ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 17, Issue 8, 2024

Online - 2455-3891
Print - 0974-2441

Research Article

A SURVEY OF ADVERSE EVENTS FOLLOWING IMMUNIZATION OF COVID-19 IN HEALTH-CARE WORKERS AT TERTIARY CARE HOSPITAL IN SOUTH GUJARAT REGION

CHAUDHARI ARCHANABAHEN G[1], PATEL BRIJALKUMAR S[2]*, TANDEL KIRTIDA R[1]

[1]Department of Pharmacology, GMERS Medical College, Valsad, Gujarat, India. [2]Department of Pharmacology, GMERS Medical College, Navsari, Gujarat, India.

*Corresponding author: Patel Brijalkumar S; Email: dr.brijalpatel@gmail.com

Received: 24 May 2024, Revised and Accepted: 10 July 2024

ABSTRACT

Objectives: The aim of the study was to evaluate adverse events following immunization (AEFI) among the health-care workers (HCWs) who received both doses of the COVID-19 vaccine either COVISHIELD or COVAXIN.

Methods: A questionnaire-based retrospective cross-sectional survey was carried out at the tertiary care teaching hospital of South Gujarat after getting approval from the Institutional Human Ethics Committee. A total of 542 HCWs who received two doses of vaccine were enrolled. Vaccine-related adverse effects and association of AEFI with demographic variables were determined.

Results: Fever, pain at the injection site, and body aches were the common adverse events reported by the participants following both doses of COVISHIELD and COVAXIN. Most of the AEFIs were reported within 6–12 h of vaccination after the 1st and 2nd doses. We found no association of AEFI with comorbidity and previous COVID-19 infection. A significant association of AEFI was found with gender, age groups, and occupation ($p<0.05$).

Conclusion: Most of the adverse events were non-serious and reported within 6–12 h of vaccination. Only few adverse events were reported after 24 h of vaccination and no serious AEFI was reported. Younger age groups, females, and HCWs are at higher risk of AEFI. Precaution needs to be taken while vaccinating these individuals.

Keywords: Adverse events following immunization, COVID-19, COVISHIELD, COVAXIN, Health-care workers.

 DOI: http://dx.doi.org/10.22159/ajpcr.2024v17i8.51554. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

The coronavirus disease (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has diseased millions of people with more than 6.9 million deaths over a period of the year to date [1]. As there is no specific therapy for COVID-19, vaccinations could be crucial in boosting community immunity, preventing serious illness, and reducing the current health crisis.

In India, the Central Drugs Standard Control Organisation has approved two vaccines for restricted use in an emergency situation, COVISHIELD (AstraZeneca's vaccine manufactured by Serum Institute of India) and COVAXIN (manufactured by Bharat Biotech Limited). The 1st phase of COVID-19 vaccination drive was started in India from January 16, 2021, initially targeting frontline workers, followed by the 2nd phase for people more than 60 years and for those older than 45 years with any of the 20 comorbidities identified by the Ministry of Health and Family Welfare and later extended to people even without comorbidities [2]. The COVISHIELD vaccine is a recombinant, replication-deficient chimpanzee adenovirus vector vaccine encoding the SARS-CoV-2 spike glycoprotein produced in genetically modified human embryonic kidney cells while COVAXIN is a whole virion inactivated coronavirus vaccine produced using a vero cell-based platform [3,4].

Adverse event following immunization (AEFI) is any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine [5]. The safety of recently marketed vaccines, for which the safety pattern could not be precisely defined in the registration studies, must be studied by post-marketing surveillance. Vaccine hesitancy was listed by the World Health Organization as one of the top ten threats to global health in 2019 [6]. The adverse effects of vaccines should be communicated transparently to raise public confidence in the vaccination programs. Hence, a precise assessment of AEFIs and continuous safety surveillance are important to alleviate public concerns surrounding vaccination. Very few studies have been conducted on AEFI following COVID-19 vaccination in India, so we conducted this survey of AEFI of COVID-19 vaccination in health-care workers (HCWs) at our tertiary care teaching hospital.

METHODS

Study design and setting

The study was carried out at our tertiary care teaching hospital in South Gujarat after getting approval from the Institutional Human Ethics Committee (MCV/IHEC/13/2021; June 2021). It was a questionnaire-based retrospective cross-sectional study involving HCWs.

Selection criteria

The study participants were all HCWs who received both doses of the COVID-19 vaccine either COVISHIELD or COVAXIN. As per the government policy, adult HCWs of any age were eligible for the COVID-19 vaccination.

Sample size and data collection

The data of eligible study participants were collected either in a printed questionnaire form or an online Google Form. The questionnaire was pre-tested and validated before starting the survey. It comprised of 24 questions and was divided into four sections. 1st section comprised participants' informed consent. Sociodemographic details, history of COVID-19 infection, comorbid conditions, etc. were included in the 2nd section. The 3rd and 4th sections comprised of questions related to AEFI after the 1st and 2nd doses of the COVID-19 vaccine, respectively.

