**How to Cite**:
Koyagura, N., Patnaik, P. K., Konda, J. P., Vedula, P., Kumar, K. V., & Anumolu, G. (2022). Adverse effects followed by immunization with COVISHIELD and COVAXIN among health care personnel in a tertiary care hospital of India. *International Journal of Health Sciences*, *6*(S4), 2725–2734. https://doi.org/10.53730/ijhs.v6nS4.7926

# Adverse effects followed by immunization with COVISHIELD and COVAXIN among health care personnel in a tertiary care hospital of India

**Narendar Koyagura**
Associate Professor, Department of Pharmacology, RVM Institute of Medical Sciences & Research Center, Siddipet- 502279, Telangana, India

**Prashanth Kumar Patnaik**
Assistant Professor, Department of Pharmacology, RVM Institute of Medical Sciences & Research Center, Siddipet- 502279, Telangana, India
*Corresponding author email: prashanthpaul86@gmail.com

**Jaya Prakash Konda**
Assistant Professor, Department of Pharmacology, RVM Institute of Medical Sciences & Research Center, Siddipet- 502279, Telangana, India

**Prasanna Vedula**
Professor & Head, Department of Pharmacology, RVM Institute of Medical Sciences & Research Center, Siddipet- 502279, Telangana, India

**Ksheerasagar Vinay Kumar**
Assistant Professor, Department of Pharmacology, RVM Institute of Medical Sciences & Research Center, Siddipet- 502279, Telangana, India

**Goparaju Anumolu**
Assistant Professor, Department of Community Medicine, RVM Institute of Medical Sciences & Research Center, Siddipet- 502279, Telangana, India

***Abstract*---**The ongoing Corona Virus Disease (COVID-19) is a pandemic disease adversely affecting health and also incurred severe financial losses globally. Vaccination is the important preventing measure to combat COVID-19 infection. Vaccine hesitancy due to the fear of side effects is a major drawback for successful implementation of immunization programs. Extensive studies on safety of COVID-19 vaccination are much needed to address this problem. The current study aims at evaluating adverse effects following vaccination against COVID-19 infection. A total of 584 healthcare personnel who received either COVISHIELD or COVAXIN were included in the study. The adverse effects after first and second dose of vaccines in different time

intervals (<24hrs, 24-48hrs, 3-7days) were recorded by using World Health Organization (WHO) based questionnaire. Among the participants, 360 received COVISHIELD and 220 received COVAXIN vaccine. Majority of the subjects experienced side effects within first 24hrs of first dose (COVISHIELD 84%, COVAXIN 90%) and also of second dose (COVISHIELD 73%, COVAXIN 89%). Side effects like general weakness, headache, fever, chills and myalgia were the most common side effects observed with both vaccines. They were self limiting and subsided within 3-7 days. None of the participants were hospitalized. Results were statistically analyzed by using Chi-square test and significance level was assumed as $p<0.05$. It revealed no significant difference between the first and second of COVISHIELD as well as COVAXIN separately. However, further studies among various age groups and populations are required for more safety data on these vaccines.

***Keywords*---**COVID-19 vaccine, covishield, covaxin, post vaccination effect.

## Introduction

Corona virus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome corona virus-2 (SARS-COV-2) which originated in China in late December 2019 emerged as a global pandemic (Hu et al., 2021). Various treatment strategies and preventive measures were employed for the management and to curtail COVID-19 spread but was rendered ineffective owing to high rate of infectivity and mutation capability of SARS-COV-2 virus (Yan et al., 2020). Researchers as well as various global and national health regulatory authorities encouraged and developed preventive vaccine strategies as a result of which many vaccines became available (Lazarus et al., 2021). The targets for vaccine development included spike protein, mRNA and inactivated viral vaccine (Ita, 2021). Some of these vaccines were given emergency utilization authorization (EUA) by FDA owing to the medical emergency and possible protective effect rendered by these vaccines (Singh and Upshur, 2021).

