ORIGINAL ARTICLE

A cross-sectional study on adverse reactions following COVID-19 vaccination from a tertiary care hospital in Uttar Pradesh

M. Amruth[1], Masuram Bharath[2], Ashish Kumar Sharma[1], Rakesh Arya[1], Arwind Kishor Shukla[1], Jawaid Hasan[1], Atul Saxena[1]

[1]Department of Community Medicine, Varun Arjun Medical College and Rohilkhand Hospital, Shahjahanpur, Uttar Pradesh, India, [2]Department of Pharmacology, Varun Arjun Medical College and Rohilkhand Hospital, Shahjahanpur, Uttar Pradesh, India

Corresponding Author:
Dr. M. Amruth,
Department of Community Medicine, Varun Arjun Medical College and Rohilkhand Hospital, Banthra, NH-24, Shahjahanpur, Uttar Pradesh, India.
Phone: +91-9964819941.
E-mail: amruth.sagara@gmail.com

Received: 02-02-2022
Accepted: 24-02-2022

How to cite this article: Amruth M, Bharath M, Sharma AK, Arya R, Shukla AK, Hasan J, Saxena A. A cross-sectional study on adverse reactions following COVID-19 vaccination from a tertiary care hospital in Uttar Pradesh. Int J Adv Integ Med Sci 2022;7(1):11-17.

Source of Support: Nil,
Conflicts of Interest: None declared.

Background: COVID-19 vaccination program was initiated in India on January 16, 2021. Covid-19 vaccines, namely, Covishield and Covaxin got emergency approval from Drugs Controller General of India and Central Drugs Standard Control Organization for restricted usage health care workers (HCWs) and frontline workers (FLWs). In this context, the present study was conducted to find out the type of adverse reactions following first dose of Covishield vaccination reported by HCWs and its association with sociodemographic factors following vaccination in a private medical college and hospital in Uttar Pradesh. **Methods:** A cross-sectional survey was undertaken during January to March 2021 and data were collected about adverse events reported voluntarily by 580 HCWs who received first dose of Covishield vaccination from the COWIN registered list of HCWs, adverse events following immunization (AEFI) register, and Google form questionnaire in Varun Arjun Medical College and Rohilkhand Hospital, Banthra in Shahjahanpur district in Uttar Pradesh. Statistical analysis was done using Epi Info software. Fisher's exact test and Pearson's Chi-square test were used to find the association between sociodemographic factors and adverse reactions following Covishield vaccination. **Results:** Five hundred and eighty HCWs received the first dose of Covishield vaccine and only 214 (36.9%) reported AEFI. The most commonly reported AEFIs were fever (85.5%), chills (68.7%), local injection site reactions (59.3%), bodyache (59.3%), headache (48.6%), and fatigue (46.7%). Most of these AEFIs were of mild-to-moderate severity and there was significant association of AEFI with male HCWs, students and younger age group. There were no serious events and anaphylaxis requiring hospitalization, and most AEFIs improved within a few days. **Interpretation:** In conclusion AEFIs such as fever, chills, local injection site reactions, bodyache, headache, and fatigue were frequently reported more commonly among male HCWs of younger age group and especially students after the Covishield vaccination. There were no serious events that required hospitalization. Sufficient explanation and preparation for expected adverse events are required to promote widespread vaccination.

KEY WORDS: Adverse reactions, COVID-19, vaccination health care workers

Access this article online	
Website: www.ijaims.in	Quick Response code

INTRODUCTION

COVID-19 vaccination program was initiated in India on January 16, 2021. During first phase of vaccination, 1 crore health care workers (HCWs) and 2 crore frontline workers (FLWs) were targeted for COVID-19 vaccination sponsored by Central Government of India. Drugs Controller General of India (DGCI)

and Central Drugs Standard Control Organization (CDSCO) had approved two vaccines for restricted use in emergency situation- Oxford-AstraZenca Company's Covishield vaccine and Bharat Biotech Company's Covaxin vaccine.[1]

In this context, the present study was conducted to find out the type of adverse reactions following first dose of Covishield vaccination reported by HCWs and its association with sociodemographic factors following vaccination in a private medical college and hospital in Uttar Pradesh.

