Journal of Cardiovascular Disease Research

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 03, 2023

RESEARCH ARTICLE

A prospective and observational study to evaluate short-term adverse event following immunization of COVID-19 vaccination

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ABSTRACT

Background: COVID-19 severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) was declared Pandemic by the World Health Organization on January 30, 2020. Vaccination represents the best possibility to resolve this pandemic. The current global challenge is the immunization against the SARS-CoV-2. However, the adverse events following immunization (AEFI) of the corona vaccine remains unclear. **Aim and Objectives:** This observational study aims to represent an accountable data of the AEFI between Covaxin and Covishield in North Indian population. **Materials and Methods:** The hospital-based prospective and observational study was employed from January 2021 to December 2021 for detecting and monitoring of AEFI in adults. All population vaccinated either covishield or covaxin with both doses were enrolled in the study as targeted population. Post-vaccination vaccinated population were telephonic follow-up with prior consent. **Results:** A total of 1015 vaccinated individuals were included in this study for assessment of AEFI. After statistical analysis of AEFI between both vaccination at 24 h $P = 0.13$, 3–7 days 0.4 and complete AEFI $P = 0.06$ observed. There is no association that was found significant $P < 0.05$ with the incidence of AEFI. **Conclusion:** The short-term outcome has not attribute any serious AEFI. This study demonstrated that both vaccines were well-tolerated and safe in generalized population.

KEY WORDS: COVID-19; Covishield; Covaxin; Immunization; Adverse Events Following Immunization.

INTRODUCTION

COVID-19 also known as novel severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) was declared Pandemic by the World Health Organization (WHO) and a Public Health Emergency of International Concern on January 30, 2020.[1] Considering that the COVID-19 vaccination represents the best possibility to resolve thispandemic. The current global challenge is the immunization against the SARS-CoV-2. Free vaccination against COVID-19 commenced in India on January 16, 2021, and the government is urging all of its citizens to be immunized, in what is expected to be the largest vaccination programin the world. Out of the eight COVID-19 vaccines that are currently under various stages of clinical trials in India, four were developed in the country. India's drug regulator has approved restricted emergency use of Covishield (the name employed in India for the Oxford-AstraZeneca vaccine) and Covaxin, the home-grown vaccine produced by Bharat Biotech.[2] However, diagnosed as CoV-19 Positive and 745 were vaccinated with Covishield and 270 with Covaxin till January 2022. An adverse event following immunization (AEFI) is defined as any untoward occurrence following immunization, and the majority of AEFIs are caused by protective immune responses stimulated by vaccines. However, the AEFI of the corona vaccine remains unclear. This observational study aims to represent an accountable dat of the AEFI between Covaxin and Covishield in North Indian population. This will be helpful for

understanding severity and post-immunization complications as well as advancing knowledge of AEFI. Although safety issue of vaccine is still under review, and the scientific and significance assessment using various AEFI data and various meta-analysis will provide an epidemiological and clinical evidence regarding a possible causal relationship between the vaccine and the adverse event. This will guide us to understand the further strategy for immunization, risk assessment, adverse event monitoring, and effective communication strategy on public health concern. Other considerations may include the perceived intensity of public or professional concern or the feasibility of additional research to help resolve scientific uncertainty regarding causal associations.[3] We focus on describing the reported AEFI in both groups of population under immunization Covishield vs. Covaxin using a comparison data model.

MATERIALS AND METHODS

The hospital-based prospective and observational study was employed from January 2021 to December 2021 for detecting and monitoring of AEFI in adults. All population vaccinated either covishield or covaxin were enrolled in the study as targeted population. The study was conducted at tertiary care hospital, India, after obtaining approval from the Institute Ethics Committee. Population aged <19 years were excluded from the study. Age group 19 years onward, understood the purpose of the study, and ready to provide information regarding their health status of all gender were included in the study. Total 1015 vaccinated population including single dose and both dose (first and second dose) of all gender were included in the study during massive vaccination drive. Post-vaccination vaccinated population were telephonic follow-up with prior consent.