In India two vaccines COVISHIELD (AstraZeneca and Serum Institute of India) and COVAXIN (Bharat biotech limited) was developed and approved by the regulatory authority (Singh et al., 2021). As per the interim 3rd phase clinical trials, the vaccines exhibited 81% and 90% efficacy for COVISHIELD and COVAXIN respectively (Kumar et al., 2021). Health care personnel are in the forefront in the management of COVID-19 and hence are at high risk of contracting COVID-19 and need vaccine protection. Hence, the government of India first started implementing the vaccine to the health care personnel. Corona vaccine administration is producing side effects such as fever, headache, fatigue, local site pain and redness, myalgia, joint pain and chills. Majority of these effects are resulting within 3 days following the vaccination (Seth, 2021). It was observed from the previous studies that fear of adverse effects was the most common cause of vaccine hesitancy (Das et al., 2019). Various studies were done to study the safety of these two vaccines. Several studies have been carried out

during post market analysis and fact sheets were released by Serum Institute of India for better understanding of the side effects of the vaccines (Luyten et al., 2021). The current study evaluated the adverse effect profiles of both COVISHIELD and COVAXIN separately. We focused on severity and duration of the side effects among the participants. In addition, we also analyzed the differences in adverse reactions of the first and second dose within and between these vaccines.

## Materials and methods

### Study design

An observational prospective cohort study was carried out in a tertiary care hospital, located in Southern part of India from January to October, 2021. Health care personnel who had two doses of either COVISHIELD or COVAXIN were included in the study. Informed consent was obtained from each participant before start of the study. A questionnaire based on WHO guidelines was given to collect the data in regards to side effects experienced following the first and second dose of vaccination (World Health Organization, 2021). The study was reviewed and approved by the Institutional Ethics Committee.

### Sample size

A total of 610 participants were recruited in this study. Out of these, only 584 participants consented for the study. Of these 584 participants, 360 participants had COVISHIELD whereas 220 received COVAXIN.

### Inclusion criterion

Health care personnel who received two doses of either COVISHIELD or COVAXIN vaccine were included in the study.

### Exclusion criterion

Subjects who did not complete two doses of vaccine, hospitalized for other reasons before or after vaccination within the period of 2 weeks, history of past or present COVID-19 infection were excluded from the study.

### Instrument

The questionnaire containing the details of vaccine type, adverse effects, duration of onset and demographic data was given to each participant. Semi open type of questions about the adverse reactions was mentioned in the list. The measures were taken to handle the post vaccination adverse effects including hospitalization also noted.

### Statistical analysis

All statistic tests were accomplished by using Statistical package for the social Sciences (SPSS) version 27.0. Chi square test was done to compare the adverse

effects following first and second dose within and between the two vaccines. p value less than 0.05 was considered as significant (P<0.05).

**Results**

This study analyzed the adverse reactions after the administration of COVISHIELD and COVAXIN individually. Among the 584 participants, 360 had COVISHIELD whereas 220 received COVAXIN. The occurrence of these adverse effects/symptoms were tabulated in different time intervals (<24hrs,24-48hrs,3-7days) andwith respect to first and second dose post vaccination separately. Most of the adverse effects were mild and less frequent. None of the participants who developed adverse effects post vaccination required hospitalization.

**Adverse effects following COVISHIELD**

Majority (84%) of the subjects noticed the side effects in first 24hrs, 11% had symptoms in between 24-48hrs period and 5% had symptoms after 3 days of first dose of COVISHIELD. Following the second dose of COVISHIELD, 73% had adverse effects in first 24hrs, 19%in between 24-48hrs period and8% had symptoms after 3 days. (Figure 1)

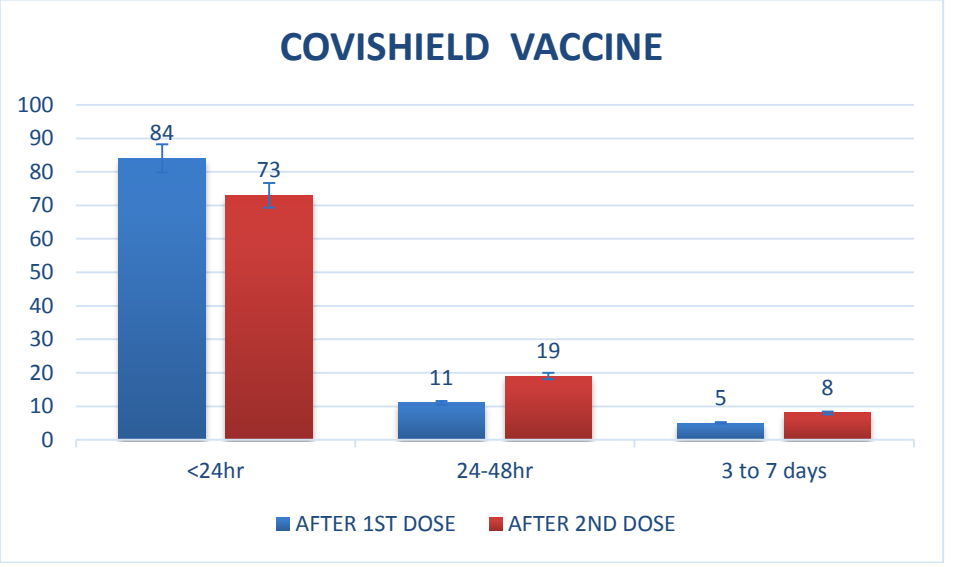


Figure 1. Data are expressed as percentage of subjects shown adverse effects following 1st& 2nd dose of COVISHIELD vaccine at various time intervals.

