Self-reported Adverse Effects in Health Care Professionals Following First and Second Dose Vaccination Against SARS-CoV 2 (Covishield)

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ABSTRACT

Introduction: The ChAdOx 1 n Cov-19 vaccine, called Covishield, was rolled out in Nepal targeting health care professionals. The study was conducted to assess the pattern of self-reported adverse events following immunization and to compare AEFI on the basis of previous COVID status.

Methods: A cross sectional study of four months duration was conducted in Shree Birendra Hospital, a tertiary care hospital, in Kathmandu, Nepal. AEFI associated with first and second dose of Covishield were assessed for a period of seven days from the day of vaccination in health care professionals and comparison was done based on COVID status.

Results: A total of 100 vaccine recipients were included in the study, out of which 83% showed AEFI. The most commonly reported AEFI after first dose were headache (56%), injection site tenderness (42%), myalgia (29%), fatigue (24%), dizziness (20%), pyrexia (19%), malaise (17%), nausea (10%), chills (8%), vomiting (2%) and arthralgia (1%) while among the AEFI after second dose were injection site tenderness (36%), headache (15%), myalgia (12%), fatigue (11%), nausea (9%), malaise (8%), pyrexia (8%), chills (5%), rashes (3%), drowsiness (3%), arthralgia (1%) and dizziness (1%). Previously infected participants were found to be prone to develop systemic adverse effects. The most of the adverse effects were subsided within four days and commonly used medication was paracetamol to relieve the symptoms.

Conclusions: AEFI following the first and second dose of vaccine were mild. Systemic adverse effects were more frequent in those with the history of COVID-19 infection.

Key Words: Adverse effect; ChAdOx 1 n Cov-19; Covishield; Vaccination

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INTRODUCTION

The ChAdOx1 nCoV-19 vaccine (AZD1222), called Covishield has been given regulatory approval by Department of Drug Administration, Nepal on 15th Jan 2021.[1] The safety data published so far is from over 20,000 participants enrolled across four clinical trials in the UK, Brazil and South Africa.[2]

The majority of adverse reactions were mild to moderate in severity which included injection site tenderness, headache, fatigue, pyrexia, chills and arthralgia which usually resolved within few days of vaccination.[2-6] Being a new vaccine, research regarding its efficacy as well as adverse effects is highly demanded.

No trials have been conducted in Nepali population and the information on adverse effects profile in Nepali population is limited. The self-reporting of adverse effects of Covishield can include a wide range of unintended harmful effects in the population thus improving awareness regarding the reporting of adverse effects. The aim of the study was to assess self-reported adverse effects in health care professionals following first and second dose of Covishield vaccine in Shree Birendra Hospital (SBH) premises.

METHODS

A cross-sectional descriptive comparative study was conducted among healthcare professionals (doctors, nurses and paramedics) who were vaccinated with Covishield vaccine in SBH, a tertiary care hospital, during early vaccination phase of the Government strategy. The study duration was four months from 26th March 2021 to 29th July 2021. The study was approved from Institutional Review Committee (IRC), Nepal Army Institute of Health Sciences (NAIHS) on March 2021 (Reg.406). Similarly, the consent from SBH administration was also taken prior to administration of questionnaire. Informed written consent was obtained from each participant before distribution of questionnaire. The health care professionals aged between 18 to 65 years of age and who were vaccinated with Covishield and gave consent for participations were included in the study. Sample size of 100 was calculated using Cochran formula, based on incidence of subject with at least one local reaction, which is 4%.[2] The total sample size was calculated using following formula: $n = p(1-p)z^2/e^2$ where, z = 1.96 at 95% confidence interval, p = estimated local adverse effect (4%), [2] e = permissible error (0.1), n = 0.04 (1-0.04) 1.96X1.96/0 .1X0.1 and n = 99.39. A structured questionnaire was developed which included socio-demographic variables like age, gender and occupation and COVID related variables like date of first and second dose with batch number, COVID status, AEFI within seven days after first dose and second dose, medications taken for adverse effects and number of rest days. Convenient sampling method was used in which the questionnaires were distributed among the vaccinated health care professionals in the designated site at the end of administration of the second dose of the vaccine and the time chosen for distribution of questionnaires was first hour of vaccination i.e. 10:30 to 11:30 am daily. The total number of questionnaires distributed were 154. Participants were instructed to fill the questionnaire and were given opportunity to ask the investigator in situation where they did not understand the statements of questionnaire correctly. The adverse effects following immunization (AEFI) i.e. first dose and second dose of Covishield vaccination till seventh day post-vaccination were recorded by the participants. The obtained data was entered and statistical analysis was done using SPSS version 21. Descriptive statistics were carried out for COVID status, adverse effects after first and second dose and medications taken for adverse effects. Inferential analysis was done to assess the association between COVID status and the adverse effects using chi-square test. P value of 0.05 was considered statistically significant.

