DOI: http://doi.org/10.4038/jccp.v53i1.7946

Research article

Adverse events following ChAdOx1 nCoV-19 (Covisheild) vaccine administered in two-dose regimen: A single centre experience from Sri Lanka

Govindapala DS[1], Senarath RMUS[1], Wijenayake W[1], Wijewardena TD[1], Nakkawita WMID[2], Senaratne UTN[3], Kawyangana P[2], De Silva AD[2], Fernando NS[2]

Journal of the Ceylon College of Physicians, 2022, **53**, 17-25

Abstract

Introduction: The ChAdOx1 nCoV-19 (Covisheild) vaccine was well tolerated with low reactogenicity in the clinical trials. However, shortly after initiating mass vaccination programmes in many countries, safety concerns resulted in vaccine hesitancy among populations.

Objectives: This prospective single-cohort study was conducted to assess adverse events following immunization (AEFI) and associated factors of the ChAdOx1 nCoV-19 vaccine among staff members of the University Hospital of General Sir John Kotelawala Defence University (UHKDU).

Methods: A total of 688 staff members who received the first dose of the ChAdOx1 nCoV-19 vaccine from 30th January to 5th February 2021 were enrolled and followed up until the completion of vaccination. Of them, 635 responded after the second dose. Data were collected using an interviewer-administered questionnaire and through telephone interviews. AEFI were classified according to WHO criteria.

Results: A total of 516 (74.9%) participants experienced AEFI after the first dose, of which 377 (73.0%) reported both systemic and local symptoms. By contrast, the incidence of AEFI was significantly less after the second dose of vaccination (n=134, 21.1%, p<0.001). Fever was the commonest adverse event after the first dose (n=389, 56.5%), and injection site pain was frequent (n=85, 13.3%) following the second dose. Two of the four participants who reported serious AEFI following the first dose had seizures. AEFI predominantly occurred within the first 24 hours after each dose (n=489, 94. 8% and n=120, 89.6%, respectively) and lasted less than 72 hours in the majority (n=409, 79.3% and n=109, 81.3%, respectively), who reported post-vaccination symptoms. The incidence of AEFI was significantly higher in females after the second dose (p=0.007).

Conclusions: The adverse events following the ChAdOx1 nCoV-19 vaccine among our population were less frequent than reported in clinical trials. Neither dose had any vaccine-related life-threatening adverse events. The vaccine appears safe in the population studied.

Key words: ChAdOx1 nCoV-19 vaccine, adverse events, reactogenicity, Covisheild, Sri Lanka

Introduction

The development of a vaccine against novel coronavirus has been a main focus since the beginning of the COVID-19 pandemic. Research teams rose to the challenge successfully and developed several vaccines within nine months of the first reported case

[1]*Department of Clinical Sciences, Faculty of Medicine, General Sir John Kotelawala Defence University, Rathmalana, Sri Lanka*
[2]*Department of Paraclinical Sciences, Faculty of Medicine, General Sir John Kotelawala Defence University, Rathmalana, Sri Lanka,* [3]*Department of Multidisciplinary Sciences, Faculty of Allied Health Sciences, General Sir John Kotelawala Defence University, Rathmalana, Sri Lanka*

Correspondence: DSG, e-mail: dumithagovindapala@kdu.ac.lk

https://orcid.org/0000-0001-6795-7913

Received 06 January 2022, accepted 28 March 2022.

of SARS-CoV-2 infection.[1] The vaccination process against COVID-19 was started in June 2020 with the approval of the CanSino vaccine for limited use on military personnel in China. Subsequently, in August 2020, the Russian Government approved the Sputnik V vaccine for emergency use.[2] Since then, many countries have initiated phased distribution of different types of vaccines, prioritizing those at the highest risk of exposure and complications, such as healthcare workers and the elderly.

