J Nepal Health Res Counc 2022 Jan-Mar; 20 (54): 59-64

Adverse Events Following the First Dose of Immunization of COVID-19 Vaccine

Bijay Bhandari,[1] Nisha Jha,[2] Imdad Hushain Khan,[1] Gaurav Rayamajhi,[1] Laxman Thapa,[1] Bihungum Bista[3]

ABSTRACT

Background: The COVID-19 pandemic has challenged the entire globe and the need for a vaccine is supreme. Since many vaccines along with Covishield have been granted emergency use authorization, the evaluation and monitoring of safety are crucial. Covishield was rolled out in Nepal on January 27, 2021. So through this study, we aim to identify the prevalence of Adverse Events Following Immunization in general with the first dose of Covishield vaccine, compare Adverse Events Following Immunization in prior COVID-19 positive cases and Adverse Events Following Immunization in co-morbid individuals.

Methods: This was a descriptive cross-sectional study conducted in 440 sample from May 2021 till July 2021 in a provincial government hospital of western Nepal. Ethical approval was received from Ethical Review Board, Nepal Health Research Council (Registration no: 279/2021 P). Simple random sampling was used. Point estimate was done at 95% confidence interval and descriptive analysis was done to identify the prevalence of Adverse Events Following Immunization within one week after Covishield vaccination in the studied population.

Results: 79.77% of the study population complaint at least one or more Adverse Events Following Immunization. Fever, myalgia, headache, pain at the injection site, arthralgia, chills, and fever are the most common Adverse Events Following Immunization. 42.73% of the study population self-medicated to manage Adverse Events Following Immunization, 7.89% took leave from work while 0.28% needed medical attention. No major Adverse Events Following Immunization relevance with prior-COVID history or co-morbidity was seen.

Conclusions: Majority of the vaccinated participants had minor adverse effects on the first-day post-vaccination while most of the Adverse Events Following Immunization subsided within seven days.

Keywords: Adverse effects; COVID-19 vaccines COVISHIELD; pharmacovigilance; side effects.

INTRODUCTION

The pandemic, COVID-19, has challenged the global health and world economy.[1-3] Since many proposed pharmacological interventions are still under trial and study,[4] the importance of vaccines seems supreme. The evaluation and monitoring of the safety of the vaccine can't be overlooked,[5] since it usually took 10-14 years on average before public use.[6]

Vaccination induces immunity by causing the recipient's immune system to react to antigens contained in the vaccine.[7] ChAdOx1 nCoV-19 vaccine's safety profile has been demonstrated in randomized controlled trials carried out in Brazil, South Africa, and the UK.[8] Covishield, rolled out on January 27 2021 in Nepal, was given to frontline workers all across the country.[9,10] When vaccines are available in a short span, vaccine hesitancy is common,[11-13] and good surveillance of Adverse Effect Following Immunization (AEFI) gets crucial.[14]

METHODS

A descriptive, cross-sectional study was conducted for 3-months duration (May-July, 2021) at Lumbini Provincial Hospital, the largest referral government hospital in Lumbini province and a major COVID-19 vaccination centre of the province. Ethical approval (279-2021) was taken from Ethical Review Board, Nepal Health Research Council. Retrospective data review

Correspondence: Dr Bijay Bhandari, Drug and Patient Safety Unit, Lumbini Provincial Hospital, Butwal, Rupandehi, Nepal. Email: drbijaybhandari@iom.edu.np, Phone: +9779863692451.

Author Affiliations

[1]Drug and Patient Safety Unit, Lumbini Provincial Hospital, Rupandehi, Nepal, [2]Department of Clinical Pharmacology, KIST Medical College and Teaching Hospital, Lalitpur, Nepal, [3]Nepal Health Research Council

of hospital-based records containing 1933 vaccines was done. After computer-generated simple random sampling, 440 sample size was taken for study. Sample size was calculated using (1-p)/ assuming p=50% at 95% confidence interval with 5% margin of error and 10% non-response rate. The study population was healthcare workers only.

