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EFFECTIVENESS OF CORONAVIRUS DISEASE-19 VACCINATION ON DISEASE TRANSMISSION, HOSPITALIZATION, AND CLINICAL OUTCOMES IN ADULTS IN NORTH INDIA

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SUMMARY

Background: Covaxin and Covishield vaccines have rapidly rolled out in India to curb the pandemic. We aimed to test the hypothesis that COVID-19 vaccination is clinically effective. Methods: This study was conducted in the Department of Physiology at MGM College, Jaipur, India after approval from the Ethics Committee. Vaccinated and non-vaccinated groups were tested on disease transmission, hospitalization, and clinical outcomes. Researchers collected data using questionnaires circulated through google forms. The association between attributes was tested using the chi-squared test. The significance level was considered at 5%.

Results: The vaccination significantly reduced disease transmission of COVID-19 [c2=4.51; p = 0.034]. However, no significant differences were seen in RTPCR positivity, chest CT findings, and hospitalization on vaccination. COVID-related symptoms and their severity were not statistically different between the two groups. Most elderly were vaccinated [c2=41.68; p < 0.001]. Most youths took one dose, while the elderly took two doses of the vaccine [c2=41.77; p < 0.001]. All age groups had similar severity of AEFIs [c2=13.22; p < 0.21]. The vaccination status across gender did not differ significantly. [c2=1.13; p < 0.288] Most males took two doses as compared to females [c2=6,57; p < 0.01]. Adverse effects post-immunization were more severe in females than males [c2=13.10; p < 0.001]. There was no association between the number of vaccine doses and the severity of AEFIs [c2=16.42; p = 0.06].

Conclusion: The present study concludes the beneficial effect of vaccination in reducing disease transmission. However, vaccination has no role in mitigating other COVID-related outcomes.

Keywords: AEFIs, Covaxin, COVID-19, Covishield, Immunization, Vaccination

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused an epidemic in Wuhan (Hubei province, China) on December 12, 2019. (1)(2). Since then, the virus has spread globally and caused thousands of deaths, and the World Health Organization (WHO) declared a pandemic on March 12, 2020. (3) As of April 3, 2022, WHO reported over 489 million cases and over 6 million deaths globally. (4) SARS-CoV-2 expressed its presence in India, with the first case diagnosed on January 30, 2020. (5) The vast extent of climatic and cultural differences in the country results in many disease transmission patterns. (6) SARS-CoV-2, a highly contagious virus, spreads by inhaling respiratory aerosols, direct human contact, and fomites. Social distancing, personal hygiene, frequent hand washing or sanitizing using alcohol (61-70%) based hand sanitizers, and disinfection of the surfaces are some steps that can protect the individuals from getting infected. (7) However, immunotherapy is considered an effective method for preventing and treating various infectious diseases and cancers, which involves the artificial triggering of the immune system to elicit the immune response. (8)

The emergence of the vaccine against SARS-CoV-2 is relevant to public health interventions, hospital management, and policy decision-making. (9)(10)(11) Many studies showed that the vaccines could prevent both symptomatic and asymptomatic infection and disease transmission in working-age adults. (12) The COVID-19 vaccination program was introduced in India on January 16, 2021. (13) The Central Drugs Standard Control Organization (CDSCO) in India granted permission to use two vaccines for emergency use that is, Covishield® (AstraZeneca's vaccine manufactured by Serum Institute of India) and Covaxin® (manufactured by Bharat Biotech Limited). (14) Many studies compared the immunogenic and reactogenic efficacy of vaccines. (15) However, the present study evaluated the effectiveness of the vaccines on post-vaccination and COVID-19 related outcomes,

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MATERIAL AND METHODS

After approval from Institutional Ethics Committee, this cross-sectional study was designed in the Department of Physiology at Mahatma Gandhi Medical College, Jaipur (Rajasthan, India). The study tested the hypothesis that COVID-19 vaccination is clinically effective. The study also evaluated post-vaccination events. The COVID-19-related outcomes were compared between vaccinated and non-vaccinated groups. The COVID-19 related outcomes include disease transmission rate, hospitalization requirement, presence of symptoms, severity of symptoms, COVID-19 findings in chest CT, and chest CT score. The disease transmission rate was calculated as a percentage of COVID-19 positive cases after 14 days of taking at least a single dose of vaccine. The vaccine-related events include the number of vaccine doses taken, adverse effects post-immunization (AEFIs), and severity of AEFIs. The majority of the Indian population took Covaxin and Covishield vaccines. Researchers collected demographic and clinical data using questionnaires circulated using google forms. The subjects over 18 years of age and willing to participate in the study were included, while those who had taken vaccines other than Covaxin and Covishield or were critically ill were excluded from the study.