Data Collection

Pertinent medical history of the vaccinated population was collected, including name, age, sex, complete address, phone number, batch number, and date of vaccination, as well as the site of simultaneous vaccination. Vaccinated population information sheets were collected and leaflet containing possible AEFI of concerned vaccine was provided.

Surveillance System

The surveillance system for AEFI was entrenched according to the WHO guidelines.[4] The adverse event may be any unfavorable or unintended sign, abnormal laboratory finding, symptom, or disease. Reported adverse events can either be "True" (resulting from the vaccine or immunization process) or "Coincidental" (not due to the vaccine or immunization process but are temporally associated with immunization). "Serious" adverse events, as per the WHO guidelines, were defined as events involving hospitalization, prolongation of existing hospitalization, life-threatening illness, or permanent disability or death. "Non-serious" adverse events were defined as any event that is not serious and does not pose a potential risk to the health of the recipient.

Surveillance

At the time of immunization, recipients were guided to report any adverse events, to the surveillance team telephonic. The recipients were telephonic followed by further next 14 days after each dose of vaccination. The first follow-up was done after 24 h of immunization. Further, follow-up was done on day 2 (24 h), 5, and 7. For any serious adverse event, it was suggested to approach hospital emergency or nearest medical center.

Statistical Analysis

The outcome measures in this study included the rate of reported AEFI. Chi-square test and *P*-value were used to establish the association of AEFI between covaxin and covishield with the variables on 24 h, 3–7 days, and complete AEFI. Serious AEFI was negligible; hence, no association was determined for the same. All the results are calculated using STATA 12.0 software version.

RESULTS

A total of 1015 vaccinated individuals were included in this study over a period of 12 months including 563 male and 452 female. Combine Covishield (1^{st} and 2^{nd}) AEFI was reported in 745 vaccinated individuals and combine Covaxin (1^{st} and 2^{nd}) AEFI was reported in 270 vaccinated

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 03, 2023

individuals including total male and female of (n = 1015) vaccinated individuals.

Table 1 describing the total no of AEFI reported at day 2on 24 h, between day 3 and day 7, and total percentage of AEFI. Description of various reported combined covishield first and second dose AEFI after vaccination is separated with the number of patients suffered with a particular adverse events- fever (75%), pain at injection site (32%), headache (23%), weakness (3%), body pain (29%), vomiting (4.5%), myalgia (2%), nausea (1%), cough (2.6%), red patches (2%), cramps (2%), chills (25%), diarrhea (3%), dizziness (7%), loss of appetite (6%), hypertension (0.52%), tachycardia (3%), flushing (1.2%), drowsiness (6%), restlessness (0.65%), stomach pain (2%), and fatigue (17%). Similarly, description of various reported combined covaxin first and second dose AEFI after vaccination is separated with the number of patients suffered with a particular adverse events – fever (63%), pain at injection site (30%), headache (22%), weakness (5%), body pain (50%), vomiting (2%), myalgia (2%), nausea (2.5%), cough (8%), red patches (2%), cramps (3.5%), chills (27%), diarrhea (2%), dizziness (5%), loss of appetite (4%), hypertension (2%), tachycardia (1.75%), flushing (1%), drowsiness (7%), restlessness (3%), stomach pain (4%), and fatigue (11%) illustrated in Figure 1. AEFI reported hypertension in both covaxin and covishield group had previous history or person with irregular medication or comorbid illness.

Detection of AEFIs was done by scrutinizing out-patient files, review of doctor's order sheet, progress report, patient interview, and follow-up. These scales categorizethe association between the reaction and the suspected immunization into one category.

An AEFI of covaxin and covishield and its association with serious and non-serious events was illustrated in Table 2. After statistical analysis of AEFI between both vaccination at 24 h, P = 0.13, 3–7 days 0.4, and complete AEFI P = 0.06 observed. There is no association that was found significant P < 0.05 with the incidence of AEFI illustrated in Figure 2.