The vaccination programme officially commenced in Sri Lanka on the 29th January 2021, using the Covisheild vaccine, the same Oxford-AstraZeneca (ChAdOx1 nCoV-19 Corona Virus Vaccine-Recombinant) vaccine, manufactured in the Serum Institute of India.[3] The ChAdOx1 nCoV-19 (AZD1222) is a non-replicating simian adenovirus-based vaccine, expressing the full-length SARS-CoV-2 spike glycoprotein gene.[4] Phase 1-3 clinical trials among several age groups have shown that ChAdOx1 nCoV-19 is well tolerated with a good safety profile. There were no serious adverse events attributable to the vaccine. Headache, malaise and fever were the common side effects reported by the participants.[5]

Nonetheless, shortly after commencing the mass vaccination programmes in many countries, there were concerns regarding vaccine-related adverse events. On the 15th March 2021, Germany suspended the ChAdOx1 nCoV-19 vaccine over thrombotic concerns, followed by several other countries in the European Economic region.[6] As of 7th April 2021, the Medicines and Healthcare products Regulatory Agency, United Kingdom, recorded 79 thrombosis cases out of 20.2 million people who received the ChAdOx1 nCoV-19 vaccine with an incidence rate of 1:250 000.[7] However, the European Medicines Agency did not restrict the use of it, stating that the overall benefits of the ChAdOx1 nCoV-19 vaccine far outweigh the risks of side effects.[8]

Concerns regarding adverse events have resulted in vaccine hesitancy among both healthcare workers and the general public in Sri Lanka. Furthermore, data on vaccine safety among Sri Lankans are scarce. Thus, we aimed to determine the occurrence of adverse events following immunization (AEFI) with two doses of the ChAdOx1 nCoV-19 (Covisheild) vaccine among the staff members of a university hospital in Sri Lanka.

Methods

This prospective observational study was conducted to profile the adverse events among staff members of the University Hospital of General Sir John Kotelawala Defence University (UHKDU) following both doses of the ChAdOx1 nCoV-19 vaccine immunisation. The staff members, who received the first dose of the ChAdOx1 nCoV-19 vaccine from 30th January to 5th February 2021, were invited to participate in this study and followed up until completion of the vaccination. The second dose was administered four months after the prime dose (30th April 2021 onwards).

All consented staff members were recruited consecutively and prospectively without applying any random selection methods. The vaccination register maintained at the vaccination centre was used as the sampling frame.

A pre-designed structured questionnaire was used to collect data regarding demographic characteristics, comorbidities, previous diagnosis of COVID-19 or exposure and adverse reactions to the vaccine. Active surveillance of the adverse events was done for up to one week. The recipients were observed for immediate AEFI during the first 30 minutes at the vaccination centre. Details about adverse events occurring in the 72-hour and one-week post-vaccine period were then collected via telephone-based interviews.

As per the WHO definition, any untoward medical occurrence following immunisation and that does not necessarily have a causal relationship with the usage of the vaccine was considered an AEFI. The adverse events resulting in hospitalization, prolonging existing hospitalisation, life-threatening illness, permanent disability, or death were defined as serious AEFI. All the other adverse events were considered non-serious AEFI.[9] Reactogenicity refers to the physical manifestations of the inflammatory response to vaccination and includes both systemic and local reactions.[10]

The data were analysed using Statistical Package for the Social Sciences (SPSS) version 25.0. Shapiro-Wilk test was used to identify normal distribution of the data. Categorical variables were described using frequencies and percentages. The median and interquartile ranges were used to describe continuous data with a skewed distribution. Proportions of the occurrence of adverse events following each dose of the vaccine were compared using the Z test. One-sided chi-square test was used to determine the association of AEFI with demographic variables and medical anamnesis. A p-value less than 0.05 was considered significant.

Results

A total of 688 vaccine recipients at the UHKDU consented to participate in this study. Of them, 28 have not obtained the second dose of the vaccine and

another 25 were lost to follow up after the second dose. Participants' median age was 32 years (IQR 28-41) and 424 (61.6%) were men. Pre-existing medical conditions were seen in 110 (16.0%) participants. Eighty participants (11.6%) had high-risk exposures to confirmed COVID-19 patients and were in quarantine prior to the first dose of the vaccine. Five participants reported a history of COVID-19 before the first dose, while 16 developed the disease after the first dose (Table 1).

Following the first dose, 516 (74.9%) reported at least one or more adverse events; of which 377 (73.0%) reported both systemic and local symptoms, 116 (22.4%) had systemic symptoms and 23 (4.4%) experienced local symptoms only. In contrast, adverse events were significantly less following the second dose (n=134, 21.1%, P<0.001) and local adverse events (n=94,70.1%) were more frequent than systemic symptoms (n=60, 44.7%) (Table 2).