A total of 545 responses were recorded. Among 545 responses, two participants did not give consent and not filled up the questionnaire while one filled form has incomplete details so we excluded 3 participants and 542 responses taken into consideration.

Statistical considerations

The data were analyzed using MS Office Excel 2010. The continuous variables were analyzed using mean and standard deviation, while the categorical variables were using frequency and percentages. The Chi-square test was used to determine the association of AEFI with the demographic variables. The results were considered to have statistical significance when $p<0.05$ and highly significant when $p<0.001$.

RESULTS AND DISCUSSION

A total of 542 HCWs gave consent for participation in the study and their sociodemographic characteristics are described in Table 1. The mean age of the study participants was 26.91±8.48 years and most of the participants were 18–30 years of age (68.82%). Female participants (56.46%) were more than that of the male participants (43.54%). The majority of our study participants (96.68%) had received the COVISHIELD vaccine. The participants were also categorized based on the occupational categories and the majority of them were undergraduate M.B.B.S students, doctors, and housekeeping staff. Only 5.9% of participants reported to have any of the co-morbidities, out of which 46.8% had either hypertension or diabetes. While 8.49% of participants reported COVID-19 infection after immunization and the majority (69.56%) of individuals acquired COVID-19 infection after receiving the 2nd dose of the COVID-19 vaccine, only 7.01% of participants had a history of COVID-19 infection in the past.

Fig. 1 shows the percentage of people who reported AEFI after receiving both doses of the COVID-19 vaccine. Participants who received the COVISHIELD vaccine reported AEFI in 88.93% of cases and in 43.7% of cases following the 1st and 2nd doses, respectively. Similarly, 83.33% of people reported AEFI following the 1st dose of COVAXIN and 72.22% after the 2nd dose.

Details of all the AEFIs for various doses of vaccination are presented in Table 2. A total of 1650 AEFIs were reported following the 1st dose of COVISHIELD and common AEFI included fever (64.12%), pain at the injection site (58.39), body ache (42.17%), and weakness (38.17%). After receiving the 2nd dose of COVISHIELD, only 27.59% of participants experienced pain at the injection site and 12.59% reported fever.

Participants who received COVAXIN (n=18) showed 34 AEFIs. The most frequent AEFI after the 1st dose was fever (55.55%) and pain at the injection site (38.89%), but only 33.33% did so after the 2nd dose of COVAXIN.

As depicted in Fig. 2, the majority of AEFIs were noted within 6–12 h of vaccination after the 1st and 2nd doses. The rate of AEFIs showed a declining trend thereafter and only a few AEFIs were noted beyond 24 h of vaccination.

The association of AEFI with demographic variables is presented in Table 3. We found that significant association of AEFI with sex and AEFIs was significantly more prevalent in females after both doses of vaccine. We found highly significant association of AEFI with age after 1st dose of vaccination and the incidence was higher in the age group of 18–30 years but it was not significant after 2nd dose of vaccine. The AEFIs also found to have a significant association with the occupation and HCWs reported to have more AEFIs. The incidence of AEFI did not have any statistically significant association with the presence of any comorbidity or history of COVID-19 infection in the past.

This study mainly focused on outlining the various AEFI following COVID-19 vaccination at our institute. The study included 542 participants who had received both doses of the vaccine. Among the participants, 43.54% were males and 56.46% were females. The mean age of the participants was 26.91±8.48 and the majority were between 18 and 30 years. The results coincide with previous studies where the majority of participants were

Table 1: Sociodemographic characteristics of study participants

Variables	Categories	N Total=542 (n)	%
Age	Mean±SD	26.91±8.48	
	18–30	373	68.82
	31–40	128	23.62
	41–50	33	6.08
	51–60	6	1.11
	>60	2	0.36
Sex	Male	236	43.54
	Female	306	56.46
Vaccine	COVISHIELD	524	96.68
	COVAXIN	18	3.32
Occupation	Doctor	77	14.21
	Students	233	42.98
	Nurse	57	10.52
	Clerk	31	5.72
	Laboratory technician	25	4.61
	Peon/Servants	98	18.08
	Others	14	2.58
Previous COVID-19 infection	Yes	38	7.01
	No	504	92.99
Post-vaccination COVID-19 infection	Yes	46	8.49
	No	496	91.51
	After 1st dose	14	30.44
	After 2nd dose	32	69.56
Comorbidities	Present	32	5.90
	Absent	510	94.09