Among the different COVID-19 vaccines available in the global market, Covishield vaccine provided by Government of India was first to roll out in Nepal to the prioritized target population.[9] Covishield™ (ChAdOx1 nCoV- 19 Corona Virus Vaccine) is a monovalent vaccine composed of a single recombinant, replication-deficient chimpanzee adenovirus vector encoding the S glycoprotein of SARS-CoV-2.[15] A hospital-based AEFI committee was formed to observe, manage and record the incidence of AEFI on the day of vaccination and follow-up via phone call till the 7th-day post-vaccination. Hospital records containing data on AEFI on days 0, 1, and 7 were screened by a team of investigators to extract information and input in the data extraction form based on WHO COVID-19 Vaccines: Safety Surveillance Manual.[14]

An AEFI has been defined as "any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine".[16] Based on its intensity vaccine reactions can be mild, moderate or severe. The event itself, however, may be of relatively minor medical significance. While, AESI (Adverse Event of Special Interest) is "a pre-identified and pre-defined medically-significant event that has the potential to be causally associated with a vaccine product that needs to be carefully monitored and confirmed by further specific studies. It is relatively new AEFI classification that started with pandemic vaccine development. AESI refers to adverse events of significant scientific, medical, and public interest among pandemic vaccines".[14,16]

AEFI can occur within minutes to days. As there are only few original studies related to AEFI of COVISHIELD vaccine in Nepal, this article will add knowledge regarding AEFI of COVISHIELD vaccine. Prior similar studies carried out in Nepal were limited to observation of AEFI until 24-48 hours but we followed study participants till 7 days to observe potential AEFI for a slight longer time duration. Also, the different modalities adapted by vaccinees who experienced AEFI post-vaccination was analysed.

The independent variable was the COVID-19 vaccine (COVISHIELD) while the dependent variable was AEFI . Descriptive analysis was done using SPSS Version 16 to identify the prevalence of AEFI in the studied population within one week, compare AEFI in non-COVID-19 patients with prior COVID-19 positive individuals and identify AEFI in vaccinated individuals with prior comorbidity.

Frequency	Occurrence among persons vaccinated in percent	Severity of reactions

Very common	≥ 10%	**Common and usually minor reactions:**
		• Are part of the immune response to vaccine,
		• Reactions settle on their own,
		• Examples include:
		  ◦ Fever,
		  ◦ Malaise.

Common (frequent)	≥ 1% and < 10%	
Uncommon (infrequent)	≥ 0.1% and < 1%	**Rare, usually more severe reactions:** 1. Usually require clinical management, 2. Examples include: • Severe allergic reaction (e.g., anaphylaxis) including an exaggerated response to the vaccine antigen or component, • Vaccine specific reactions, such as BCG osteitis.
Rare	≥ 0.01% and < 0.1%	
Very rare	< 0.01%	

Figure 1. Operational definition of frequency and severity of adverse vaccine reaction.

RESULTS

Out of 440 samples taken for the study among 1933, 247 (56.14%) of them were below 35 years of age and the rest above 35. The distribution of male 242 (55.00%) and female 198 (45.00%) was almost uniform. 72 (16.40%) vaccines have co-morbid conditions and 60 (13.60%) had a history of COVID-19 infection. Table.1 shows the socio-demographic and health-related information of the participants.

AEFI on 1st-day post-vaccination shows 351 (79.77%) vaccines complained at least one AEFI or more. There were 835 AEFIs reported and almost all of them were minor, except one that needed special attention. These AEFI were classified as very common, common, and uncommon as per their incidence. The most commonly observed AEFIs were fever, myalgia, headache, pain at the injection site, arthralgia, chills, fatigue. Table 2. shows the incidences of AEFI post COVISHIELD vaccination.

Upon observation of AEFIs in prior COVID-19 and non-COVID-19 populations as tabulated in Table 3 and as illustrated by Fig.1, no major difference was found. Most of the AEFIs were minor to moderate self-limiting in nature and remaining requiring medications like analgesics, anti-pyretic, and anti-histaminics. Many participants, 188 (42.73%) people self-medicated themselves to manage the symptoms post-vaccination. On the 7th day follow-up, 9 participants had not responded to the phone call while 38 (8.82%) still complained of the presence of at least one AEFI, 34 (7.89%) stated they took a leave from their work during this course of

a week and 1 (0.28%) needed treatment by a hospital visit. Fig.2 demonstrates different modalities adopted by COVISHIELD vaccine recipients to manage AEFI.

A 24-year-old female presented in emergency of Lumbini Provincial Hospital with history of sudden fall down with impact over occipital region of head after 1 day of COVISHIELD vaccination. She complained of dizziness, fever, pain in vaccinated arm. On examination, she was ill-looking, conscious and well oriented. Local examination revealed 4cm X 1cm lacerated injury over occipital region of head. There was no active bleeding. Her vitals were stable and systemic findings were normal. On evaluation, her base line investigations and CT scan head were normal. She was discharged after 12 hours of observation.

Table 1. Socio-demographic and health-related information of the participants.