MATERIALS AND METHODS

A cross-sectional survey was undertaken in Varun Arjun Medical College and Rohilkhand Hospital, Banthra in Shahjahanpur district in Uttar Pradesh. First dose of Covishield vaccine was given to pre-registered HCWs in this institution on 22, 28, 29, January 22, 28, and 29–February 15, 2021. Study period was from January to March 2021.

The minimal sample size required for the study was estimated to be 384, anticipating that 50% of study subjects will have adverse events following immunization (AEFI) with 5% level of significance and 5% absolute error margin at a 95% confidence interval. Five hundred and eighty HCWs who received first dose of Covishield vaccination were selected for the study. Ethical approval was obtained from the ethics and research committee of the hospital.

All HCWs aged 18 years and above who received first dose of Covishield Vaccination. HCWs who were pregnant, lactating up to 6 months and those with any acute illness were not given vaccination and hence excluded from the study.

Study data were collected by the authors from the COWIN registered list of HCWs, register and Google form questionnaire which was used to collect information about adverse events reported voluntarily by vaccinated HCWs. Common adverse reactions such as local injection site pain, tenderness, redness, swelling, and systemic reactions such as fever, headache, flu-like illness, bodyache, nausea, vomiting, abdominal pain, dizziness, syncope, excessive sweating, and fatigue were reported by vaccinated subjects within 7 days after first dose of vaccination were collected.

Data were entered in Microsoft Excel and then analyzed using Epi Info software by CDC, USA. Fisher's exact test and Pearson's Chi-square test were used to find the association between sociodemographic factors and adverse reactions following Covishield vaccination.

RESULTS

Total number of HCWs who received first dose of Covishield vaccine was 580 including 318 male (54.8%) and 262 (45.2%) female HCWs. Table 1 containing the baseline data of study population shows that the majority of the HCWs belongs to younger age group of 18–44 years (87%) and students by occupation (52.2%).

Out of 580 HCWs, only 214 (36.9%) reported AEFIs after the first dose. The Figures 1-3 describes about the characteristics of HCWs reporting AEFI. Majority of them were belonging to younger age group of 18–44 years, 202 (94.4%) and remaining were 45–59 years, 6 (2.8%) and above 60 years 6 (2.8%). Majority were male participants about 129 (60.3%) and females were about 85 (39.7%). Majority were students 149 (69.7%), medical officers or doctors were 45 (21%) and nurses, and others were 20 (9.3%).

Table 2 and Figure 4 show that fever was the most common adverse event (85.5%) reported by the vaccinated HCWs. Chills with or without fever (68.7%) was the second most common

Table 1: Baseline data of study population

Variables	HCWs (580)	
	No.	%
Sex		
Male	318	54.8
Female	262	45.2
Age group		
18–44	505	87.0
45–59	49	8.5
60 and above	26	4.5
Occupation		
Medical officers	87	15.0
Students	303	52.2
Nurses and others	190	32.8

HCWs: Health care workers

Table 2: Occurrence of AEFI reported by HCWs after Covishield vaccination

Types of AEFI	No. of HCWs (214)
Fever	183 (85.5%)
Chills	147 (68.7%)
Headache	104 (48.6%)
Bodyache	127 (59.3)
Dizziness	38 (17.8%)
Syncope	1 (0.5%)
Fatigue	100 (46.7%)
Flu like symptoms	12 (5.6%)
Excessive sweating	17 (7.9%)
Nausea	27 (12.6%)
Vomiting	25 (11.7%)
Pain abdomen	16 (7.5%)
Loss of appetite	35 (16.4%)
Body Itching	6 (2.8%)
Local reactions	127 (59.3%)

HCWs: Healthcare workers, AEFI: Adverse events following immunization

adverse event reported followed by local reactions (59.3%) and bodyache (59.3%). Local reactions include pain, tenderness, redness, swelling, and itching at the site of injection and restricted hand movements due to pain was reported by majority of the HCWs post-vaccination. Systemic reactions mainly include headache was reported by 48.6% and fatigue was reported by 46.7% of HCWs. Other less common systemic reactions were dizziness (17.8%), loss of appetite (16.4%), pain abdomen (7.5%), nausea (5.6%), vomiting (5.6%), flu-like symptoms (cold symptoms [5.6%]), excessive sweating (5.6%), body itching (2.8%), and syncope was reported by 2 HCWs (0.5%).