SD: Standard deviation

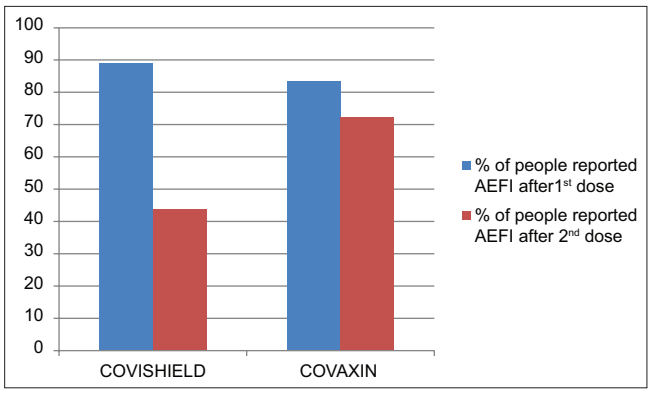

Fig. 1: Self-reported AEFI after 1st and 2nd doses of COVISHIELD and COVAXIN. AEFI: Adverse event following immunization

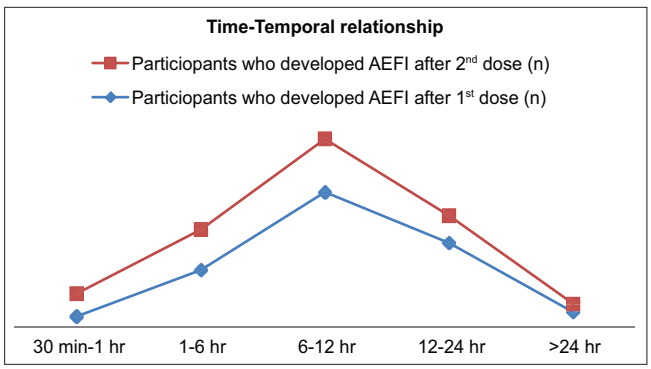

Fig. 2: Time-temporal relationship of vaccine and AEFI. AEFI: Adverse event following immunization

Table 2: AEFI after 1st and 2nd dose of COVISHIELD and COVAXIN

S. No.	AEFI	COVISHIELD (n=524)				COVAXIN (n=18)			
		1st dose		2nd dose		1st dose		2nd dose	
		n	%	n	%	n	%	n	%
1.	Fever	336	64.12	66	12.59	10	55.55	06	33.33
2.	Chills	195	37.21	26	4.96	02	11.11	0	0
3.	Pain at the injection site	306	58.39	143	27.29	07	38.89	06	33.33
4.	Swelling at injection site	55	10.49	17	3.24	01	5.56	01	5.56
5.	Headache	169	32.25	49	9.35	05	27.78	02	11.11
6.	Bodyache	221	42.17	43	8.21	04	22.23	03	16.67
7.	Joint pain	71	13.54	12	2.29	0	0	0	0
8.	Weakness	200	38.17	41	7.82	02	11.11	02	11.11
9.	Drowsiness	54	10.30	09	1.72	01	5.56	0	0
10.	Abdominal pain	05	0.95	0	0	0	0	0	0
11.	Diarrhea	06	1.14	0	0	0	0	0	0
12	Nausea	13	2.48	01	0.19	01	5.56	0	0
13.	Vomiting	10	1.91	01	0.19	01	5.56	0	0
14.	Allergic reaction	01	0.19	0	0	0	0	0	0
15	Others	08	1.53	03	0.57	0	0	0	0

AEFI: Adverse event following immunization

Table 3: Factors associated with AEFI among study participants (n=542)

Variables	Categories	AEFI-first dose		p-value	AEFI-second dose		p-value
		Yes (n)	No (n)		Yes (n)	No (n)	
Sex	Female	288	18	<0.00001	154	152	0.0017
	Male	193	43		87	149	
Age	18–30	337	36	0.0009	171	202	0.2227
	31–40	114	14		50	78	
	41–50	26	7		18	15	
	>50	4	4		2	6	
Occupation	Doctor	65	12	0.012	30	47	0.006
	Nurse	52	5		22	35	
	Students	212	21		104	129	
	Admin Staff	54	2		38	18	
	Housekeeping	79	19		41	57	
Comorbidity	Yes	26	6	0.1667	11	21	0.2363
	No	455	55		230	280	
Previous COVID-19 infection	Yes	32	6	0.8414	16	22	0.7614
	No	449	55		225	249	

*p<0.05 indicates significant association between variables and *P*<0.001 denotes highly significant association. AEFI: Adverse event following immunization

20–30 years old, and a smaller number (8.4%) were above 50 years [7]. About 5.9% of the study participants had comorbidities while in previous studies on AEFI in India, 34.1% of the participants were found to have comorbidities. Furthermore, comorbidities such as hypertension and diabetes topped the list similar to previous studies [8].