Variables	N (Frequency)	Percentage(%)
Age (years)		
18-35	247	56.14
36-55	172	39.09
55+	21	4.77
Gender		
Male	242	55.00
Female	198	45.00
Comorbidities		
Yes	72	16.40
No	368	83.60
Prior COVID-19		
Yes	60	13.60
No	380	86.40

Table 2. Magnitude of AEFI post Covishield vaccination.

Very Common (>1/10)	Common (≥1/100 to <1/10)	Uncommon (≥1/1000 to <1/100)
Fever	Nausea	Cough
Myalgia	Dizziness	Sore throat
Headache	Swelling at injection site	Insomnia
Pain at injection site	Runny nose	Increased appetite
Arthralgia	Diarrohea	Discoloration at injection site
Chills	Anorexia	Dry nasal mucosa
Fatigue	Vomiting	Dry mouth
		Burnings sensation at injection site
		Regurgitation
		Redness at injection site
		Somnolence
		Skin Rashes
		Hyperglycemia
		Abdominal pain
		Ageusia

Table 3. Systemic AEFI post COVISHIELD vaccination in groups with prior COVID-19 and with no history of COVID-19.

Symptoms	COVID group (N/%)	Non-COVID group (N/%)
Fever	31 (62.00)	145 (48.17)
Chills	12 (24.00)	54 (17.94)
Pain at injection site	13 (26.00)	97 (32.22)
Myalgia	23 (46.00)	113 (37.54)
Fatigue	10 (20.00)	34 (11.33)
Dizziness	3 (6.00)	19 (6.31)
Headache	16 (32.00)	95 (31.56)
Nausea	5 (10.00)	23 (7.64)
Diarrhea	0 (0.00)	5 (1.64)
Arthralgia	17 (28.33)	76 (25.24)

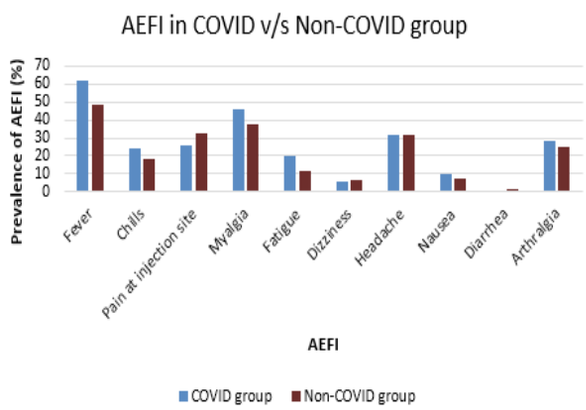

Figure 2. Proportion of AEFI prevalence in groups with prior COVID-19 infection and with no history of COVID-19.

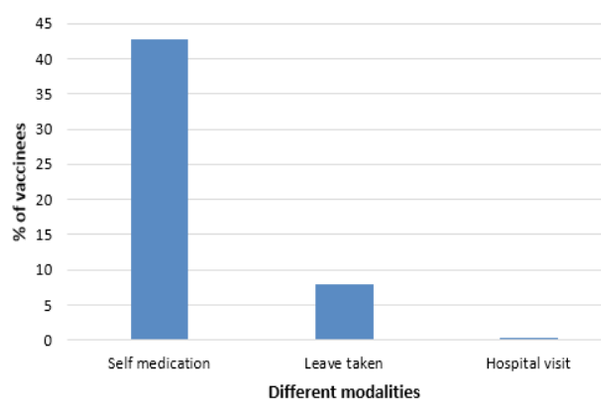

Figure 3. Percentage of different modalities of AEFI management adapted by vaccinated people.

DISCUSSION

In this study, AEFIs were observed in 79.77% of the study population, which resembles the study carried out by Adhikari P. which was 78.90%.[18] The occurrence of AEFI is comparable to the study conducted in Nepal by Shrestha S. (85.04%),[19] and another in Saudi Arabia by Alhazmi A. (84.00%),[20] while, the study in South India by Inbaraj LR. shows a little lower incidence (69.70%).[21] The most common adverse effects encountered in our study were fever, myalgia, headache, pain at the injection site, arthralgia, chills, and fatigue which were very similar to the study by Shrestha S.[18] Local and systemic reactions such as pain or fever are expected to occur as part of the immune response by reacting to the antigens contained in the vaccine, while other components used in vaccines (e.g. adjuvants, stabilizers, and preservatives) can also trigger reactions.[7]

The study in Saudi Arabia by Alhazmi A. also states fatigue, pain at the injection site, fever, chills, and headache as their very common AEFI along with nausea and vomiting which were commonly seen in our study.[20] The study in South India by Inbaraj LR. lists body ache, headache, and fever as their highly observed AEFI.[21] The incidence of AEFI in co-morbid and non-comorbid populations was not of much difference, likewise with people of different gender and people with or without co-morbid conditions.