Statistical Analysis:

The descriptive statistics for quantitative data were expressed as the median and interquartile range (IQR), and qualitative data were expressed as percentages. The continuous variable age was discretized to find relationships with other attributes. The association between attributes was tested using the chi-squared test. The significance level was considered at 5% (α=0,05). Researchers used Google Sheets for data collection, Microsoft Excel 2019 to prepare the database, MATLAB 2019a for graphics visualization, and used R 4.1.2 statistical package for statistical analysis.

Table 1. *Comparison of vaccinated and non-vaccinated individuals on COVID-19 related outcomes*

Attribute	Levels	Vaccination Status		χ^2 value	*p*
		Nonvaccinated	Vaccinated		
COVID Status	Non-COVID	155(81.579)	221(88.755)	4.515	0.034
	COVID	35(18.421)	28(11.245)		
RT-PCR positivity	Negative	6(17.647)	2(7.407)	1.385	0.239
	Positive	28(82.353)	25(92.593)		
chest CT	Covid finding absent	12(46.154)	9(52.941)	0.19	0.663
	Covid finding present	14(53.846)	8(47.059)		
CT Score	Less than 8	9(56.25)	8(72.727)	1.173	0.556
	9 to 15	3(18.75)	2(18.182)		
	More than 15	4(25)	1(9.091)		
Hospitalization	Not Hospitalized	27(84.375)	26(96.296)	2.278	0.131
	Hospitalized	5(15.625)	1(3.704)		

Table 2. *Comparison of vaccinated and non-vaccinated individuals on COVID symptomatology*

Attribute	Levels	Vaccination Status		χ^2 value	*p*
		Non-vaccinated	Vaccinated		
Presence of Symptoms	Asymptomatic	4(12.903)	2(7.407)	0.47	0.493
	Symptomatic	27(87.097)	25(92.593)		
Fever	Absent	6(18.182)	4(15.385)	0.081	0.776
	Present	27(81.818)	22(84.615)		
Cough	Absent	12(36.364)	8(30.769)	0.203	0.652
	Present	21(63.636)	18(69.231)		
Loss of taste or smell	Absent	14(42.424)	11(42.308)	8.09E-05	0.993
	Present	19(57.576)	15(57.692)		
Severity of Symptoms	Mild	13(43.333)	12(46.154)	0.567	0.753
	Moderate	14(46.667)	10(38.462)		
	Severe	3(10)	4(15.385)		

Table 3. *Association of vaccination-related events with various age groups in persons susceptible for COVID-19*

Attributes	Levels	Age groups (years)						χ^2 value	*p*
		< 20	21-30	31-40	41-50	51-60	> 60		
Vaccination Status	Vaccinated	90	38	59	38	27	10	41.688	< .001
	Non-vaccinated	75	58	44	11	3	0		
Number of vaccine doses	One dose	64	19	12	12	13	4	41.773	< .001
	Two doses	26	19	47	26	14	6		
Severity AEFIs	Mild	43	14	25	19	15	8	13.216	0.212
	Moderate	26	13	12	8	6	0		
	Severe	9	3	2	1	0	0		

Table 4. *Association of vaccination-related events with gender in persons susceptible for COVID-19*

Attributes	Levels	Gender		χ^2 value	*p*
		Male	Female		
Vaccination Status	Vaccinated	146	113	1.13	0.288
	Non-vaccinated	116	73		
Number of vac doses	One dose	58	63	6.572	0.01
	Two doses	88	50		
Severity AEFIs	Mild	76	48	13.099	0.001
	Moderate	22	40		
	Severe	5	10		

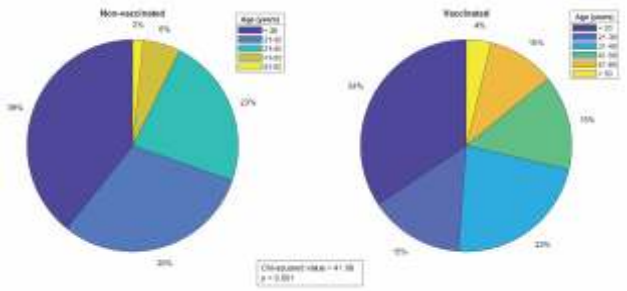

Figure 1. *Pie charts showing the distribution of age groups across vaccinated and non-vaccinated groups*