In the present study, higher AEFIs were reported among COVISHIELD beneficiaries who took the 1st dose (88.93%) when compared to the 2nd dose (43.7%) while 83.33% and 72.22% reported AEFI following the 1st and 2nd dose, respectively, among COVAXIN beneficiaries. However, based on the findings in the present study, it cannot be concluded that more AEFI were observed among COVAXIN beneficiaries following the 2nd dose as in our study, participants who received COVAXIN are very less (3.32% vs. 96.68%).

In our study, the most common AEFI reported in the local reaction was pain at the injection site, while the most common systemic reaction observed was fever followed by body aches following both doses of COVISHIELD and COVAXIN. These results are in accordance with a study done in Gujarat where the most common local reaction reported was pain at the injection site following both doses of vaccination, whereas the most common systemic reaction was fever and headache [9]. As per the interim analysis data, the most frequently reported adverse reactions to COVISHIELD were injection site tenderness (>60%); injection site pain, headache, fatigue (>50%); myalgia, malaise (>40%); and pyrexia, chills (>30%) while pain at the injection site, followed by headache, fatigue, and fever were the common adverse events reported to COVAXIN [3,4]. The most common medication used to resolve the AEFI was paracetamol (500/650 mg) after both doses of vaccine.

We observed that the majority of AEFIs reported were non-serious in nature; no serious AEFI was reported among vaccine recipients. This supports the findings of phase 1 and phase 2/3 trials of ChAdOx1 nCoV-19 vaccines wherein the majority of recipients reported with non-serious AEFI [10,11]. These findings demonstrate the higher safety profile of COVID-19 vaccines. In the present study, more AEFIs were noted after the 1st dose of COVISHIELD than the 2nd dose. It may be due to the prophylactic use of paracetamol after having a vaccine dose. Similar observations of more number of AEFI after the 1st dose were reported from the interim analysis of clinical trials for COVISHIELD [3,10].

Most of the AEFIs were reported within 6–12 h of vaccination after the 1st and 2nd doses. The rate of AEFIs showed a declining trend thereafter and only a few AEFIs were reported after 24 h of vaccination. A similar declining trend was observed in other studies as well [12]. Chaudhary *et al*. reported that most of the adverse events were reported after 30 min but within the first 24 h of vaccination [13].

We have discovered a significant association between gender and AEFI, with females reporting higher AEFI rates after both dosages than

males. Similar conclusions were drawn from a study carried out in North India [14]. In contrast to this, no gender difference was reported in a study done by Kamal *et al*. from South India [15]. We found that more AEFI were reported among younger age groups. Our findings are statistically significant after 1st dose while not after the 2nd dose, which might be due to prophylactic measures taken by individuals. Kaur *et al*. also reported higher AEFI among younger participants [16]. In our study, a significant association was also found between occupation and AEFI with a higher incidence of AEFI in HCW whereas most of the studies found no significant association between occupation and AEFI [14]. Differences in the incidence of AEFI with age groups, gender, and occupation in our study might be due to the type of study population (HCW). We found no significant association between comorbidity and AEFI while comorbidity was significantly associated with AEFI in a study done by Khalil *et al*. [17]. We did not find any correlation between previous COVID-19 infection and AEFI while in previous studies; a higher incidence of reactogenicity was reported in participants with previous SARS-CoV-2 infection [18].

Our study has few limitations. First of all, it is an observational cross-sectional study and hence, cause and effect relationship cannot be established. This study is subject to some extent to recall bias in self-reported AEFIs. Since it is a single-centric study, multi-centric studies are required to explore the effects of different socio-demographic factors on the AEFI of COVID-19 vaccines.

CONCLUSION

The study showed that COVID-19 vaccines carry a good safety profile and was well tolerated by the study population. All the AEFI were non-serious in nature and the majority of them reported within 6–12 h of vaccination. Younger age groups, females, and HCWs are at higher risk of AEFI. The vaccines should be administered to these individuals with adequate observation. Further long-term follow-up studies are required to understand the safety of these vaccines in multiple age groups and with comorbidities for the delayed adverse effect.

ACKNOWLEDGMENTS

The authors are thankful to the Head of the Institute and the Ethics Committee for allowing us to carry out this study at our institute. We are also grateful to all the health-care professionals for providing their support to accomplish this study.

AUTHORS' CONTRIBUTIONS

Dr. Archana Chaudhari, Dr. Brijal Patel: Conceptualization. Dr. Kirtida Tandel, Dr. Brijal Patel, Dr. Chaudhari: Methodology. Dr. Archana Chaudhari, Dr. Brijal Patel, Dr. Kirtidatandel: Data acquisition and data analysis. Dr. Brijal Patel, Dr. Archana Chaudhari: Manuscript preparation and editing. Dr. Kirtida Tandel, Dr. Archana Chaudhari: Final review.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

AUTHORS' FUNDING

None.

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