The common systemic adverse events reported after the first dose were fever (n=389, 56.5%), muscle /body aches (n=306, 44.5%), arthralgia (n=200, 29.1%) and headache (n=124, 18.0%). Pain around the injection site was the most frequent local adverse event following the first (n=369, 53.6%) and second doses (n=89,14.0%) of the vaccination (Table 3).

Table 1. Sociodemographic data and medical anamnesis of the study population

Variables		*First dose recipients (N = 688)*	*Second dose recipients (N = 635)*
Age	Median (IQR)	32 (28-41)	32 (28-41)
Gender	Male	424 (61.6%)	388 (61.1%)
	Female	264 (38.4%)	247 (38.9%)
Occupation	Consultant	45 (6.5%)	43 (6.8%)
	Medical Officer	51 (7.4%)	51 (8.0%)
	Nursing Officer	143 (20.8%)	137 (21.6%)
	Health care assistant	32 (4.7%)	30 (4.7%)
	Paramedical staff	19 (2.8%)	18 (2.8%)
	Admin Staff	34 (4.9%)	32 (5.0%)
	Other*	364 (52.9%)	324 (51.0%)
Comorbidities**	Yes	110 (16.0%)	101 (15.9%)
	No	578 (84.0%)	534 (84.1%)
Allergies	Yes	70 (10.2%)	66 (10.4%)
	No	617 (89.9%)	569 (89.6%)
Past History of COVID-19	Yes	5 (0.7%)	21 (3.3%)
	No	683 (99.3%)	614 (96.7%)
Past History of quarantined	Yes	80 (11.6%)	No data
	No	608 (88.4%)	No data

* Supporting and security staff of the UHKDU

** Diabetes, hypertension, dyslipidaemia, ischemic heart disease, asthma, COPD, chronic liver cell disease, chronic kidney disease, cancer, thyroid disorders, anaemia

Table 2. Reporting of solicited adverse events by the recipients of the ChAdOx1 nCoV-19 vaccine

Variables		*1st dose (n=688)*	*2nd dose (n=635)*	*Significance*
Presence of AEFI following immunisation	Yes	516 (75.0%)	134 (21.1%)	Z =19.6 P<0.001
	No	172 (25.0%)	501 (78.9%)	
Local AEFI only	Yes	23 (3.3%)	74 (11.6%)	Z=5.8 P<0.001
	No	665 (96.6%)	561 (88.3%)	
Systemic AEFI only	Yes	116 (16.9%)	40 (6.3%)	Z=5.8 P<0.001
	No	572 (83.1%)	595 (93.7%)	
Both local and systemic AEFI	Yes	377 (54.8%)	20 (3.1%)	Z=20.3 P<0.001
	No	311 (45.2%)	615 (96.9%)	

The onset of reported adverse reactions was frequent within the first 24 hrs (n=489, 94.7%) and resolved completely within 72 hours in 409 (79.3%) participants after the first dose of vaccination. A similar trend was observed for the second dose, where the majority reported onset of symptoms within 24 hours (n=120, 89.5%) and recovery within 72 hours (n=109, 81.3%). However, a small proportion of participants reported symptoms lasting more than a week following each doses (3.7% and 0.9%, respectively) (Figure 1).

