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Adverse Reaction Monitoring following Coronavirus Disease (COVID-19) Immunization among Health Care Workers of a Tertiary Care Hospital in India

Suraj B. Panchal[1], Latha Shivanand.[2], Rakesh Navale[3], Somashekara S. Chikkannasetty.[1*], Amrutha D. Tori[1], Rameez Ahmed[1], Satish Ghatage[4]

[1]Department of Pharmacology, ESIC Medical and Hospital, India
[2]Department of Pharmacology, Shri BM Medical College, India
[3]Department of Paediatrics, ESIC Medical and Hospital, India
[4]Department of Community Medicine, Al-Ameen Medical and Hospital, India

Abstract

With the unprecedented and devastating impact of Corona Virus Disease (COVID-19) pandemic on public health, high coverage of safe and efficacious vaccines against COVID-19 disease could contribute to the control of the COVID-19 pandemic. However, in India vaccination strategy against COVID-19 was implemented to overcome this catastrophe as early as January 2021. Considering the novelty in adverse events and the dearth of research studies about the adverse event following immunization (AEFI) associated with COVID-19 vaccine, the present study aimed to determine the incidence and types of adverse events following COVID-19 vaccination among healthcare workers (HCWs). It was a prospective, observational study conducted among the HCWs of a tertiary care hospital who received the first dose of the ChAdOx1 nCoV-19 vaccine between January-March 2021. Systemic and local adverse events experienced up to the first 24 hours of vaccination were surveyed using Google Forms. Of the total 1045 HCWs who were vaccinated, 666 HCWs responded completely to the Google form. The majority (79.3%) of the participants were 18-30 years old. The most commonly reported AEFI were pain at the injection site (68.8%), fatigue (40.1%), myalgia (35.4), and malaise (35.0%). Among the systemic adverse events, the incidence of fatigue, and local adverse events, the pain at the injection site was considerably greater in the 18-30 years age group than in the other HCWs group ($P < 0.001$). The severity of most AEFI was mild-to-moderate in nature. Hence, this study concludes that AEFI associated with the ChAdOx1 nCoV-19 vaccine after a single dose was safe and tolerable. The maximum number of participants accepted AEFI because minor reactions would be common and treatable.

Keywords: Adverse Events Following Immunization, ChAdOx1 nCoV-19 vaccine, COVID-19, Health Care Workers.

Corresponding Author: Somashekara S.C., Department of Pharmacology, ESIC Medical and Hospital, India.
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Introduction

A novel coronavirus disease (COVID-19) was first reported in Wuhan, the capital city of Hubei Province of China, in November 2019.[1] In India first case of COVID-19 infection was reported in the Kerala district on January 27, 2020.[2] With the alarming level of spread, World Health Organization (WHO) declared COVID-19 as a pandemic on March 11, 2020.[3] Since then SARS-CoV-2 pandemic has claimed over 3,811,561 lives and affected over 175,987,176 persons worldwide by 16th June 2021.[4] However, in India, the situation is still grim, with more than 865,432 active cases and 379,573 deaths related to the same virus.[5] As the COVID-19 pandemic shows no signs of aborting globally, efforts to prevent infection by developing vaccines have become an urgent international priority. Having widespread community immunity across the age span and around the globe through a vaccination strategy may be the best way to bring this pandemic under control.

COVID-19 vaccination in India was initiated in early January 2021. However, healthcare workers (HCWs), frontline workers (FLWs), and the population above 50 years of age[6] were prioritized and were administered with Covaxin (Bharat Biotech, ICMR India) or ChAdOx1 nCoV-19 Corona Virus Vaccine (Serum Institute of India). An acceptable safety profile for Covaxin has been reported by randomized controlled trials[7] and from the assessment report of the European Medicines Agency for ChAdOx1-S [recombinant] as a favorable safety profile.[8]

Considering the prevailing conditions in India with a high number of active cases, COVID-19 vaccination inoculation rate on larger scale could possibly contain the disease spread by enhancing immunity. However, several adverse events associated with COVID-19 vaccines have been reported, including thrombosis associated with thrombocytopenia[9] and transverse myelitis.[10]

Vaccines are unique as they are administered to large cohorts of mostly healthy individuals. Therefore, it is unacceptable for vaccines to induce a significant burden of side effects, even where the illness itself can produce severe or fatal side effects.[11]

Moreover, there is a dearth in research studies about AEFI associated with the COVID-19 vaccination in the Indian population at large, the present study aimed to determine the incidence and types of adverse events following COVID-19 vaccination.

