasing age, presence of comorbidity, and shorter duration of stay remained associated with mortality [Table 2].

The subgroup analysis was done for the type of vaccination. Similar results were observed for both Covaxin and Covishield [Table 3].

Discussion

COVID-19 vaccines have been provided EUA and hence there is little evidence for long-term effects, safety, and effectiveness of the vaccines in different settings. In India, vaccine rollout is mostly Covishield and Covaxin.[10] We did a case-control with mortality as an outcome among moderate to severe COVID-19 cases.

Our study did not find the effectiveness of the vaccine in reducing mortality among moderate to severe cases in either partially vaccinated or fully vaccinated participants. In a study in the UK, the data published shows first dose vaccine effectiveness (Covishield) ChAdOx1nCoV-19 was 80.4%.[11] A study published by Jamie Lopez Bernal *et al*.[12] in England reveals that a single dose of ChAdOx1-S vaccine was about 80% effective at preventing admission to hospital with covid-19. Another study published by Baden *et al*.[13] the England New journal of medicine shows that the mRNA-1273 vaccine showed 94.1% efficacy at preventing Covid-19 illness, including severe disease. The studies have shown that severe COVID-19 cases and death are rare in the vaccinated population (0.015% for severe disease and 0.0033% for death).[14] Studies conducted in India also showed that the vaccine is effective in preventing severe cases and death among participants.[15,16]

Though there are many studies on the effectiveness of vaccines amongst healthy individuals yet, none of the studies has compared outcomes among vaccinated and non-vaccinated moderate and severe cases. The present study fills that gap. None of the vaccines provide sterilizing immunity. Hence there are cases that progressed from moderate to severe COVID-19 cases even among vaccinated. Once the case has progressed to severe COVID-19 disease, there was no difference in mortality of vaccinated or non-vaccinated individuals. The reason may be related to the pathogenesis of the disease. The severity of the cases indicates that the infection has already overwhelmed the immunity of the body system. Our study shows that vaccination may not prevent deaths in such cases. On subgroup analysis, there was no difference in the effectiveness of any vaccine.

Our study also finds that there is no difference in survival in terms of gender (OR = 0.71 *P* value 0.05) when we adjusted with other variables in the study. The study conducted among 11278 COVID-19 cases with outcomes in India observed that the male sex may be at higher risk of mortality.[17] A smaller sample size could be one of the reasons. Since we did not have data on the medical parameters at the individual level many other factors like differential admission could not be looked into as this may also be one of the reasons for the different observations of sex in mortality.

The study findings that old age and co-morbidity are related to higher mortality are in congruence with the findings of other studies.[17,18]

Table 1: Characteristics of cases and controls with their vaccination status (*n*=735)

Characteristics	Case (*n*=326) number, %	Control (*n*=409) number, %	*P*
Vaccination			
Unvaccinated	193, 59.20%	280, 68.46%	0.02
Partial Vaccinated	98, 30.06%	101, 24.69%	
Full vaccinated	35, 10.74%	28, 6.85%	
Age Years mean (SD*)	52.8 (14.1)	60.9 (14.7)	<0.001
Stay Days mean (SD)	5.5 (4.85)	8.2 (5.7)	<0.001
Sex			
Female	134, 41.1%	137,33.5%	0.034
Male	192, 58.9%	272,66.5%	
Co -morbidities			
0	40.18% (*n*=131)	56.72% (*n*=232)	<0.001
1	26.38% (*n*=86)	33.99% (*n*=139)	
2	22.70% (*n*=74)	8.07% (*n*=33)	
3	10.74% (*n*=35)	1.22% (*n*=05)	

*SD=Standard deviation

Table 2: Logistic regression model with different variables among cases and controls

Characteristics	Unadjusted OR	95%CI	*P*	Adjusted OR	95%CI	*P*
Age	1.04	1.03-1.05	<0.001	1.03	1.02-1.04	<0.001
Stay	0.90	0.87-0.93	<0.001	0.90	0.87-0.93	<0.001
Sex						
Female	Ref					Ref
Male	0.72	0.53-0.97	0.34	0.71	0.51-1.002	0.05
Co-morbidity						
0	Ref					
1	1.09	0.77-1.5	0.60	0.87	0.60-.1.2	0.48
2	3.97	2.49-6.3	<0.001	2.9	1.8-4.7	<0.001
3	12.39	4.7-32.41	<0.001	8.8	3.2-24.1	<0.001
Vaccination status						
Unvaccinated	Ref			Ref		
Partial Vaccinated	1.40	1-1.9	0.04	1.1	0.75-1.61	0.61
Full vaccinated	1.81	1.06-3.0	0.02	1.2	0.67-2.2	0.50

Table 3: Multiple logistic regression for each vaccine subtype

Characteristics	Covaxin (*n*=141)		*P*	Covishield (*n*=118)		*P*
	Adjusted OR	95%CI		Adjusted OR	95%CI	
Vaccination status						
Unvaccinated	Ref			Ref		
Partial Vaccinated	1.2	0.8-2	0.9	0.8	0.5-1.4	0.4
Full vaccinated	1.4	0.6-3.3	0.8	0.9	0.4-2	0.8
Age	1.03	1.02-1.05	<0.001	1.03	1.02-1.04	<0.001
Stay	0.90	0.87-0.93	<0.001	0.91	0.88-0.94	<0.001
Sex						
Female	Ref					Ref
Male	0.65	0.45-0.94	0.022	0.8	0.6-1.2	0.3
Co-morbidity						
0	Ref					
1	0.9	0.7-1.4	0.60	0.8	0.5-.1.2	0.2
2	2.7	1.6-4.7	<0.001	2.6	1.5-4.6	0.001
3	6	2.1-17.1	0.001	9.5	3.1-29.1	<0.001

The present study is a case-control study so it has all the limitations of the case-control study for the generation of evidence. Second, we could not get detailed clinical conditions and laboratory parameters of the patients in both group and hence were not able to adjust for clinical variables in the analysis. Third, as the predominant strain of the virus in the community are different at different times so the findings of the study may be applicable to the variant predominant at the time. Fourth, genetic studies to identify the variant of the SARS-COV-2 were beyond the scope of the study. The past history of the COVID infection could not be taken, which could also influence immunity and mortality.

The present study brought out that there is no association between vaccination and mortality among moderate to severe COVID-19 cases admitted to a makeshift hospital in Delhi. However, the findings of the present study may be confirmed by a better observational study design.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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