Subjects who received first dose of COVISHIELD had complained of general weakness (202), fever (198), myalgia (159), headache (153), chills (110), joint pains (78), fatigue (39), giddiness (32), nausea(11), vomiting(9), and rashes (1). Subjects who took second dose of COVISHIELD had experienced side effects like general weakness (97), myalgia (84), fever (74), headache (58), chills (30), Joint pain (29), fatigue (12) and giddiness (5). It is interesting to note that none had vomiting and only 3 participants developed rashes. (Table 1)

Table 1
Number of subjects reported adverse effects after COVISHIELD vaccination

| Adverse effects | | COVISHIELD | | Chi-square | p-value* |
|---|---|---|---|---|---|
| | | 1st dose | 2nd dose | | |
| General weakness | Present | 202 | 97 | 63.06 | <0.0001S |
| | Absent | 158 | 263 | | |
| HEADACHE | Present | 153 | 58 | 60.50 | <0.0001S |
| | Absent | 207 | 302 | | |
| CHILLS | Present | 110 | 30 | 56.75 | <0.0001S |
| | Absent | 250 | 330 | | |
| FEVER | Present | 198 | 74 | 90.85 | <0.0001S |
| | Absent | 162 | 286 | | |
| FATIGUE | Present | 39 | 12 | 15.38 | <0.0001S |
| | Absent | 321 | 348 | | |
| NAUSEA | Present | 11 | 2 | 6.35 | 0.0118S |
| | Absent | 349 | 358 | | |
| VOMITING | Present | 9 | 0 | 9.11 | 0.0025S |
| | Absent | 351 | 360 | | |
| MYALGIA | Present | 159 | 84 | 34.94 | <0.0001S |
| | Absent | 201 | 276 | | |
| JOINTPAIN | Present | 78 | 29 | 26.36 | <0.0001S |
| | Absent | 282 | 331 | | |
| GIDDINESS | Present | 32 | 5 | 20.77 | <0.0001S |
| | Absent | 328 | 355 | | |
| RASHES | Present | 1 | 3 | 1.01 | 0.3160NNS |
| | Absent | 359 | 357 | | |

*- P<0.05 there is a significant association between Adverse effects and COVISHIELD doses by using chi-square. NS: Non-significant S: Significant

**Adverse effects following COVAXIN**

Following the first dose of COVAXIN, 90% had adverse effects in 24 hrs., 8% in 24-48hrs whereas 2% after 3days. Post second dose of COVAXIN, 89% participants had side effects in 24hrs, 7% in 24-48hrs and 4% after 3days. (Figure 2)