RESULTS

Out of 154 questionnaire form distributed, completely filled questionnaires were 100, incompletely filled were 18 and remaining 36 forms were not returned. Majority of recipients were from age group 30 to 39 years (52%) and least recipients from 50 to 59 years (1%). The maximum age of recipient was 50 years and minimum age was 22 years. The mean age of recipient was found to be 33.43 ± 9.08 years. The number of male and female recipients were 73 and 27 respectively. The male to female ratio was 2.7. The vaccinated people were doctors (18%), nurses (26%) and paramedics (56%). About 53% of recipients had a previous history of COVID-19 infection as confirmed by Polymerase Chain Reaction (PCR) test (male:40; female:13) while 47% were without the previous COVID infection (male:33, female:14).

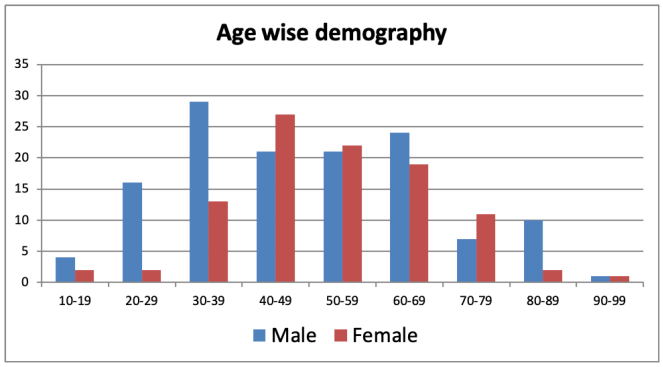

Figure 1. AEFI after first and second dose of vaccine

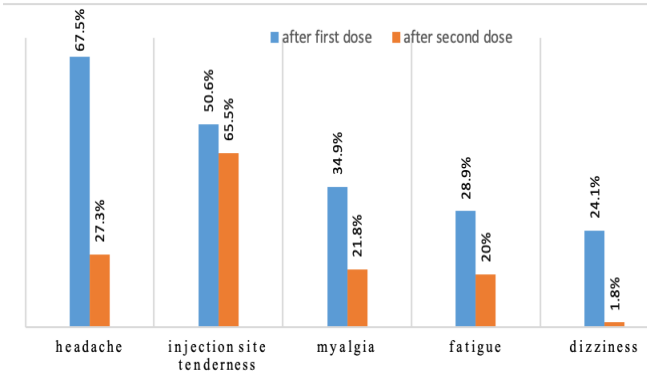

Figure 2. Common AEFIs after first and second dose

The number of vaccinated health care professionals who showed AEFI after first and second dose is illustrated in figure 1. Among those who showed symptoms, 82.19% were males and 66.66% were females.