No considerable difference has been found in the incidence of AEFI among the population below and above 35 years of age, while the study in Chitwan, Nepal by Adhikari P. [18], and another study conducted

in the Czech Republic by Riyad A. show a greater incidence of AEFI in the study population of younger age.[22] On analyzing, no significant difference was found in the overall prevalence of AEFI in a population with prior history of COVID-19 v/s non-COVID-19. Similarly, two studies from Nepal by Adhikari P. and Shrestha S. show no significant difference in AEFI on the aspect of prior-COVID and non-COVID populations.[18,19] However, several studies by support higher reactogenicity in those with a history of COVID-19 infection following mRNA COVID-19 vaccination.[23,24] In response to the AEFI, 42.73% self-medicated, 7.89% took leave from the work and 0.28% had to visit a hospital and the data pattern shows congruency with the study conducted in Patan by Shrestha S.[19]

As the study population were healthcare workers, many of them were well aware of how to treat common illnesses which gives us a supportive indication that the percentage of self-medication was high, limiting the number of hospital visits. Though no mortality or any AESI was observed in our study, this doesn't exclude the rationale of the vaccine pharmacovigilance system. In the long run, rigorous monitoring of adverse drug reactions in real-time can ensure vaccine safety.[24]

Since the studied population were healthcare workers, so the response received on query in regard to AEFI is more credible in comparison to general population. However, there is a possibility of interviewer's bias from investigators' side and recall bias from participants' side during follow-up call. Moreover, our study is of single site, AEFI surveillance requires data from multiple sentinel sites to identify unusual adverse events.

CONCLUSIONS

Majority of the vaccinated participants had minor adverse effects on the first-day post-vaccination while most of the AEFI subsided within seven days. This study didn't notice any AESI and mortality cases associated with vaccination while one case needed a hospital visit. From this study it can be concluded that there are minor side effects from COVISHIELD vaccination.

ACKNOWLEDGEMENTS

We would like to thank Dr. Rajendra Prasad Khanal, Indradeep Yadav, Kamala Hamal, Shubham Sarkar and Shree Ram Pandey of Lumbini Provincial Hospital, Butwal, Rupandehi, Nepal for their support during the study.

CONFLICT OF INTEREST

None.

REFERENCES

1. Baldwin RE, Evenett SJ. COVID-19 and trade policy why turning inward won't work [Internet]. Centre for Economic Policy Research; 2020 [cited 2021 Jul 7]. [Article]

2. Meo SA, Alhowikan AM, Al-Khlaiwi T, Meo IM, Halepoto DM, Iqbal M, et al. Novel coronavirus 2019-nCoV: prevalence, biological and clinical characteristics comparison with SARS-CoV and MERS-CoV. Eur Rev Med Pharmacol Sci. 2020;24:2012–9. [Article]

3. Meo SA, Bukhari IA, Akram J, Meo AS, Klonoff DC. COVID-19 vaccines: comparison of biological, pharmacological characteristics and adverse effects of Pfizer/BioNTech and Moderna Vaccines. Eur Rev Med Pharmacol Sci. 2021;25:1663–9. [Article]

4. Tobaiqy M, Qashqary M, Al-Dahery S, Mujallad A, Hershan AA, Kamal MA, et al. Therapeutic Management of COVID-19 Patients: A systematic review. Infect Prev Pract [Internet]. 2020 Apr 17 [cited 2021 Jun 28];2(3):1–26. [Article]

5. Shakir S, Lane S, Davies M. How to Investigate a Serious Adverse Event Reported During a Clinical Trial for a COVID-19 Vaccine. Drug Saf [Internet]. 2021 Jan [cited 2021 Jun 21];44(1):1–5. [Article]

6. Petousis-Harris H. Assessing the Safety of COVID-19 Vaccines: A Primer. Drug Saf [Internet]. 2020 Dec [cited 2021 Jun 21];43(12):1205–10. [Article]

7. WHO. MODULE 3 – Classification of AEFIs - WHO Vaccine Safety Basics [Internet]. [cited 2021 Jun 30]. Available from: https://vaccine-safety-training.org/classification-of-aefis.html