Methods

Study Design and Participants

A prospective, single-centred observational study of three months duration (January-March 2021) was conducted among HCWs of tertiary care hospital at Karnataka, India. After the ethical approval (No: ESIC/GLB/IEC/21/2021) from the Institutional Ethics Committee (IEC) was obtained, a convenience sample involving HCWs[6] [Doctors, Dentist, Nursing officers and supervisors, Lab Technicians, OT technicians, Pharmacist, Radiographer, Nursing orderlies, Ward boys, Drivers, Security staff, Sanitation workers, Students (Medical, Dental, Nursing, Paramedical)] aged ≥ 18 years up to 62 years of either sex, willing to give consent, and to share the information following the first dose of ChAdOx1 nCoV-19 Corona Virus Vaccine (Covishield) vaccination were included. Among the vaccinated HCWs, those who did not give consent, had incomplete responses, pregnant and lactating women, severely allergic to any vaccine ingredient(s), and those not willing to share information were excluded from the current research.

Vaccination Protocol

Details of the study participants with their contact information were obtained from the Nodal officer of the Hospital. After permission from District Health Officer, the study participants were counseled regarding the importance of reporting AEFI to AEFI team. A document was provided to the study participants, containing the information regarding vaccine reactions and contact details of investigators and IEC member Secretary. Study participants were educated to note such events and provide the same information to the investigators. The vaccination session site had designated separate entry and exit, with three separate rooms (waiting room, vaccination room, and observation room) to avoid criss-cross movement of participants at the session site. The preliminary details of HCWs were entered in Co-WIN software as per the government recommendations and registered for vaccination. Skilled nurses administered the vaccine in the left deltoid region, and adverse events were monitored for 30 minutes.

Adverse Events Reporting System

All study participants were interviewed at the vaccination site and then were asked to fill out the Google form to report online to capture demographic data, clinical variables, and system organ class-wise adverse events. The information was collected by adding the participants on the social platform (Whatsapp, Email) by creating groups daily with a consent form attached to them. However, the Google form link was sent after 24 hours of vaccination to collect adverse events experienced up to 24 hours after receiving the vaccination. Those study participants unable to fill out the Google form were interviewed at the vaccination site after 24 hours. However, study participants were told to contact the research team for any difficulties understanding the research questions or the nodal officer of the hospital. The telephonic interview was conducted for those who couldn't visit the vaccination site and could not fill out the Google form. Information regarding the adverse events among the study participants was shared with the Nodal Officer of the hospital and IEC on time, depending on the severity of the event. AEFI management was carried out by a team of physicians and anesthetists.

The results were analysed by using statistical software SPSS (version 17, IBM Corporation, New York, United States). Descriptive statistics was used for the categorical variables and were reported as frequencies and percentages. Continuous variables were expressed as mean with standard deviation. Chi square test was performed for qualitative variables. A p-value of ≤ 0.05 was considered statistically significant.

Results and Discussion

Of the total 1045 HCWs who were vaccinated, 666 HCWs attributing to 63.7%, responded. The mean age of the participants was 23.5 ± 7.3 years (range, 18-62 years), among which 52.1% were male (n = 347). The majority of HCWs responded were medical students (54.1%, n = 360) followed by doctors (11.0%, n = 73) and nursing officers (9.8%, n = 65). (Table 1). Thirty-six participants (5.4%) had a history of allergy, and 46 (6.9%) reported a family history of allergy. The most common (0.019%, n = 13) comorbidity associated was respiratory disease. All of these results are presented in Table 1.

The incidence and types of adverse events were analysed, which presented in Table 2. Fatigue (40.1%, n = 267) myalagia (35.4%, n = 236) and malaise (35.0%, n = 233) were most commonly reported systemic adverse events. A low percentage of HCWs reported nausea (4.4%) and abdominal pain (2.7%).

However, pain (68.8%; n = 458) at the injection site was the most commonly reported local adverse event. All AEFI that were reported were minor in nature. Four participants complained of dyspnoea and dizziness within 30 minutes after vaccination, and were immediately attended by AEFI team. Subsequently, the participants improved and did not require hospitalisation and, therefore, classified as immunisation anxiety related reactions. However, for symptomatic relief of adverse events; nearing 18.2% of participants took NSAIDs.