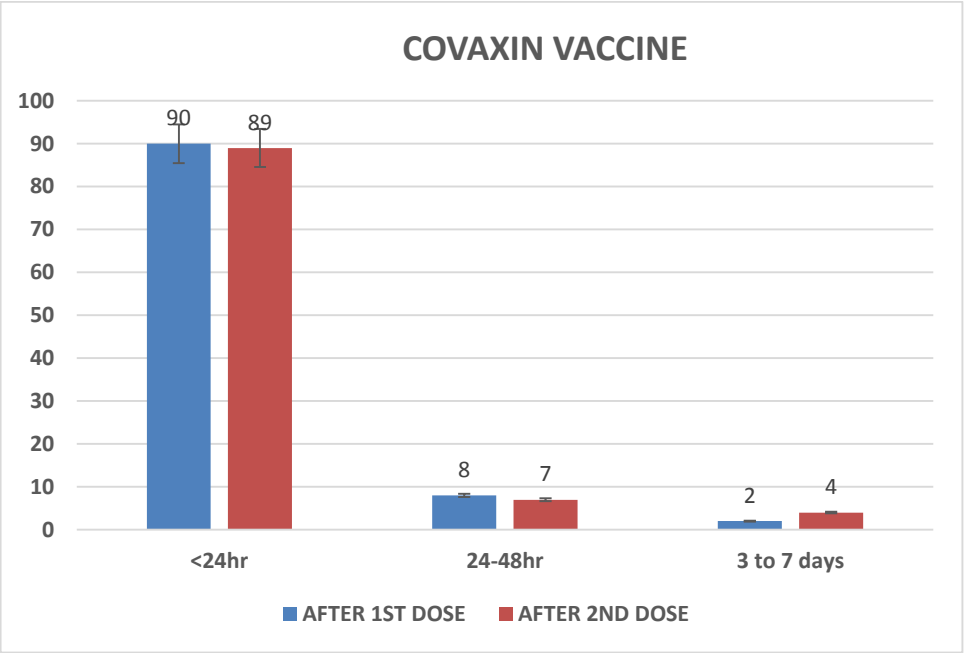


Figure 2. Data are expressed as percentage of subjects shown adverse effects following 1st& 2nd dose of COVAXIN vaccine at various time intervals.

Subjects who took first dose of COVAXIN noticed the adverse effects such as fever (108), general weakness (100), myalgia (88), headache (84), chills (60), joint pain (43), fatigue (15), giddiness (12), vomiting (5) and nausea (4). None of the participants developed rashes. General weakness (56), fever (45), myalgia (40), headache (30), joint pain (15), chills (15), fatigue (6), giddiness (3), vomiting (1), nausea (1) and rashes (1) were experienced by study subjects after second dose of COVAXIN.

Table 2
Number of subjects reported Adverse effects after COVAXIN vaccination

| Adverse effects | | COVAXIN | | Chi-square | p-value* |
|---|---|---|---|---|---|
| | | 1st dose | 2nd dose | | |
| General weakness | Present | 100 | 56 | 19.04 | <0.0001S |
| | Absent | 124 | 168 | | |
| HEADACHE | Present | 84 | 30 | 6.42 | 0.0113S |
| | Absent | 140 | 194 | | |
| CHILLS | Present | 60 | 15 | 32.43 | <0.0001S |
| | Absent | 164 | 209 | | |
| FEVER | Present | 108 | 45 | 39.49 | <0.0001S |
| | Absent | 116 | 179 | | |
| FATIGUE | Present | 15 | 6 | 4.05 | 0.0443S |
| | Absent | 209 | 218 | | |
| NAUSEA | Present | 4 | 1 | 1.82 | 0.1773NS |
| | Absent | 220 | 223 | | |

| | | | | | |
|---|---|---|---|---|---|
| VOMITING | Present | 5 | 1 | 2.70 | 0.1002NS |
| | Absent | 219 | 223 | | |
| MYALGIA | Present | 88 | 40 | 25.2 | <0.0001S |
| | Absent | 136 | 184 | | |
| JOINTPAIN | Present | 43 | 15 | 15.53 | <0.0001S |
| | Absent | 181 | 209 | | |
| GIDDINESS | Present | 12 | 3 | 5.59 | 0.0180S |
| | Absent | 212 | 221 | | |
| RASHES | Present | 0 | 1 | 1.01 | 0.3168NNS |
| | Absent | 224 | 223 | | |

*- P<0.05 there is a significant association between Adverse effects and COVAXIN doses by using chi-square. NS: Non-significant S: Significant

**Discussion**

COVID-19 is highly infectious and hence its prevention is a public health priority and need of the hour owing to non-availability of specific pharmacotherapy. Vaccines have been approved by public health authorities of various countries to immunize the general population which is expected to control the spread of the infection by raising the level of herd immunity and thereby reducing the mortality and morbidity (DeRoo et al., 2020). Although the vaccines became available for the prophylaxis of COVID-19, its hesitancy in public poses a major challenge in effective implementation of immunization programme (Sallam, 2021). During the past two years, many researchers across the globe have conducted studies for proving the safety of COVID-19 vaccines (Forman et al., 2021; Kaur and Gupta, 2020). In continuation of these efforts, we explored the possible adverse effects of COVISHIELD and COVAXIN with respect to first or second dose in Indian population. Earlier studies on these vaccines reported the side effects like general weakness, fever, myalgia and headache, etc. Pain at injection site is commonly complained by vaccine recipients but not considered in this study since it is subjective and varies with injection technique (Ozdemir et al., 2013).