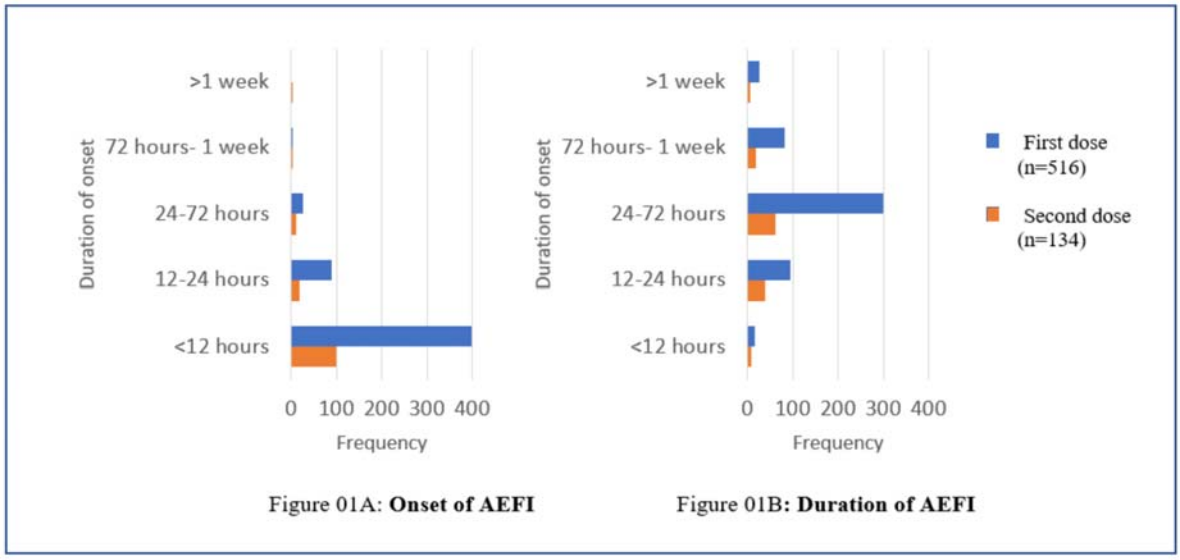

Figure 1. Onset and duration of adverse events following the ChAdOx1 nCoV-19 vaccine.

Table 3. Incidence of adverse events following the ChAdOx1 nCoV-19 vaccine

Frequencies	*1st dose (n=688)*	*2nd dose (n=635)*
Very common ≥10%	**Local Symptoms:** Injection site pain (53.6%) **Systemic symptoms:** Fever (56.5%) Muscle/body aches (44.5%) Arthralgia (29.1%) Headache (18.0%) Chills (17.3%) Feeling tired (11.5%)	**Local Symptoms:** Injection site pain (14.0%)
Common (frequent) ≥1% and <10%	**Local Symptoms:** Swelling (8.4%) Redness (3.3%) Warmth (2.5%) Bruising (1.9%) Induration (1.5%) Itching (1.2%) **Systemic symptoms:** Back pain (10.8%) Reduced appetite (8.3%) Nausea and vomiting (9.6%) Dizziness (2.2%) Abdominal pain (1.0%)	**Systemic symptoms:** Feeling tired (2.8%) Fever (2.3%) Headache (2.2%) Muscle/body aches (2.2%)
Uncommon (infrequent) ≥0.1% and <1%	**Systemic symptoms:** Rash (0.1%) Seizure (0.3%)	**Local Symptoms:** Swelling (0.6%) Redness (0.5%) Itching (0.1%) **Systemic symptoms:** Arthralgia (0.9%) Nausea and vomiting (0.3%) Dizziness (0.6%) Chills (0.1%) Reduced appetite (0.1%) Rash (0.1%)

Almost all reported adverse events were self-limiting except for four participants who required hospital admission after the first dose of vaccination. Two of them had high fever with body aches. One participant was admitted with a generalized tonic-clonic seizure lasting less than five minutes. Another recipient was evaluated for altered behaviour and possible atonic seizure and recovered completely within 24 hours. Both participants presented on the same day of receiving the vaccine. No seizure recurrence or neurological sequelae were observed in them.

Given the evidence from previous studies suggesting higher reactogenicity among females, young age groups, and individuals previously infected with SARS-CoV-2, we analysed data to determine these associations. There was no statistically significant association between age or the presence of comorbidities and the incidence of adverse events. No significant difference in the occurrence of adverse events was observed among individuals with a previous COVID-19 infection than those without a past infection. Although there was no gender difference in the frequency of adverse events after the first dose (P=0.147), higher reactogenicity was observed among females following the second dose (P=0.007). Most notably, of the 516 participants who reported adverse reactions following the first dose, only 102 (19.8%) had post-vaccination symptoms for the second dose (P=0.739) (Table 4).