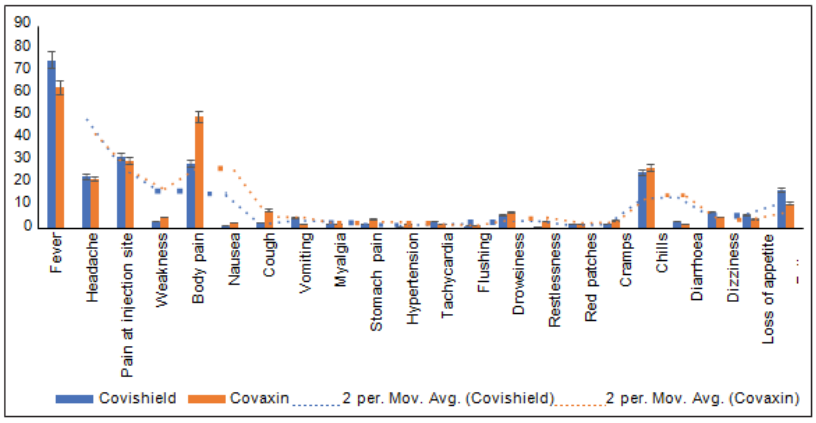

Figure 1: Various adverse events following immunization between both vaccine recipients

Table 1: AEFI of both vaccines reported on 2-time points followed by 7 days

AEFI (n=1015)	Covishield (n=745)			Covaxin (n=245)		
	24 h (Day 2)%	Day (3–7) %	Total	24 h (Day 2) %	Day (3–7) %	Total
Fever	65	10	75	60	3	**63**
Headache	22	1	23	17	5	**22**
Pain at injection site	29.5	2.5	32	25	5	**30**
Weakness	2.5	0.5	3	4	1	**5**
Body pain	25	4	29	47	3	**50**
Nausea	1	0	1	2	0.5	**2.5**
Cough	2	0.6	2.6	7	1	**8**
Vomiting	4.5	0	4.5	2	0	**2**
Myalgia	2	0	2	2	0	**2**

Stomach pain	2	0	2	3	1	**4**
Hypertension	0	0.52	0.52	0.5	1.5	**2**
Tachycardia	2.5	0.5	3	1.7	0	**1.7**
Flushing	1.2	0	1.2	1	0	**1**
Drowsiness	5	1	6	6	1	**7**
Restlessness	0.65	0	0.65	3	0	**3**
Red patches	1	1	2	1	1	**2**
Cramps	1	1	2	2	1.5	**3.5**
Chills	24	1	25	25	2	**27**
Diarrhea	2.4	0.6	3	1	1	**2**
Dizziness	5	2	7	4	1	**5**
Loss of appetite	5	1	6	1	3	**4**
Fatigue	14	3	17	8	3	**11**
AEFI: Adverse events following immunization						

DISCUSSION

The most of the reported AEFI of covaxin and covishield were non-serious. Our study also found that there is noassociation that was established between both of vaccine.We also observed that there is no association established with different time point of AEFI. Overall percentage of adverse events following reporting time line decreased from 24 h to 3–7 days. Fever, body pain, fatigue, myalgia, and pain at injection site were reported more common and scored high percentage in both illustrated Figure 1. In covishield vaccinated recipient hypertension (0.52%) and in covaxin recipient 2% was reported in first 24 h with the previous history and irregular medication. The study reported that covishield has a generally favorable safety profile, with AEFI rates that are significantly lower than those seen with other adenoviral vaccines. Females, those with hypertension, those with a history of allergies, and those with hypothyroidism, may require extra caution when receiving vaccines.[5]

A similar study post-vaccination adverse event targeting medical students reported and localized pain in the injection site during the first dose with 25 (45%) reports and the booster dose with 34 (67%) reports. Then, followed by malaise, the first dose with 20 (36%) reports and the booster dose with 21 (41%) reports. Other symptoms such as headache, fever, shivering, sleepiness, nausea, dysphagia,and cold were also reported.[6]

Table 2: Association of AEFI events between covishield and covaxin at different time interval

AEFI (*n*=1015)	Chi-square	*P*-value
24 h	188.84	0.13
3–7 days	55.97	0.4
Total AEFI	259.42	0.06