The common AEFI profile seen among those who were vaccinated after first dose and second dose are shown in figure 2. Others less frequent AEFIs after first dose were pyrexia (19%), malaise (17%), nausea (10%), chills (8%), vomiting (2%) and arthralgia (1%) while among the AEFI after second dose were nausea (9%), malaise (8%), pyrexia (8%), chills (5%), rashes (3%), drowsiness (3%), arthralgia (1%) and dizziness (1%).

AEFI was compared for those with the previous history of COVID-19 infection with those without any previous infection, both after the first dose and the second dose which is illustrated in figures 3 and 4 respectively. The Chi-square test didn't show significant difference between those two groups after first dose of vaccination when five common AEFIs including local reaction were compared ($p = 0.875$; CI 95%) however, systemic adverse effect showed significant difference ($P = 0.032$; CI 95%). Also, there was statistically significant difference between common systemic AEFIs after first and second dose when compared individually as illustrated in table 1.

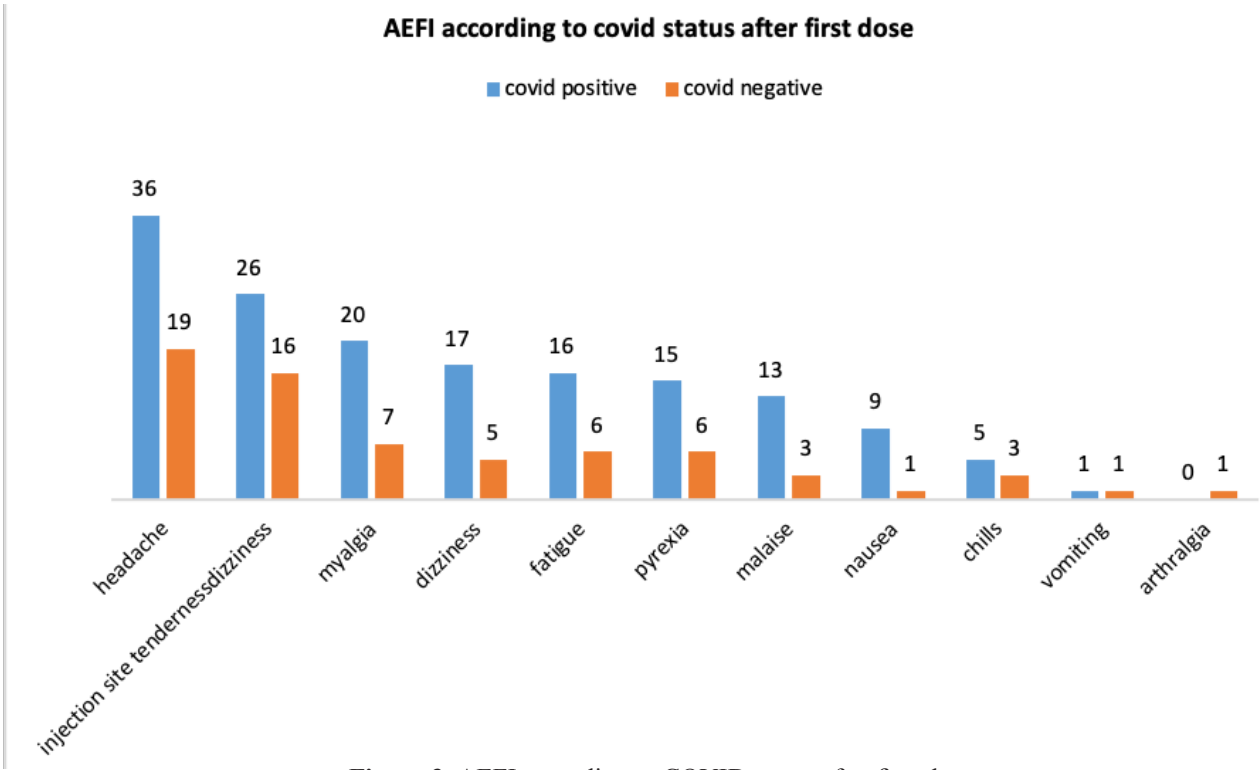

Figure 3. AEFI according to COVID status after first dose

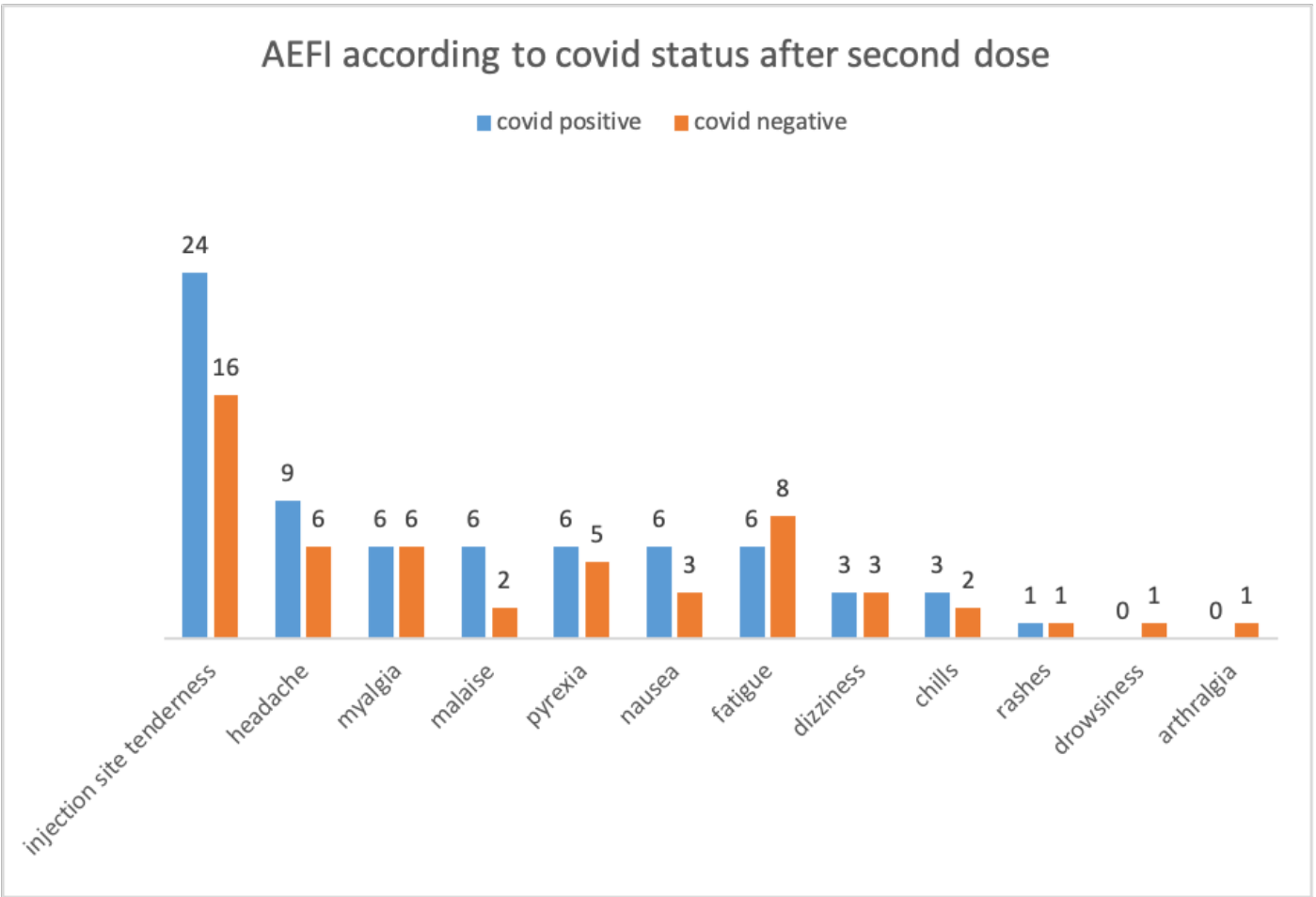

Figure 4. AEFI according to COVID status after second dose

Table 1. Common AEFIs after first dose in vaccine recipients with/ without previous history COVID-19 infection