Table 4. Adverse events following the ChAdOx1 nCoV-19 vaccine stratified by demographic characteristics and medical anamnesis

Variables		*AEFI- First dose (n=688)*				*AEFI- Second dose (n=635)*			
		Yes (n, %)	No (n, %)	Chi-square (n, %)	P value (n, %)	Yes (n, %)	No (n, %)	Chi-square (n, %)	P value (n, %)
Age	18 - 39	370 (74.3%)	128 (25.7%)	0.579	0.749	96 (19.3%)	402 (80.7%)	0.317	0.853
	40 - 59	113 (77.4%)	33 (22.6%)			28 (19.2%)	118 (80.8%)		
	≥ 60	33 (75.0%)	11 (25.0%)			10 (22.7%)	34 (77.3%)		
Gender	Male	310 (73.1%)	114 (26.9%)	2.098	0.147	69 (16.3%)	355 (83.7%)	7.229	**0.007**
	Female	206 (78.0%)	58 (22.0%)			65 (24.6%)	199 (75.4%)		
History of COVID-19 infection	Yes	03 (60.0%)	02 (40.0%)	0.604	0.437	03 (14.3%)	18 (85.7%)	0.372	0.542
	No	513 (75.1%)	170 (24.9%)			131 (19.6%)	536 (80.4%)		
Comor-bidities	Yes	84 (76.4%)	26 (23.6%)	0.130	0.719	28 (25.5%)	82 (74.5%)	2.983	0.084
	No	432 (74.7%)	146 (25.3%)			106 (18.3%)	472 (81.7%)		

Discussion

The present study assessed the adverse events and associated factors following ChAdOx1 nCoV-19 vaccine immunisation among 688 recipients. Our study group represents a relatively young population, with the majority being men, because of the inclusion of healthcare workers and other staff members of the UHKDU. We found that adverse events were less in the studied population than in the clinical trials. Nearly two-thirds of study participants experienced adverse events following the first dose and most of them reported both local and systemic symptoms. The incidence of adverse events was significantly less after the second dose with predominant local reactions. Serious adverse events were uncommon, and no life-threatening adverse events were reported. There were no age-related differences in the occurrence of adverse events. We observed that the frequency of adverse events was significantly higher in females than in males following the second dose.

Of the study population, 74.9% after the first dose and 21.1% following the second dose of the ChAdOx1 nCoV-19 vaccine experienced at least one adverse reaction during the study period. Following the first dose, the incidence of adverse events was substantially lower in our study population than in the single-blind, randomized, controlled, phase 2/3 trial (COV002) of the ChAdOx1 nCoV-19 vaccine.[11] In the phase 2/3 trial, 86% of participants aged 18-55 years who received the first dose of the vaccine have reported systemic adverse events, whereas we found a lower rate of 71.7% in the overall sample. Similarly, local adverse events following the first dose were reported at much lower frequencies than in the clinical trials.[11]

Systemic adverse events were more common than local reactions in all age groups of the studied population after the first dose. In contrast, a community survey in the UK showed the highest proportion of reported adverse events were due to local reactions.[12] In numerous studies, fatigue, muscle aches, and headache were the commonest systemic symptoms reported after the first dose of the ChAdOx1 nCoV-19 vaccine.[11-15] However, fever was the most frequent systemic adverse event in our population, experienced by more than half of them. Interestingly, fever was the most reported systemic symptom after the first dose of the ChAdOx1 nCoV-19 vaccine in two other studies from South East Asia.[16,17] Similar to many other studies, the injection site pain was the predominant local symptom after the first dose of vaccination.[12,14,17] Our findings for the onset and duration of adverse events following the first dose are in accordance with previous studies.[12,16] Most recipients experienced symptoms within 24 hours of receiving the first dose and the symptoms lasted less than 72 hours in the majority.

Compared to the first dose, the incidence of adverse events after the second dose of vaccination was significantly less in our population. These findings are similar to the Phase 2/3 clinical trial observations and data from two regional studies.[11,17,18] However, the adverse events were reported at much lower rates than anticipated in the clinical trials.[11] Pain at the injection site was the only adverse event denoted as very common following the second dose.