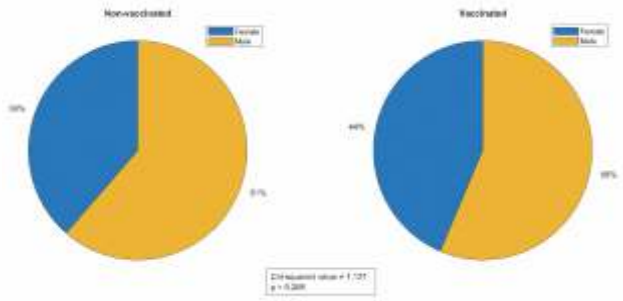

***Figure 2**. Pie charts showing the distribution of gender across vaccinated and non-vaccinated groups*

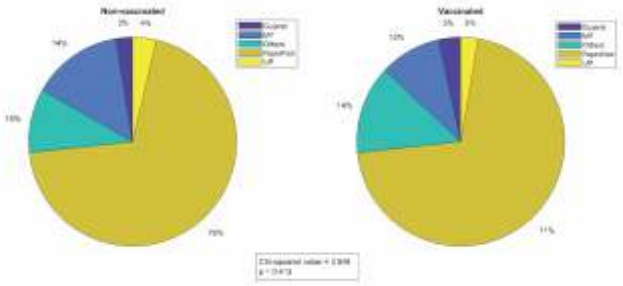

***Figure 3**. Pie charts showing the state-wise distribution across vaccinated and non-vaccinated groups*

RESULTS

A total of 453 responses were obtained from google forms. The median age of participants was 26 years (minimum = 18 and maximum = 72), with a male preponderance (58.5%). (Figures 1 and 2) Most of the responses were from the state of Rajasthan (70.2%), followed by Madhya Pradesh (11.5%). The percentage of vaccinated individuals was 57.8% (Figure 3)

The vaccine had a significant effect on the reduction of transmission of COVID-19 [c^2=4.51; p = 0.034]. However, no significant differences were seen in RTPCR positivity, chest CT findings, CT score, and hospitalization. (Table 1) Similarly, the presence of symptoms, fever, cough, loss of taste, and severity of symptoms was not substantially different in vaccinated and non-vaccinated individuals. (Table 2) The persons in higher age groups were more vaccinated [c^2=41.68; p < 0.001]. Most individuals less than 20 years had taken one dose of vaccine, while higher age groups took two doses of vaccine [c^2=41.77; p < 0.001]. No significant differences were found between age groups and severity of AEFIs [c^2=13.22; p < 0.21]. (Table 3) The vaccination status across gender did not differ significantly. [c^2=1.13; p < 0.288] Most of the males had taken two doses as compared to females [c^2=6,57; p < 0.01]. Adverse effects post-immunization were more severe in females than males [c^2=13.10; p < 0.001]. (Table 4) There was no association between the number of vaccine doses and the severity of AEFIs [c^2=16.42; p = 0.06].

DISCUSSION

The primary role of any vaccination drive is disease prevention and reduction in transmission of infection, hospitalization events, and mortality. (16)(11) The vaccine's effectiveness depends on multiple factors, including age, gender, ethnic inequality, drugs, diabetes, and blood groups. (17) (18)(19)(20) Verma et al. described the prominent role of diabetes and hypertension in the mortality of vaccinated individuals; otherwise, COVID-19 vaccines were very efficacious against COVID-19. (21) Two vaccines were rolled out to curb the ongoing pandemic in India- Covishield and Covaxin. Covishield (ChAdOx1-S) is a Covid 19 vaccine developed by Oxford Astra Zeneca and manufactured at the Serum Institute of India. The Covishield vaccine used the Viral Vector Platform. It involves modifying a chimpanzee adenovirus to carry the Covid19 spike protein. (22) On the other hand, Covaxin is a whole virion inactivated (WVI) SARS-CoV-2 vaccine (BBV152), adjuvanted with aluminum hydroxide gel (Algel), or TLR7/8 agonist chemisorbed Algel. It is manufactured by Bharat Biotech, Hyderabad, collaborating with the ICMR- National Institute of Virology, Pune. (23) Ella et al. conducted a phase I human trial and found that BBV152 led to tolerable safety outcomes and enhanced immune responses. Both Algel-IMDG formulations were selected for phase 2 immunogenicity trials. (24) In the second phase of the clinical trial, BBV152 showed better reactogenicity and safety outcomes and enhanced humoral and cell-mediated immune responses compared with the phase 1 trial. The 6 µg with Algel-IMDG formulation was selected for the phase 3 efficacy trial. (25) During a phase trial III, Ella et al. found BBV152 was highly efficacious against laboratory-confirmed symptomatic COVID-19 disease in adults. The vaccine was well tolerated, with no safety concerns raised in this interim analysis. (26)

Yadav et al. discussed challenges and tools to test the effectiveness of vaccines. Different testing methodologies are available in various laboratories worldwide, and there is no standardized measurement process to know the protective immune response. The authors focused on the requirement of a suitable antibody test that can be used to check whether the vaccine has triggered a sufficient immune response. Further, the method needs to have the ability to measure the valid quantity of antibodies generated, and it should be traceable to the international unit. (27) another aspect of measurement of vaccine effectiveness is clinical outcomes, such as rate of transmission, presence and severity of symptoms, hospital admissions, and mortality.