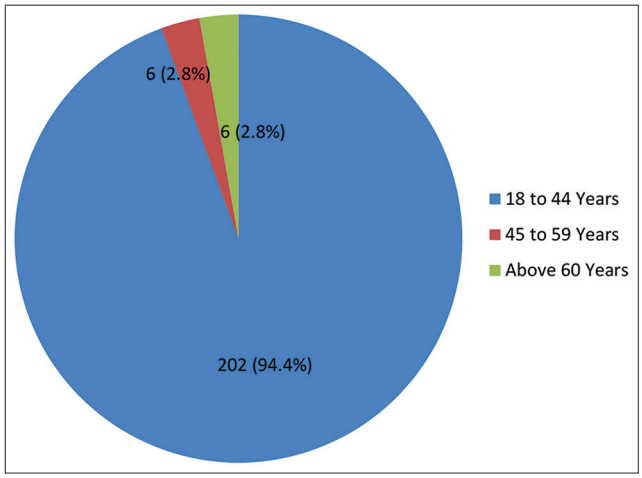

Figure 1: Age distribution of health care workers reporting adverse events following immunization

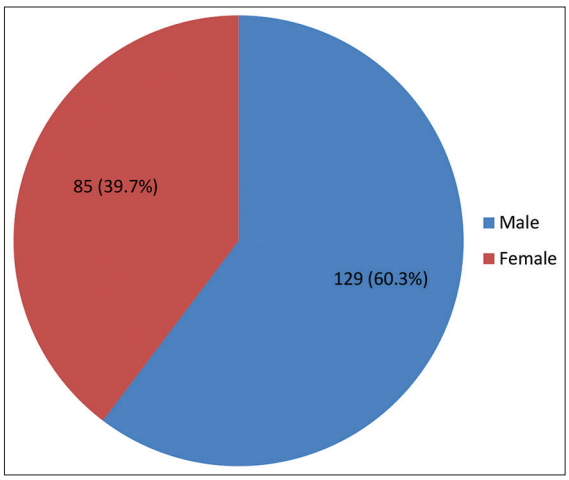

Figure 2: Sex distribution of health care workers reporting adverse events following immunization

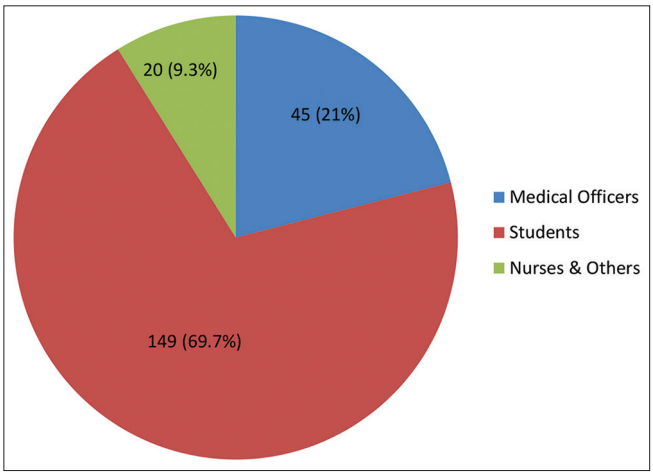

Figure 3: Occupational distribution of health care workers repoting adverse events following immunization

Figure 5 shows that Paracetamol tablet was most commonly used (91.6%) to treat the AEFI, followed by Diclofenac tablets (7.5%), Cetrizine (5.6%), Pantoprazole and Domperidone (5.1%), IV Fluids (1.9%), and ORS (0.9%). Only about four HCWs required admission at hospital casualty department for day care observation and treated symptomatically for fever, nausea, vomiting, and pain abdomen.

Table 3 shows that male HCWs reported AEFIs such as fever, chills, headache, bodyache, fatigue, loss of appetite body itching, and local reactions more frequently than female HCWs. However, female HCWs reported dizziness, syncope, flu like symptoms, excessive sweating, nausea, vomiting, and pain abdomen more frequently than male HCWs. However, this difference between both the genders was not statistically significant except for dizziness, which was more significant among female HCWs ($P < 0.01$).