Different operational definitions were used in the previous studies for the severity grading of adverse reactions. Adverse effects requiring hospitalization were considered serious and reported by four participants of our study group. Corroborating findings were reported from Nepal, where only three out of 5591 recipients of the ChAdOx1 nCoV-19 vaccine required hospitalisation.[16] On the contrary, 12% (n=188) of HCWs required medical consultation or hospitalisation after the first dose of the vaccine in Togo.[15]

Considering the four serious adverse events reported in this study, the patient admitted with a generalised convulsion was a previously healthy female with no history or risk factors for epilepsy. The second patient who presented with confusion and possible atonic seizure was also a healthy female with no history of epilepsy. Investigations including MRI brain were normal and causality was not confirmed in both of them. Both feared the adverse effects and avoided obtaining the second dose, despite no seizure recurrences after the initial event. Although the generalised convulsions have proven to be associated with immunization, seizures following the ChAdOx1 nCoV-19 vaccine are rarely reported.[19-21] Two other hospitalized patients with high-grade fever and severe body aches made a complete recovery with symptomatic treatment and were discharged after a short period of hospital stay.

Previous studies have reported a significantly high prevalence of AEFI in women and younger age groups.[12-14] We found a significant association of AEFI with the female gender following the second dose of vaccination (P=0.007). Although the incidence of AEFI was higher in women than in men after the first dose, the observed difference was statistically not significant. Age and comorbidity were not significantly associated with vaccine-related adverse events. Moreover, our study did not demonstrate the high reactogenicity observed among individuals with past SARS-CoV-2 infection in the previous studies.[12,14] More than 90% of our study participants were below 55 years of age with a low prevalence of comorbidities. Furthermore, only

a small proportion of participants had a history of COVID-19. These population characteristics may explain the contrasting differences in our findings to the literature.

One main limitation of this study is self-reported data, which may have underestimated or overestimated adverse events. Another limitation is that previous SARS-CoV-2 infections among study participants were entirely based on history and no pre-vaccination antibodies were performed. Hence, asymptomatic infections would have been missed. Further, the study was conducted on a cohort of hospital staff to evaluate the short-term adverse effects of the ChAdOx1 nCoV-19 vaccine, making it difficult to extrapolate the results to the broader population. Hence, long-term surveillance in the general population is required to strengthen the findings of this study.

Conclusions

In the studied population, adverse reactions were less frequent than reported in clinical trials. The adverse events following the second dose of the vaccine were significantly lower than the first dose in all age groups. The post-vaccination symptoms were self-limiting and short-lived. Severe adverse events requiring hospital admission were reported only by four participants. Neither thrombotic events linked to the vaccine nor life-threatening adverse events were observed in our population. Hence, our study results reiterate that ChAdOx1 nCoV-19 is a safe and well-tolerated vaccine.

Declarations

Availability of data and material: The supporting data and material of this study are available from the corresponding author on reasonable request. Patient's de-identification will be maintained in sharing the data.

Conflict of interest

The authors declare that they have no competing interests.

Funding

This work was supported by the General Sir John Kotelawala Defence University (KDU Research Grant [KDU/RG/2021/FOM/005]).

Ethics approval

Ethics approval for this study was obtained from of the General Sir John Kotelawala Defence University.

Author contributions

Conceptualization: DG; Design of research study: DG, DN, WW, NSF; Data acquisition: DG, USS, TDW, DN, TNS, PK; Data analysis: DG, WW, USS, NSF, PK, TNS; Interpretation of results: DG, WW, NSF, PK, TNS; Writing the manuscript: DG, USS, WW, ADS, NSF

All authors contributed and approved the final draft of the manuscript.

Acknowledgement

The staff of the University Hospital KDU for their cooperation.