AEFI: Adverse events following immunization

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 03, 2023

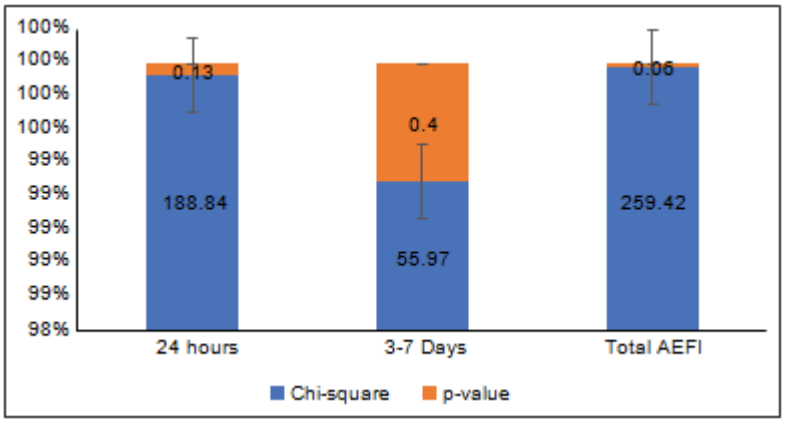

Figure 2: Statistical association between adverse events following immunization of both vaccine recipients

The prevalence of AEFI was 79.8%, with 68.0% of local AEFI and 59.7% of systemic AEFI, respectively. Tenderness at the injection site was the most prevalent symptom. Local and systemic symptoms disappeared in 96.8% and 98.7% of vaccines, respectively, in <1 week. Females were shown to be more likely than males to develop AEFI (AOR = 1.7, 95% CI = 1.2–2.4).[7] Most of the AEFIs found (95.3%) were of low severity, with no serious AEFIs found according to the WHO severity categorization. Based on findings, the ChAdOx1 nCoV-19 coronavirus vaccine (recombinant) is proved to be safe, as the majority of AEFIs seen were of minor severity.[8] A study following covaxin immunization AEFI described, no severe adverse events were reported, and about 1.6% had moderate AEFI. Pain at the injection site (14.6%), fever (9.7%), and myalgia (5.9%) were the common adverse events reportedby the participants. AEFI incidence was higher in the first dose (38.1%) when compared to the second dose (26.4%), and this finding was significant with $P <$ 0.001.[9] Overall, covaxin (BBV152) has a favorable safety profile and is well accepted by adults. AEFI is more common among younger people, women, those with comorbidities, people with a history of allergies, and people who have had an acute infection in the recent 3 months. Because covaxin is an inactivated vaccine that is safer than mRNA vaccinesthat can be considered for widespread use, the vaccinations should be delivered to these persons with an adequate observation period following immunization.[9] The first 48 h were dominated by short-term AEFI. In both doses, the rate of recurrence reduced in consecutive weeks, with no occurrence after 15 days. The symptoms were modest and only lasted a few days. There have been no significant AEFIs linked to vaccinations.[10] Myalgia was the most common side effect, followed by local pain at the injection site after the first dose. The second dose of the vaccination had no effect on 92% of the individuals.[11] There were no serious adverse event noted after first dose as well as seconddose of covishield vaccination.

A study within health-care providers reported following first and second dose of vaccination, (44%) and (28.40%) experienced local as systemic kind of. Most common local and systemic reaction was pain at injection site and fever, respectively.[12] The similar finding with some more details was also found in our study. Although vaccines have adverse effects, none are as serious as the disease itself. Active surveillance for vaccine-related adverse events is a useful tool for discovering and assessing minor side effects.

The precision and accuracy of data are more reliable because all data were collected though experienced health- care professional team. All the vaccinated recipients were followed by medical team precisely. Vaccinated recipients were not closely monitored in hospital setup and small population size could considered as limitation of the study. This is neither guidelines nor possible in this pandemic situation.

CONCLUSION

The short-term outcome has not attribute any serious AEFI. Hence, direct association was not established between both of the vaccine recipient, neither covaxin nor covishield. This study demonstrated that both vaccines were well-tolerated and safe in generalized population.

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