In this study, COVISHIELD received subjects had reported adverse reactions more after first dose when compared to the second dose. More number of adverse effects was noted within 24hrs following first (84%) and second dose (73%) post vaccination when compared to other time intervals. General weakness, fever, myalgia and headache were the significant symptoms observed. In concordance with earlier studies, myalgia and fatigue were the most common effects of vaccination, followed by fever (Zhu et al., 2020; Mohakuda et al., 2021) Similar to other studies, mild adverse effects were reported after the vaccination but resolved in 3 to 7 days (Shrestha et al., 2021). In our study, all the symptoms resolved within 1week and many of them got treated with over-the-counter drugs. Other research works also did not reveal any serious side effect after the 7 days follow up and none of those patients were hospitalized and no fatality was recorded (Mohakuda et al., 2021; Anitha et al., 2021).

Two doses of COVAXIN reported to have 81% efficacy in preventing Corona virus infection. But the safety profile of COVAXIN is not being studied extensively (Ella et al., 2021). Therefore, our study focussed to analyze the possible association of adverse effects following the COVAXIN administration at different time intervals.

We observed similar percentage (90% & 89%) of adverse effects in 24hrs following the first and second dose of COVAXIN respectively. In contrast, a study in different ethnic population observed more adverse reactions with second dose when compared to first dose (Lee et al., 2021). The present study observed the significant side effects such as general weakness, fever and myalgia, Whereas other studies have reported the side effects like headache and fatigue considered to be most common with COVAXIN (Menni et al., 2021; Polack et al., 2020). Notwithstanding with results of the present study, the side effects were mild and disappeared in 3 to 7 days. No life threatening adverse events were seen with the vaccination.

As suggested by WHO 'vaccine should be able to produce high efficacy rate with minimal to no side effects and confer safety up to one year after administration (Kaur et al., 2020). Extensive research is required in various geographical populations to evaluate these parameters like safety and efficacy to combat COVID infection globally. We focussed on the safety measurements by studying the adverse effects in post COVID vaccination. More comparative studies are required to understand the immunological changes which alter the immunogenic response after each dose that will add further knowledge in planning and implementing booster doses.

## Conclusion

The present comparative study on COVISHIELD and COVAXIN vaccines concluded that these vaccines are safer and well tolerated. The adverse reactions resulted were mild and short-lived, eventually subsided within 3-7 days. The frequency and duration of adverse events were almost similar in both the vaccines. However, extensive evaluation is required to assess the long term complications of vaccination that may help for the better planning and implementation of booster dose programmes to curb the disease completely.

## Acknowledgements

The authors are thankful to the management of RVM Institute of Medical Sciences & Research Centre, Hyderabad for their constant support to complete this project.

## References

1. Darbar S, Agarwal S, Saha S. (2021). COVID19 Vaccine: COVAXIN-India's First Indigenous Effective Weapon to Fight against Coronavirus (A Review). *Parana Journal of Sciences Education*, 7(3), 1-9. http://tiny.cc/PJSE24476153v7i3p001-009
2. Das L, Meghana A, Paul P, Ghosh S. (2021). Are We Ready For Covid–19 Vaccines?–A General Side Effects Overview. *Current Medical Research Opinion,* 4(02), 830-841. https://doi.org/10.15520/jcmro.v4i02.398
3. DeRoo SS, Pudalov NJ, Fu LY. (2020). Planning for a COVID-19 vaccination program. *Jama*, 323(24), 2458-2459. https://doi.org/10.1001/jama.2020.8711
4. Forman R, Shah S, Jeurissen P, Jit M, Mossialos E. (2021). COVID-19 vaccine challenges: What have we learned so far and what remains to be