Table 4 shows that fever (87.6%) and chills (69.8%) were the most common adverse event reported by younger age group HCWs (18–44 years) compared to middle age (45–59 years) and elderly

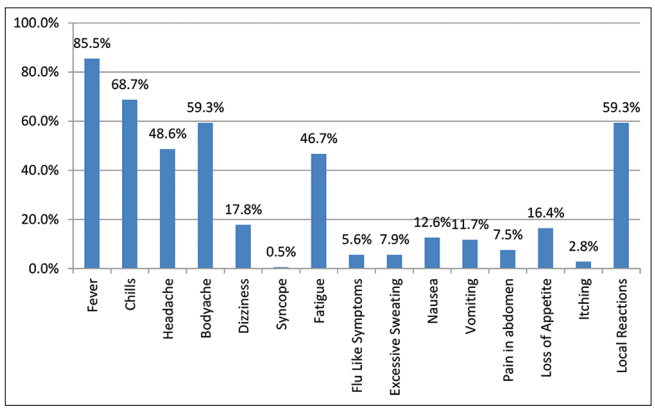

Figure 4: Bar graph showing health care workers reporting adverse events following immunization after Covishield vaccination

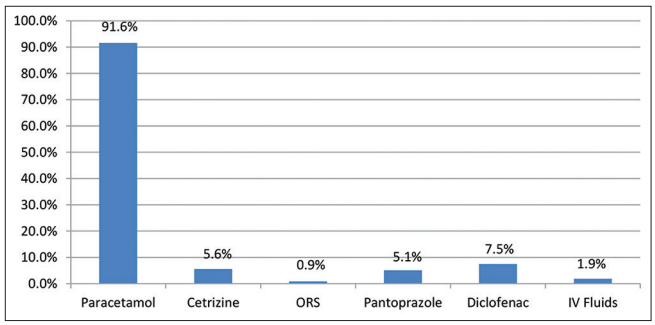

Figure 5: Bar graph showing commonly used medications for treating adverse events following immunizations

age groups (above 60 years). Bodyache (61.9%), local reactions (59.9%), headache (51%), and fatigue (48.5%) were other most common adverse events reported by younger age group HCWs. The incidence and severity of AEFIs including fever, headache, bodyache, and fatigue were significantly higher in the younger HCWs group than in the older HCWs group ($P < 0.05$).

Table 5 show that the AEFI symptoms were more commonly reported by students ($P < 0.01$) compared to medical officers, nurses, and other occupational groups except for fever and chills, commonly reported by all the three groups of occupation after Covishield vaccination.

The Table 6 shows that the adverse reactions were significantly more prevalent in male HCWs than in female HCWs ($P < 0.05$). Adverse reactions were significantly more prevalent in younger age group (18–44 years) than 45–59 years and above 60 years ($P < 0.01$). Furthermore, the adverse reactions were significantly more prevalent in students than medical officers and nurses and others ($P < 0.01$).

Table 3: Comparison of AEFI between male and female HCWs

Types of AEFI	Sex		*P* value
	Male (129)	Female (85)	
Fever	114 (88.4%)	69 (81.2%)	0.143
Chills	90 (69.8%)	57 (67.1%)	0.675
Headache	63 (48.8%)	41 (48.2%)	0.931
Bodyache	81 (62.8%)	46 (54.1%)	0.206
Dizziness	15 (11.6%)	23 (27.1%)	0.003*
Syncope	0 (0)	1 (0.8%)	NA
Fatigue	64 (49.6%)	36 (42.4%)	0.297
Flu like symptoms	6 (4.7%)	6 (7.1%)	0.453
Excessive sweating	9 (7.0%)	8 (9.4%)	0.519
Nausea	14 (10.9%)	13 (15.3%)	0.338
Vomiting	14 (10.9%)	11 (12.9%)	0.641
Pain abdomen	8 (6.2%)	8 (9.4%)	0.382
Loss of appetite	23 (17.8%)	12 (14.1%)	0.472
Body itching	4 (3.1%)	2 (2.4%)	0.745
Local reactions	78 (60.5%)	49 (57.6%)	0.681

*$P<0.01$, indicating strong significant difference. HCWs: Health care workers, AEFI: Adverse events following immunization

INTERPRETATION

In our study, 580 HCWs received the first dose of Covishield (ChAdOx1 nCoV-19) vaccine and only 214 (36.9%) reported AEFI. The most commonly reported AEFIs were fever (85.5%), chills (68.7%), local injection site reactions (59.3%), bodyache (59.3%), headache (48.6%), and fatigue (46.7%). Most of these AEFIs were of mild-to-moderate severity and there was significant association of AEFI with male HCWs, students, and younger age group. There were no serious events and anaphylaxis requiring hospitalization, and most AEFIs improved within a few days.