8. Voysey M, Clemens SAC, 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 Lond Engl. 2021 Jan 9;397(10269):99–111. [Article]

9. COVID-19 vaccination drive to commence from Wednesday in Nepal - The Himalayan Times [Internet]. [cited 2021 Jun 28]. Available from: https://thehimalayantimes.com/nepal/covid-19-vaccination-drive-to-commence-from-wednesday-in-nepal

10. WHO. Nepal launches nationwide COVID-19 vaccination

drive with health workers and frontline workers [Internet]. [cited 2021 Jun 28]. Available from: https://www.who.int/nepal/news/detail/27-01-2021-nepal-launches-nationwide-covid-19-vaccination-drive-with-health-workers-and-frontline-workers

11. Schattner A. Consequence or coincidence?: The occurrence, pathogenesis and significance of autoimmune manifestations after viral vaccines. Vaccine [Internet]. 2005 Jun 10 [cited 2021 Jun 28];23(30):3876–86. [Article]

12. Agorastos T, Chatzigeorgiou K, Brotherton JML, Garland SM. Safety of human papillomavirus (HPV) vaccines: A review of the international experience so far. Vaccine [Internet]. 2009 Dec 9 [cited 2021 Jun 28];27(52):7270–81. [Article]

13. Demicheli V, Rivetti A, Pietrantonj CD, Clements CJ, Jefferson T. Hepatitis B vaccination and multiple sclerosis: evidence from a systematic review. J Viral Hepat [Internet]. 2003 [cited 2021 Jun 28];10(5):343–4. [Article]

14. WHO. COVID-19 vaccines: safety surveillance manual [Internet]. World Health Organization; 2020 [cited 2021 Jun 30]. [PDF]

15. COVISHIELD™ ChAdOx1 nCoV- 19 Corona Virus Vaccine (Recombinant) [product insert]. Pune, India: Serum Institute of India [Internet]. [cited 2021 Oct 29]. [PDF]

16. CIOMS/WHO Working Group on Vaccine Pharmacovigilance, editor. Definition and application of terms for vaccine pharmacovigilance: report of CIOMS/WHO Working Group on Vaccine Pharmacovigilance. Geneva: World Health Organization; 2012. 193 p. [PDF]

17. MODULE 1 – Adverse events: Frequency and severity - WHO Vaccine Safety Basics [Internet]. [cited 2021 Oct 27]. Available from: https://vaccine-safety-training.org/frequency-and-severity.html

18. Adhikari P, Adhikari K, Gauli B, Sitaula D. Acceptance of covid-19 vaccine and pattern of side effects in nepalese context: a post vaccine cross-sectional study among health care workers in a tertiary care hospital. 2021;11(2):5. 34-38. [Article]

19. Shrestha S, Devbhandari RP, Shrestha A, Aryal S, Rajbhandari P, Shakya B, et al. Adverse events following the first dose of ChAdOx1 nCoV-19 (COVISHIELD) vaccine in the first phase of vaccine roll out in Nepal. J Patan Acad Health Sci [Internet]. 2021 Apr 29 [cited 2021 Jun 23];8(1):9–17. [Article]

20. Alhazmi A, Alamer E, Daws D, Hakami M, Darraj M, Abdelwahab S, et al. Evaluation of Side Effects Associated with COVID-19 Vaccines in Saudi Arabia. Vaccines [Internet]. 2021 Jun [cited 2021 Jun 27];9(6):674. [Article]

21. Inbaraj LR, George CE, Franklyn NN. How safe is Covishield (ChAdOx1nCoV-19) vaccine? Experience from a tertiary care hospital in South India. Curr Med Pract. 2021 Jul 5;19(3):162–4. [Article]

22. Riad A, Pokorná A, Attia S, Klugarová J, Košík M, Klugar M. Prevalence of COVID-19 Vaccine Side Effects among Healthcare Workers in the Czech Republic. J Clin Med [Internet]. 2021 Apr 1 [cited 2021 Jun 22];10(7):1428. [Article]

23. COVID symptom Study. Vaccine after effects more common in those who already had COVID [Internet]. 2021 [cited 2021 Jun 28]. Available from: https://covid.joinzoe.com/post/vaccine-after-effects-more-common-in-those-who-already-had-covid

24. Krammer F, Srivastava K, the PARIS team, Simon V. Robust spike antibody responses and increased reactogenicity in seropositive individuals after a single dose of SARS-CoV-2 mRNA vaccine [Internet]. Allergy and Immunology; 2021 Feb [cited 2021 Jun 28]. [Article]