		COVID positive (n = 53)	Non-COVID (n = 47)	P value (< 0.05)
Headache	+	36 (67.92%)	19 (40.43%)	0.005801
	-	17 (32.08%)	28 (59.57%)	
Myalgia	+	20 (37.74%)	7 (14.89%)	0.010230
	-	33 (62.26%)	40 (85.11%)	
Dizziness	+	17 (32.08%)	5 (10.64%)	0.009799
	-	36 (67.92%)	42 (89.36%)	
Fatigue	+	16 (30.19%)	6 (12.77%)	0.032627
	-	37 (69.81%)	41 (87.23%)	
Injection site tenderness	+	26 (49.06%)	16 (34.04%)	0.1289489
	-	27 (50.94%)	31(65.96%)	

+ Present, - Absent

Out of 83% who showed AEFI, number of participants 30% took medications to relieve the symptoms. The most frequently used medication was paracetamol 25 (83.33%), followed by the combination of paracetamol and ibuprofen 2 (6.67%), combination of codeine and paracetamol 2 (6.67%) and the least commonly used one was ondansetron 1 (3.33%). The vaccine recipients took rest for maximum of four days (1%), 4% of them took leave for three days, 7% for two days and minimum of one day leave was taken by 9%. The mean days of leave was calculated to be 0.42 ± 9.90 days.

DISSCUSSION

This cross-sectional study involved 100 vaccine recipients and male preponderance was observed which is similar to study done by Jeskowaik I et al.[7] Ours being Army Hospital, more army personnel may have been provided vaccine which could also skew the male preponderance of vaccination. The target age was between 18 - 65 years when the vaccine was first rolled out in Nepal and worldwide, health care professionals being the prioritized group. Among those enrolled in this study, majority of them were from 30 to 39 years age group (52%) which is in contrast to the findings of

Jeskowaik et al. [19-30 years (51.4%)] and Adhikari P et al. [less than 30years (42.6%)].[7,8]

The overall adverse effects associated with Covishield vaccine in our study was 83% which is in congruence with the findings of the study done by Bae S et al (80%).[9] Bae S et al also reported that adverse effects after the first dose were more frequent in female health care professionals than in male which is contrast to our study which showed male predominance.[9,10] This could be due to unequal gender distribution in sample size.

The five common adverse effects seen after first dose of vaccine were headache (56%), injection site tenderness (42%), myalgia (29%), fatigue (24%) and dizziness (20%) which is comparable to data from interim analysis of pooled data on adenoviral vector COVID-19 vaccine from four clinical trials conducted in UK, Brazil and South Africa and study conducted by Jeskowiak I et al[2,7] Our study had similarity with that done in Nepal by Shrestha S et al. where injection site tenderness (55%), fever (37.1%), myalgia (30.1%), lethargy (27.6%) and headache (26.3%) were common adverse effects.[1] Headache (52.6%) was the most commonly reported adverse effect in terms of systemic adverse effects by interim analysis of four clinical trials which is consistent with our study (56%) that is similar to the study findings reported by Bae S et al., Dutta S et al and Azimi M et al .[2,6,9,11] However, headache was reported as less prevalent adverse effect in Raid et al. study where injection site tenderness (72.8%) was the most common adverse effect, followed by systemic adverse effects like fatigue (73.9%), muscle pain (55.4%).[12] Compared to first dose of vaccine, we found decreased incidence of self-reported adverse effects after second dose. Similar kind of reporting was done by Bae et al. where adverse effects after second dose of ChAdOx1 vaccine were less common than after first dose as compared to BNT162n2 where AEFI after second dose were more common than after its first dose.[9] Manufacturers have also reported lower frequency and intensity of adverse effects with second dose.[13] Phase 2/3 trial of ChAdOx1 nCov-19 by Ramasamy MN et al. had similar reporting regarding the frequency of AEFI after second dose.[14] Further studies need to be carried out to determine whether the frequency of AEFIs differ between vaccinations.