A similar, prospective, and observational study was conducted by Kamal *et al.*[2] in a tertiary care COVID dedicated hospital of Southern India from January 16–April 15, 2021. Nine hundred and eighty-one HCWs who received two doses (4 weeks apart) were enrolled. Active and passive surveillance was conducted after 48 h, and at days 8, 15, 22, and 28 for both doses. One thousand and twenty non-serious and two serious AEFI (altered sensorium) were reported within 48 h of first dose. Two hundred and twenty non-serious AEFI were reported within 48 h of second dose. No AEFI was reported after 15 days for

Table 4: Comparison of AEFI between different age groups

Types of AEFI	Age			*P* value
	18–44 years (202)	45–59 Years (6)	Above 60 years (6)	
Fever	177 (87.6%)	3 (50.0%)	3 (50.0%)	0.003**
Chills	141 (69.8%)	4 (66.6%)	2 (33.3%)	0.203
Headache	103 (51.0%)	1 (16.6%)	0 (0)	0.011*
Bodyache	125 (61.9%)	0 (0)	2 (33.3%)	0.001**
Dizziness	37 (18.3%)	1 (16.6%)	0 (0)	0.834
Syncope	1 (0.5%)	0 (0)	0 (0)	NA
Fatigue	98 (48.5%)	0 (0)	2 (33.3%)	0.051*
Flu like symptoms	12 (5.9%)	0 (0)	0 (0)	NA
Excessive sweating	17 (8.4%)	0 (0)	0 (0)	NA
Nausea	26 (12.9%)	1 (16.6%)	0 (0)	0.810
Vomiting	24 (11.9%)	1 (16.6%)	0 (0)	0.784
Pain abdomen	16 (7.9%)	0 (0)	0 (0)	NA
Loss of appetite	34 (16.8%)	1 (16.6%)	0 (0)	0.833
Body itching	5 (2.5%)	1 (16.6%)	0 (0)	0.295
Local reactions	121 (59.9%)	2 (33.3%)	4 (33.3%)	0.433

*$P<0.05$, indicating significant difference, **$P<0.01$, indicating strong significant difference. AEFI: Adverse events following immunization

Table 5: Comparison of AEFI between different occupational groups of HCWs

Types of AEFI	Occupation			*P* value
	Medical Officers (45)	Students (149)	Nurses and Others (20)	
Fever	38 (84.4%)	126 (84.0%)	19 (95.0%)	0.571
Chills	28 (62.2%)	100 (66.7%)	19 (95.0%)	0.013*
Headache	3 (6.7%)	97 (64.7%)	4 (20.0%)	0.001**
Bodyache	19 (42.2%)	105 (70.0%)	3 (15.0%)	0.001**
Dizziness	1 (2.2%)	35 (23.3%)	2 (10.0%)	0.001**
Syncope	0 (0)	0 (0)	1 (5.0%)	NA
Fatigue	19 (42.2%)	78 (52.0%)	3 (15.0%)	0.004*
Flu like symptoms	1 (2.2%)	11 (7.3%)	0 (0)	0.284
Excessive sweating	0 (0.0%)	17 (11.3%)	0 (0)	NA
Nausea	2 (4.4%)	24 (16.0%)	1 (5.0%)	0.093
Vomiting	1 (2.2%)	23 (15.3%)	1 (5.0%)	0.024*
Pain abdomen	0 (0.0%)	16 (10.7%)	0 (0)	NA
Loss of appetite	1 (2.2%)	33 (22.0%)	1 (5.0%)	0.001**
Body itching	3 (6.7%)	1 (0.7%)	2 (10.0%)	0.007**
Local reactions	22 (48.9%)	101 (67.3%)	4 (20.0%)	0.001**

*P<0.05, indicating significant difference, **P<0.01, indicating strong significant difference. HCWs: Health care workers, AEFI: Adverse events following immunization