Summary of incidence of adverse events categorised by the participants' age group are presented in Table 3. It were observed that both systemic and local adverse events were reported relatively more frequent among participants below the age of 30 years old than among other HCWs age group. Among the systemic adverse events occurred, the incidence of fatigue, and among the local adverse events, the incidence of pain at the injection site was considerably higher in the 18-30 years age group than in the other HCWs age group (specifically among 18-30 years age group. Incidence of fatigue in the systemic adverse events and the incidence of pain at the injection site in the local adverse events was significantly higher than the other HCWs age group) ($p< 0.001$).

The present study considered January-March 2021 as the study duration, as the rollout of vaccination was started on a larger scale during

Table 1. Demographic Characteristics and Clinical Variables of Participants (n = 666)

		Frequency	Percentage
Gender	Male	347	52.1
	Female	319	47.9
Occupation	Doctor	73	11.0
	Dentist	36	5.4
	Intern	25	3.8
	Nursing officer	65	9.8
	Support staff	43	6.5
	Medical student	360	54.1
	Dental student	56	8.4
	Nursing student	8	1.2
History of allergy (to vaccine, drugs or food)	Present	36	5.4
	Absent	599	89.9
	Unknown	31	4.7
Family history of allergy	Present	46	6.9
	Absent	574	86.2
	Unknown	46	6.9
Comorbidities	Cardiovascular disease	8	0.012
	Respiratory disease	13	0.019
	Diabetes	4	0.006

Table 2. Incidence and Types of Adverse Events

Adverse Events		Total (n = 666)	
		Frequency	Percentage
Systemic AEFI*	Fatigue	267	40.1
	Myalgia	236	35.4
	Malaise	233	35.0
	Headache	228	34.2
	Fever	210	31.5
	Chills	135	20.3
	Dizziness	87	13.1
	Flu like symptoms	58	8.7
	Loss of appetite	47	7.0
	Nausea	29	4.4
Local AEFI*	Pain	458	68.8
	Warmth	40	6.0
	Swelling	37	5.6
	Tenderness	28	4.2
	Induration	27	4.1
	Erythema	19	2.9

***Multiple choice options: did not add up to 100 percentage; AEFI denotes: Adverse Event Following Immunization**

early January 2021 and was introduced phase-wise, keeping in mind the risk of exposure of HCWs and other general population to novel Coronavirus infection. In the present study, the incidence and types of adverse events among HCWs following the first dose of ChAdOx1 nCoV-19 coronavirus vaccine was found to be relatively safe and well tolerated across the age groups, more so in the 31-60 years age group.

The most frequently reported adverse events were fatigue, myalgia, malaise, and pain at the injection site. Most of the adverse events reported were mild to moderate in severity, and none reported any unexpected serious adverse reactions. Most of the adverse events were managed symptomatically by NSAIDs.

In a randomised controlled phase 2/3 trials conducted in United Kingdom (UK) on the ChAdOx1 nCoV-19 vaccine administered in young adults, the most commonly reported adverse reactions were tenderness at the injection site (76%), pain at the injection site (61%), fatigue (76%) and headache (65%). Considering the severity of adverse reactions, most were mild to moderate in nature.[12] However, a higher incidence of pain at the injection site (68.8%) was observed in our study, with a relatively lower incidence of tenderness (4.2%), headache (34.2%), and fatigue (40.1%) which could be attributed to the difference in the ethnicity, because the nature of reporting which was subjective and considering only those events experienced within first 24 hours of vaccination.

None of the participants reported severe local symptoms after receiving ChAdOx1 nCoV-19 vaccine[12] and were in line with our study. Five percent of participants showed a severe systemic reaction after receiving prime vaccination in a clinical trial.[12] However, none of the participants showed a severe systemic reaction in our study, which could be due to follow-up of data restricting up to 24 hours after vaccination.

Systemic symptoms reported across the age groups (Table 3) in our study showed relatively decreasing reactogenicity with increasing age; although the numbers of participants in the age groups (31-45 and 46-60 years) were lesser, a similar trend was observed after the first dose in randomized controlled phase 2/3 trials conducted in UK[12] and in a prospective study conducted by Menni *et al.*[13] in UK during March 2021.