The present study considered clinical measures and showed that nCoV-19 vaccines (BBV152 and ChAdOx1) were associated with a significant reduction in disease transmission of SARS-CoV-2. However, there was no significant decrease in hospital admissions, presence and severity of symptoms, and chest CT score. The present study considered CT score an outcome as it has an independent role in diagnosing COVID-19. (28). Furthermore, Covishield and Covaxin were equally effective in post-vaccination effects and COVID-19 related characteristics.

Many researchers proved the immunogenicity and protective efficacy of an inactivated SARS-CoV-2 vaccine. (29)(30)(31) Bhattacharya et al. evaluated the association between disease severity and vaccination status. The odds of hospitalization were 0.12 (95% CI: 0.03–0.45), and ICU admission/death was 0.07(95% CI: 0.01–0.36) among fully vaccinated individuals. On the contrary, the present study showed no significant association between vaccination status on disease severity. (32) Kamal et al. studied adverse events following immunization (AEFIs) in health care workers with two doses of the Covishield vaccine. Active and passive surveillance was conducted after 48 hours and on days 8,15, 22, and 28 for both doses. The researchers found 1020 non-serious and two serious AEFI (altered sensorium) within 48 hours of the first dose, while 220 non-serious AEFI were reported within 48 hours of the second dose. No AEFIs were

reported after 15 days for both doses. (33) Sachdeva et al. conducted a cross-sectional study on 1,145 individuals to evaluate the adverse effects of vaccination. The authors found that adverse effects were expected in 18-27 years (73%) and were more in females. The most typical symptom was pain at the injection site (85.2%), followed by fever (62.6%). (34) On the contrary, the present study found no association between AEFIs and age, but the severity of AEFIs was more in females. Arora et al. studied adverse effects and breakthrough infections in vaccinated individuals and found that females encountered more adverse effects than males ($p < 0.05$) than the present study. (35) Selvaraj et al. designed a study to determine the rate of post-vaccination infectivity and clinical manifestations using questionnaires prepared on google forms. Researchers found COVID infection in vaccinated and non-vaccinated individuals to be 26% and 44.5%, respectively (odds ratio = 2.27). The majority of the fully vaccinated individuals had a gap of 4–5 weeks for the second dose (37.1%) followed by 5–6 weeks (11.2%). The present study also showed cohort of vaccinated individuals had a lower disease transmission rate. (36) Basvaraj et al. evaluated adverse events following COVID-19 vaccination from a tertiary care hospital in South India within the first 90 days of vaccination. Among 11,656 vaccine doses, 445 AEFIs were reported from 269 subjects (incidence rate = 3.48%) mostly in age group 18-65 years. The most common AEFI was in the system organ class of 'General disorders and administration site conditions, as shown by the present study. (13) Contrary to the present study, Abhilash et al. assessed vaccination (Covishield and Covaxin) effects among symptomatic patients of COVID-19 during the second wave of the pandemic in India. As compared to unvaccinated individuals, at least one dose of vaccine reduced the need for hospitalization (RR: 0.40; 95% CI: 0.35-0.47), oxygen (0.33; 0.27-0.40), NIV (0.23; 0.17-0.32), ICU admission (0.18; 0.12-0.27) and mortality (0.18; 0.11-0.29).(37) However, the present study showed no significant effect of vaccination on hospital admissions and disease severity.

CONCLUSION

The present study concludes the beneficial effect of vaccination in reducing disease transmission, which is the primary objective of any immunization program. However, vaccination did not mitigate disease severity, hospitalization, and chest CT findings. In addition, no effect was shown on subsiding symptoms and their severity in vaccinated and non-vaccinated individuals.

The study also assessed the distribution of vaccination events, such as the number of doses and AEFIs across age groups and gender. Further, it evaluates the effect of the number of doses on disease severity.

Limitations of the study:

The sample represents the outcome of people with a good education level who can fill out google forms. The sample represented specific strata of the population. Studies involving more wider groups are required in the future.

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