done?. *Health Policy*, 125(5), 553-567. https://doi.org/10.1016/j.healthpol.2021.03.013
5. Hu B, Guo H, Zhou P, Shi ZL. (2021). Characteristics of SARS-CoV-2 and COVID-19. *Nature Reviews Microbiology*, 19(1), 141-154. https://doi.org/10.1038/s41579-020-00459-7
6. Ita K. (2021). Coronavirus disease (COVID-19): Current status and prospects for drug and vaccine development. *Archives of Medical Research*, 52(1), 15-24. https://doi.org/10.1016/j.arcmed.2020.09.010
7. Jaiswal KM, Dudhgaonkar S, Raghute L, Uike P, Kohli S, Anand I. (2021). An assessment of AEFI COVID-19 vaccination in health care workers at a tertiary health care centre in central India. *Microbiology Research International,* 9(2), 46-50. https://doi.org/10.30918/MRI.92.21.017
8. Kaur SP, Gupta V. (2020). COVID-19 Vaccine: A comprehensive status report. *Virus Research,* 288(1), 1-12. https://doi.org/10.1016/j.virusres.2020.198114
9. Kaur U, Ojha B, Pathak BK, Singh A, Giri KR, Singh A, et al. (2021). A prospective observational safety study on ChAdOx1 nCoV-19 corona virus vaccine (recombinant) use in healthcare workers-first results from India. *E Clinical Medicine,* 38(1), 1-11. https://doi.org/10.1016/j.eclinm.2021.101038
10. Kumar VM, Pandi-Perumal SR, Trakht I, Thyagarajan SP. (2021). Strategy for COVID-19 vaccination in India: the country with the second highest population and number of cases. *NPJ Vaccines*, 6(1), 1-7. https://doi.org/10.1038/s41541-021-00327-2
11. Lazarus JV, Ratzan SC, Palayew A, Gostin LO, Larson HJ, Rabin K, et al. (2021). A global survey of potential acceptance of a COVID-19 vaccine. *Nature Medicine*, 27(2), 225-8. https://doi.org/10.1038/s41591-020-1124-9
12. Lee YW, Lim SY, Lee JH, Lim JS, Kim M, Kwon S, et al. (2021). Adverse reactions of the second dose of the BNT162b2 mRNA COVID-19 vaccine in healthcare workers in Korea. *Journal of Korean Medical Science*, 36(21), 1-12. https://doi.org/10.3346/jkms.2021.36.e153
13. Luyten J, Bruyneel L, Van Hoek AJ. (2019). Assessing vaccine hesitancy in the UK population using a generalized vaccine hesitancy survey instrument. *Vaccine,* 37(18), 2494-2501. https://doi.org/10.1016/j.vaccine.2019.03.041
14. Menni C, Klaser K, May A, Polidori L, Capdevila J, Louca P, et al. (2021). 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. *The Lancet Infectious Diseases*, 21(7), 939-949. https://doi.org/10.1016/S1473-3099(21)00224-3
15. Mohakuda SS, Nigam A, Rajesh K, Sashindran VK, Sharma H, Singh B, et al. (2021). Covishield India: Demystifying Myths Through an Early Multicenter Safety Study. *American Journal of Managed Care,* 27(10), 1-10. https://doi.org/10.37765/ajmc.2021.88694
16. Ozdemir, L, Pnarc, E, Akay B N, Akyol A. (2013). Effect of Methylprednisolone Injection Speed on the Perception of Intramuscular Injection Pain. *Pain Management Nursing*, 14(1), 3–10. https://doi.org/10.1016/j.pmn.2010.03.002
17. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. (2020). Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *The New England Journal of Medicine*, 383(27), 2603-2615. https://doi.org/10.1056/NEJMoa2034577

18. Sallam M. (2021). COVID-19 vaccine hesitancy worldwide: a concise systematic review of vaccine acceptance rates. Vaccines, 9(2), 160. https://doi.org/10.3390/vaccines9020160.
19. Seth PK. (2021). A Brief Report of the NASI Webinar on Building Confidence on COVID Vaccines. *National Academy Science Letters*, 44(4), 373-376. https://doi.org/10.1007/s40009-021-01058-7
20. Shrestha S, Devbhandari RP, Shrestha A, Aryal S, Rajbhandari P, Shakya B, et al. (2021). 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 Health Sciences,* 8(1), 9-17. https://doi.org/10.3126/jpahs.v8i1.36242
21. Singh JA, Upshur RE. (2021). The granting of emergency use designation to COVID-19 candidate vaccines: implications for COVID-19 vaccine trials. *The Lancet Infectious Diseases,* 21(4), e103-109. https://doi.org/10.1016/S1473-3099(20)30923-3.
22. World Health Organization - Global Manual on Surveillance of Adverse Events Following Immunization. Available at: https://www.who.int/vaccine_safety/publications/Global_Manual_on_Surveillance_of_AEFI.pdf. Accessed: 10 January 2021.
23. Yan Y, Shin WI, Pang YX, Meng Y, Lai J, You C, et al. (2020). The first 75 days of novel Coronavirus (SARS-CoV-2) outbreak: Recent advances, prevention, and treatment. *International Journal of Environmental Research and Public Health,* 17(7), 1-23. https://doi.org/10.3390/ijerph17072323.
24. Zhu FC, Li YH, Guan XH, Hou LH, Wang WJ, Li JX, et al. (2020). Safety, tolerability, and immunogenicity of a recombinant adenovirus type-5 vectored COVID-19 vaccine: a dose-escalation, open-label. *Lancet,* 395(10240), 1845-1854. https://doi.org/10.1016/S0140-6736(20)31208-3