Table 6: Association of AEFI occurrence with sex, age group, and occupation

Variables	AEFI – First dose		Chi-square	*P* value
	Yes (214)	No (366)		
Sex				
Male (318) % of total (580)	129 (22.2%)	189 (32.6%)	4.071	0.043*
Female (262) % of total (580)	85 (14.7%)	177 (30.5%)		
Age group				
18–44 (505) % of total (580)	202 (34.8%)	303 (52.2%)	17.011	0.0002**
45–59 (49) % of total (580)	6 (1.1%)	43 (7.4%)		
60 and above (26) % of total (580)	6 (1.1%)	20 (3.4%)		
Occupation				
Medical officer (87) % of total (580)	45 (7.8%)	42 (7.2%)	84.581	0.00001**
Students (303) % of total (580)	149 (25.7%)	154 (26.6%)		
Nurses and others (190) % of total (580)	20 (3.4%)	170 (29.3%)		

*P<0.05, indicating significant association. **P<0.01, indicating strong significant association. AEFI: Adverse events following immunization

both the doses. In contrast to our study findings, they found no association of AEFI with sex and profession ($P > 0.5$). Similar to our study, they found significant association of AEFI with younger age group ($P < 0.01$)

A similar cross-sectional study was conducted by Khalil *et al.*[3] in Dhaka, Bangladesh in May 2021. Three hundred and five persons fulfilling the inclusion criteria were asked over the telephone-based on a predesigned questionnaire. The rates of adverse events were 54.1% and 41.3% after the first and second dose of vaccine, respectively, and the difference was statistically significant ($P < 0.001$). Pain at the injection site was the most common adverse event (32.5% following the first dose and 27.9% following the second dose). All of the symptoms were mild and lasted for about 2 days. Age and comorbidities were significantly associated with the adverse events ($P < 0.001$). Neither doses had any vaccine-related life-threatening adverse event.

In a retrospective study by Jeon *et al.*[4] from Busan, Korea, during March 2021, out of 1503 HCWs 994 reported AEFIs after the first dose of ChAdOx1 nCoV-19 vaccine. The most commonly reported AEFIs were tenderness at the injection site (94.5%), fatigue (92.9%), pain at the injection site (88.0%), and malaise (83.8%). Similar to our study, the severity of most AEFIs was mild-to-moderate, and the severity and number of AEFIs were less in the older age group.

A comparative study by Kim *et al.*[5] from Changwon, Korea, 1301 of 1403 ChAdOx1 nCoV-19 vaccine recipients and 38 of 80

BNT162b2 vaccine recipients reported AEs, respectively, (90.9% vs. 52.5%): injection-site pain (77.7% vs. 51.2%), myalgia (60.5% vs. 11.2%), fatigue (50.7% vs. 7.5%), headache (47.4% vs. 7.5%), and fever (36.1% vs. 5%; $P < 0.001$ for all). Young HCWs reported more AEs of mild-to-moderate severity with ChAdOx1 nCoV-19 than with BNT162b2. No incidences of anaphylaxis were observed. Only one serious adverse event required hospitalization for serious vomiting, and completely recovered. In conclusion, reported AEs were more common in recipients with ChAdOx1 nCoV-19 vaccine than in those with BNT162b2 vaccine.

In an interim analysis of four clinical trials on the ChAdOx1 nCoV-19 vaccine, the most frequently reported adverse reactions were tenderness at the injection site (63.7%), pain at the injection site (54.2%), headache (52.6%), and fatigue (53.1%). The majority of the adverse reactions were mild-to-moderate in severity and usually resolved within a few days of vaccination.[6,7] Compared to this report, a higher incidence of systemic AEFIs were reported in our study. In a safety analysis of the clinical trials, 8.9% of the participants were aged 65 or above; in contrast, there were only 17 (2.33%) from this age group in our study.[6] The incidence and severity might have been underestimated due to the involvement of more elderly participants in the clinical trials since these studies reported that reactogenicity was generally milder and reported less frequently in older adults (≥65-years-old).

Huh *et al.*[8] reported that the incidence of anaphylaxis associated with vaccination tended to increase in Korea. As of March 26, 2021, according to the status of reports of adverse reactions after vaccination against COVID-19 in Korea, 96 suspected cases of anaphylaxis were reported (96/771, 284, 0.01%).[9] However, in our study, only one HCW presented with syncope, which spontaneously resolved without any specific treatment.