Regarding the COVID status, 53% participants were previously infected by SARS-CoV-2 in our study which is in contrast to study of Raid A et al. which found only 8.7% had previous history of COVID-19 infection.[12] Gender distribution was unequal in our study in terms of previous exposure with COVID-19 (male 75.5%, female 24.5%) which was different from that of Raid A et al (male 38.1%, female 38%). Statistically significant correlation was found by Jaeskowiak I et al. regarding women susceptibility to COVID-19 infection as compared to male.[7] Mathioudakis AG et al in his study showed significant association between prior COVID-19 infection and higher incidence and severity of self-reported adverse effects after vaccination.[15] Likewise, individuals with prior COVID-19 infections showed more adverse effects than non-COVID in Menni et al study.[16] But our study had different findings than that of Alexander G et al and Menni et al i.e. no significant difference in number of AEFIs who had previous COVID-19 infection. However, our findings were similar to the study done by Adhikari et al in Nepal.[8] Nevertheless; there was statistically significant difference between common systemic AEFIs after first and second dose in regard to COVID status. The period between recovery date and the first vaccination dose has not been taken into consideration in our study. Frequency of adverse effects could be correlated with the previous infection and residual antibodies. Compared with first dose, our study found decreased incidence of self-reported adverse effects after second dose when recipients had been previously exposed to viral antigen which is similar to the findings of Rajpurohit P et al.[17] Study done by Jaeskowaik et al reported the occurrence of stronger adverse effects with previous COVID-19 infection after the first dose and similar stronger adverse effects were seen after second dose in participants without prior infection.[6,18] This could be partly due to weakened antibody-dependent enhancement (ADE) which corresponds to the situation where antibodies that normally alleviate the consequences of viral infection end up doing the opposite. This ADE fail to control the virus pathogenicity by failing to neutralize or enhance the viral reproduction potential or by triggering an extensive and misadapted reaction thereby causing damage to the host organs through hyper-inflammation or cytokine storm.[7] In our study, however, there was no significant difference in adverse effects after first and second dose among the participants who had not been exposed to viral antigen unlike that reported by Jaeskowaik et al.[7] Among all the adverse effects, headache was significantly more after first dose than after second dose in those who had no prior COVID-19 infection.

The majority of adverse effects lasted for one to four

days which indicated that adverse effects would resolve within four days after vaccination. Similar findings were reported by Raid A et al. where post vaccination adverse effects resolved within three days and by European Medical Agency (EMA) which claimed that majority of adverse effects resolved within few days. [12,19]

Our study observed that about 30% vaccine recipients with AEFI took medications which is in consistent with study done by Shrestha S et al. in Nepal (32%) which mostly included paracetamol and combination of paracetamol with ibuprofen.[1] There are important limitations of this study. The sample size is small and it has included only the health care professionals which make generalization of the result difficult. It was based on self-reported adverse effects, rather than direct observation, which are prone to subjectivity and might result in overestimation or underestimation of severity and frequency of adverse effects. AEFIs for both the first as well as second dose was collected after the second dose of vaccination so there might be recall bias. Additionally, there was an inconsistent gap between the first and the second dose. Lastly, the survey was intended to collect AEFI seen within seven days following vaccination so the adverse effects that occurred thereafter were not evaluated so we could have missed important events.

CONCLUSIONS

Following the Covishield vaccinations among the healthcare workers, AEFIs were observed more after first dose than second dose and most of them were mild. Previously infected participants were found to be prone to develop systemic adverse effects. Self-reporting of adverse effects after vaccination needs to be encouraged and further studies need to be conducted with large sample size for longer duration in multiple centers.

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Conflict of Interest: None declared

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