References

1. Rawat K, Kumari P, Saha L. COVID-19 vaccine: A recent update in pipeline vaccines, their design and development strategies. *Eur J Pharmacol.* 2021; **892**: 173751. doi: 10.1016/j.ejphar.2020.173751.
2. UPDATED Comparing COVID-19 Vaccines: Timelines, Types and Prices. *Bio Space.* 2021. Available from: https://www.biospace.com/article/comparing-covid-19-vaccines-pfizer-biontech-moderna-astrazeneca-oxford-j-and-j-russia-s-sputnik-v/
3. Progress Report of COVID -19 Immunization. Epidemiology Unit, Ministry of Health, Sri-Lanka. 2021. Available from: https://www.epid.gov.lk/web/index.php?option=com_ontent&view=article&id=231&Itemid=426&lang=en
4. Watanabe Y, Mendonça L, Allen ER, et al. Native-like SARS-CoV-2 Spike Glycoprotein Expressed by ChAdOx1 nCoV-19/AZD1222 Vaccine. *ACS Cent Sci.* 2021; **7**(4): 594-602. doi:10.1021/acscentsci.1c00080
5. Folegatti PM, Ewer KJ, Aley PK, et al. Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial. *Lancet* 2020; **396**(10249): 467-78. doi:10.1016/S0140-6736(20)31604-4
6. Wise J. COVID-19: How AstraZeneca lost the vaccine PR war. *BMJ* 2021; **373**: n921. doi:10.1136/bmj.n921
7. Coronavirus Vaccines-summary of Yellow Card reporting. Medicines & Healthcare products Regulatory Agency, Government of UK.2021 Available from: http://www.nationalarchives.gov.uk/doc/open-government-licence/
8. Benefits of COVID-19 Vaccine AstraZeneca outweigh risks of blood clots. *Reactions Weekly* 2021; **1848**(1): 2. doi:10.1007/s40278-021-93004-3
9. COVID-19 vaccines: SAFETY SURVEILLANCE MANUAL. World Health Organization. 2020. Available from: https://apps.who.int/iris/bitstream/handle/10665/338400/9789240018280-eng.pdf?sequence=1&isAllowed=y
10. Hervé C, Laupèze B, Del Giudice G, Didierlaurent AM, Tavares Da Silva F. The how's and what's of vaccine reactogenicity. *NPJ Vaccines* 2019; **4**: 39. doi:10.1038/s41541-019-0132-6

11. Ramasamy MN, Minassian AM, Ewer KJ, et al. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial. *Lancet* 2021; **396**(10267): 1979-93. doi:10.1016/S0140-6736(20)32466-1

12. Menni C, Klaser K, May A, et al. Vaccine side-effects and SARS-CoV-2 infection after vaccination in users of the COVID Symptom Study app in the UK: a prospective observational study. *Lancet Infect Dis.* 2021; **21**(7): 939-49. doi:10.1016/S1473-3099(21)00224-3

13. Song JE, Oh GB, Park HK, Lee SS, Kwak YG. Survey of Adverse Events After The First Dose of The ChAdOx1 nCoV-19 Vaccine: A Single-Center Experience in Korea. *Infect Chemother.* 2021; **53**(3): 557-61. doi:10.3947/ic.2021.0044

14. Riad A, Pokorná A, Mekhemar M, et al. Safety of ChAdOx1 nCoV-19 Vaccine: Independent Evidence from Two EU States. *Vaccines (Basel)* 2021; **9**(6): 673. doi:10.3390/vaccines9060673

15. Konu YR, Gbeasor-Komlanvi FA, Yerima M, et al. Prevalence of severe adverse events among health professionals after receiving the first dose of the ChAdOx1 nCoV-19 coronavirus vaccine (Covishield) in Togo, March 2021. *Arch Public Health* 2021; **79**(1): 207. doi:10.1186/s13690-021-00741-x

16. 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. *Journal of Patan Academy of Health Sciences.* 2021; **8**(1): 9-17. doi: 10.3126/jpahs.v8i1.36242

17. Khalil MM, Mahbub-Uz-Zaman K, Hossain AS, et al. Adverse Events Following COVISHIELD Vaccination Among Adult Population in Bangladesh. *SN Compr Clin Med.* 2021; **3**(11): 2207-13. doi:10.1007/s42399-021-01021-z

18. 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**(Suppl 2): S283-S288. doi: 10.1016/j.mjafi.2021.06.014

19. Chen RT. Brighton Collaboration Safety Platform for Emergency vaccines (SPEAC) Project World Health Organization.2020. Available from: https://www.dcvmn.org/IMG/pdf/8._cepi_speac_presentation_bob_chen.pdf

20. Ghosh R, Dubey S, Roy D, Mandal A, Naga D, Benito-León J. Focal onset non-motor seizure following COVID-19 vaccination: A mere coincidence? *Diabetes Metab Syndr.* 2021; **15**(3): 1023-4. doi: 10.1016/j.dsx.2021.05.003

21. Aladdin Y, Shirah B. New-onset refractory status epilepticus following the ChAdOx1 nCoV-19 vaccine. *Journal of Neuroimmunology* 2021; **357**: 577-629. doi.org/10.1016/j.jneuroim.2021.577629.