Table 3. Incidence of Adverse Events by Age Groups

Adverse Events		18-30 years (n = 528)	31-45 years (n = 121)	46-60 years (n = 17)	Total (n = 666)	p-value
Systemic AEFI*	Fatigue	232 (43.9%)	33 (27.3%)	2 (11.8%)	267 (40.1%)	0.001**
	Malaise	187 (35.4%)	42 (34.7%)	4 (23.5%)	233 (35.0%)	0.578
	Headache	185 (35.0%)	39 (32.2%)	4 (23.5%)	228 (34.2%)	0.540
	Fever	178 (33.7%)	27 (22.3%)	5 (29.4%)	210 (31.5%)	0.051
	Chills	119 (22.5%)	13 (10.7%)	3 (17.6%)	135 (20.3%)	0.014
	Dizziness	70 (13.3%)	16 (13.2%)	1 (5.9%)	87 (13.1%)	0.673
	Flu-Like Symptoms	51 (9.7%)	6 (5.0%)	1 (5.9%)	58 (8.7%)	0.233
	Nausea	23 (4.4%)	5 (4.1%)	1 (5.9%)	29 (4.4%)	0.947
	Abdominal Pain	15 (2.8%)	3 (2.5%)	0 (0.0%)	18 (2.7%)	0.766
	Vomiting	5 (0.9%)	1 (0.8%)	0 (0.0%)	6 (0.9%)	0.916
Local AEFI*	Pain	387 (73.3%)	63 (52.1%)	8 (47.1%)	458 (68.8%)	0.001**
	Warmth	34 (6.4%)	6 (5.0%)	0 (0.0%)	40 (6.0%)	0.473
	Swelling	33 (6.2%)	4 (3.3%)	0 (0.0%)	37 (5.6%)	0.265
	Tenderness	20 (3.8%)	8 (6.6%)	0 (0.0%)	28 (4.2%)	0.234
	Induration	24 (4.5%)	3 (2.5%)	0 (0.0%)	27 (4.1%)	0.403
	Erythema	16 (3.0%)	3 (2.5%)	0 (0.0%)	19 (2.9%)	0.733

***Multiple choice options: did not add up to 100 percentage;**
****denotes: significant difference between the groups**

On March 2021, none of the serious adverse events reported to the National AEFI Committee of India was due to the COVID-19 vaccine.[14] However, the current study discovered that 4 HCWs complained of dyspnoea and dizziness within 30 minutes after vaccination, but none required hospitalisation, which corroborated with the retrospective study conducted by Jeon *et al.*[15] in 1,503 HCWs in the Republic of Korea in March 2021.

The majority of the adverse events (both systemic and local) in the present study were mild to moderate in severity which correlated

with a preliminary report of Folegatti *et al.*[16] and from studies of ChAdOx1-vectored vaccines.[17-19] Similar data from other geographical locations and ethnicity would not only help address the initial concerns about adverse events following COVID-19 vaccination and vaccine hesitancy, which plays an important role in accepting mass immunization in adults in this unprecedented COVID-19 situation worldwide.

Strengths and Limitations of Study

The study's strength is that it included a larger number of HCWs of the tertiary care centre and encouraged them to report those who could not respond to the electronic form at the vaccination site. Using the Google form platform saved time and paper, avoided exchanging materials among HCWs, and allowed them to follow COVID-19 protocol. To manage the adverse events, AEFI team was constituted to monitor and treat accordingly effectively. Therefore it is pivotal to test the effectiveness of vaccines and equally important to have a holistic approach and to frame a protocol for systemic surveillance of safety concerns. By setting up a web-based Institutional surveillance program, an attempt was made to capture the self-reporting of adverse events while keeping in view the lockdown situation and adequately managing adverse events. Such surveillance programs alleviate the concerns about adverse events and associated vaccine hesitancy and contribute to improving the inoculation rate. Although the questions designed were focused on the study's primary and secondary objectives, the applicability to each participant could not be verified considering the nature of reporting as self-reporting; hence, bias cannot be ruled out. A further limitation is possible that the results might not be generalisable as it is a single centre study and comprised of participants below 60 years of age with the mostly younger population. Although very few were reported to have comorbidities, not considering older age groups and adequate comorbidities, the results might not be illustrative of the general older population. Additionally, the findings of the adverse event are restricted to the first 24 hours and were not followed up to know further safety and tolerability. In conclusion, ChAdOx1 nCov-19 was safe and tolerable; most adverse events were managed with NSAIDs (paracetamol) without hospitalisation.

Conclusion

AEFI associated with the ChAdOx1 nCoV-19 vaccine after a single dose was safe and tolerable. Maximum participants experienced AEFI, which was accepted by them because minor reactions would be expected and treatable.

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Conflict of Interest

None declared.

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