Moreover, no serious AEFIs that required hospitalization or death were reported during the monitoring period. These results are consistent with the results of the ChAdOx1 nCoV-19 vaccination among HCWs in Nepal.[10] Such mild-to-moderate AEFIs are acceptable if we compare the risk-benefit ratio for the vaccine. Our study results are helpful in addressing the vaccine hesitancy among the public.

Limitations of the Study

There are few limitations of the present study. First, AEFIs were voluntarily reported by HCWs; thus, they were not objective. Second, since this study was conducted at a single center among HCWs, the results might not be generalizable. Third, we did not collect the history of comorbidities. The possibility of bias due to unobserved variables cannot be excluded from the study.

CONCLUSION

AEFIs such as fever, chills, local injection site reactions, bodyache, headache, and fatigue were frequently reported more commonly among male HCWs of younger age group and especially students after the Covishield vaccination. There were no serious events that required hospitalization. To develop a novel vaccination strategy against emerging infectious diseases, the sharing of accurate and abundant information is important, and it will be helpful to use a mobile based adverse event monitoring system such as COWIN app for reporting of AEFIs. Sufficient explanation and preparation for expected adverse events are required to promote widespread vaccination.

ACKNOWLEDGMENT

The authors sincerely acknowledge all the study participants. We would like to thank the Department of Community medicine, Department of Pharmacology, Department of General Medicine, Medical Superintendent, Nursing Superintendent, Pharmacy College, Nursing College, DMLT and DMRT College and the Management of VAMC and RH, Banthra, Shahjahanpur, Uttar Pradesh for their support for this research work.

REFERENCES

1. Health Secretary, MOHFW, Government of India. All Preparations are on Track for COVID-19 Vaccine Roll-out from 16th January 2021. Available from: https://www.pib.gov.in/pressreleasepage.aspx?PRID=1688036 [Last accessed on 2021 Mar 26].
2. Kamal D, Thakur V, Nath N, Malhotra T, Gupta A, Batlish R. Adverse events following ChAdOx1 nCoV-19 vaccine (COVISHIELD) amongst health care workers: A prospective observational study. Med J Armed Forces India. 2021;77:S283-8.
3. Khalil MM, Mahbub-Uz-Zaman K, Hossain AS, Ahmed F, Chowdhury MF, Khan ST, *et al*. Adverse events following COVISHIELD vaccination among adult population in Bangladesh. SN Compr Clin Med 2021;3:2207-13.
4. Jeon M, Kim J, Oh CE, Lee JY. Adverse events following immunization associated with coronavirus disease 2019 vaccination reported in the mobile vaccine adverse events reporting system. J Korean Med Sci 2021;36:e114.
5. Kim SH, Wi YM, Yun SY, Ryu JS, Shin JM, Lee EH, *et al*. Adverse events in healthcare workers after the first dose of ChAdOx1 nCoV-19 or BNT162b2 mRNA COVID-19 vaccination: A single center experience. J Korean Med Sci. 2021;36:e107.
6. Voysey M, Clemens SA, Madhi SA, Weckx LY, Folegatti PM, Aley PK, *et al*. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: An interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. Lancet 2021;397:99-111.
7. European Medicines Agency. Assessment Report COVID-19 Vaccine AstraZeneca. Available from: https://www.ema.europa.eu/en/documents/assessment-report/vaxzevria-previously-covid-19-vaccine-astrazeneca-epar-public-assessment-report_en.pdf [Last accessed on 2021 Mar 26].
8. Huh K, Kim YE, Radnaabaatar M, Lee DH, Kim DW, Shin SA, *et al*. Estimating baseline incidence of conditions potentially associated with vaccine adverse events: A call for surveillance system using the Korean national health insurance claims data. J Korean Med Sci 2021;36:e67.

9. Korea Centers for Disease Control and Prevention. COVID-19 Domestic Occurrence and Vaccination Status. South Korea: Korea Centers for Disease Control and Prevention. Available from: http://www.cdc.go.kr/board/board.es?mid=a20501010000&bid=0015&list_no=712838&cg_code=&act=view&npage=1 [Last accessed on 2021 Mar 26].
10. Sah R, Shrestha S, Mehta R, Sah SK, Rabaan AA, Dhama K, *et al*. AZD1222 (Covishield) vaccination for COVID-19: Experiences, challenges, and solutions in Nepal. Travel Med Infect Dis 2021;40:101989.