ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Adverse events following immunization to booster dose (precautionary dose) of COVID-19 vaccine among health-care professionals in a tertiary care teaching institute

Kandula Chaitanya[1], Mary Rohini P[2], Bhuvaneshwari G[3], Edavaluru Shravya[4], Praneeth Reddy O[5]

[1,5]Final Year Postgraduate Resident, [2]Assistant Professor, [3]Professor and Head, Department of Pharmacology, Gandhi Medical College, Secunderabad, [4]Intern, Department of Medicine, Kamineni Academy of Medical Sciences and Research Centre, Hyderabad, Telangana, India

Submission: 16-02-2023 Revision: 03-05-2023 Publication: 01-06-2023

ABSTRACT

Background: The worldwide coronavirus disease-2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus. The Government of India announced the booster dose for patients aged 18 or older on April 10, 2022. The booster dose effectively prevented and controlled the spread of COVID-19. This booster dose was effective against Omicron variant as well. **Aims and Objectives:** The aims of this study were to find out the type of adverse events following immunization to booster dose (precautionary dose) and the treatment for the adverse drug reactions developed to booster dose (precautionary dose) of COVID-19 vaccine. **Materials and Methods:** A prospective study was conducted among 157 health-care professionals over a period of 6 months, in a tertiary care teaching hospital. Subjects were interviewed for any adverse events at the time of vaccination and followed up at 6 months for delayed adverse effects. The data were collected and entered in Microsoft Excel sheet and analyzed using SPSS software. **Results:** Total 157 number of health-care professionals received Booster dose (Precautionary dose) of COVID-19 vaccine in our study. Among 157 recipients, 146 were administered with Covishield vaccine (Group 1) and 11 recipients were given Covaxin (Group 2). Majority of health-care professionals were in the age group of 31–40 years. In them majority of females than males. Six recipients tested positive for COVID-19 virus with Covishield and three with Covaxin (Adverse events noted were fever, headache, body aches, chills, cough, cold, and swelling at the inj. site). There was a statistically significant difference between these two groups with P = 0.01. **Conclusion:** This study concludes that all the reported adverse events to booster dose of COVID-19 vaccine were non serious and were mild to moderate, which have subsided with treatment. Even though few studies on first and second dose of COVID-19 vaccine have evaluated cardiac manifestations, these findings are not evident in the present study. Hence, long-term follow-up studies are required to understand the safety of these vaccines in multiple age groups and with comorbidities.

Key words: Covishield; Covaxin; Pandemic; Vaccines; Corona virus

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v14i6.52569

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

The worldwide corona virus disease-2019 (COVID-19) pandemic is caused by severe acute respiratory syndrome coronavirus.[1] COVID was declared by the World Health Organization as a pandemic caused by Novel Coronavirus and was under Public Health Emergency of International Concern on January 30, 2020.[2]

In India, COVID-19 affected approximately 43 million people and has contributed to 524,706 deaths as of June 06, 2022.[3] India has an important role in the COVID-19

Address for Correspondence:
Dr. Mary Rohini P, Assistant Professor, Gandhi Medical College, Secunderabad, Telangana, India. **Mobile:** +91-9908521401.
E-mail: drmaryrohini@yahoo.co.in

vaccination (first dose and second dose) as it is the second-largest populated country with one of the biggest pharmaceutical manufacturing capacities.[4]

Covaxin includes inactivated virus that is incapable of infecting the receiver but prepares the immune system to act against such viruses.[5-8] Since the vaccine's introduction, 74% of the population has received the first dose, and 65% have received the second dose until June 06, 2022.[9]

A booster dose was introduced in India for the healthcare workers, frontline workers, patients older than age 50, and those with comorbidities (Phase 1) on January 10, 2022.[10] The Government of India announced the booster dose for patients aged 18 or older on April 10, 2022.[11] The booster dose effectively prevented and controlled the spread of COVID-19.[12] This booster dose was effective against Omicron variant as well.

Very little is known about the safety of these vaccines intended to be used in health-care professionals beyond the clinical trial environment. As far as our knowledge goes, there are no studies published to date on adverse events following immunization to booster dose of COVID-19 vaccines.

Hence, this study was initiated to find out the adverse events following immunization to booster dose of COVID-19 vaccines among health-care professionals in a tertiary care teaching hospital, to study adverse events following immunization to booster dose (Precautionary dose) of COVID-19 vaccine among health-care professionals, and to determine the type of adverse events following covishield and covaxin and management for the adverse drug reactions (ADRs) developed to both COVID-19 vaccines.

Aims and objectives

To study Adverse events following immunization to Booster dose (Precautionary dose) of covid-19 vaccine among health care professionals.

To find out the type of Adverse events following immunization to booster dose (Precautionary dose) and the treatment for the ADRs developed to Booster dose (Precautionary dose) of covid-19 vaccines.

MATERIALS AND METHODS

This prospective study was initiated after getting approval from the Institutional Ethics Committee. This study was conducted over a period of 6 months in a tertiary care teaching hospital among the health-care professionals. The data regarding adverse events with covishield and covaxin were collected by interview method at the time of vaccination after taking consent from health-care professionals in tertiary care teaching hospital. Immediately, after the vaccination, recipients were monitored for 24 h for immediate adverse effects, as a part of pharmacovigilance program.

Inclusion criteria

The following criteria were included in the study:

- All health-care professionals who were due for booster dose (precautionary dose) of COVID-19 vaccine.

Exclusion criteria

The following criteria were excluded from the study:

- All health-care professionals who were not willing to take booster dose (precautionary dose) of COVID-19 vaccine were excluded from the study
- Allergic and anaphylactic reactions to previous dose of COVID-19 vaccine.

Later on, vaccine recipients were contacted for type of vaccine, adverse events, and management of ADRs following booster dose (Precautionary dose) of COVID-19 vaccine until 1 month and followed up until 6 months for further ADRs. These adverse events following immunization were handed over to the AMC Center, for further reporting to the National Pharmacovigilance Center, Ghaziabad.

Statistical analysis

The data collected were entered into the Microsoft Excel sheet and analyzed as percentages. P-value was calculated using Fisher exact test. $P<0.05$ is considered as statistically significant.

RESULTS

This study was conducted among health-care professionals who received booster dose (Precautionary dose) of COVID-19 vaccine in tertiary care teaching hospital. Total 157 number of health-care professionals received booster dose (Precautionary dose) of COVID-19 vaccine in our study. Among 157 recipients, 146 were administered with Covishield vaccine (Group 1) and 11 recipients were given Covaxin (Group 2).

Majority of health-care professionals who developed adverse events following immunization were in the age group of 31–40 years (n=32, 26.6%) and only 1.6% (n=2) of health-care professionals were above 70 years of age (Figure 1).

Most of the recipients who developed adverse events following immunization were females (n=65.54%) when compared to males (n=55, 46%) (Figure 2).

Flow chart 1 shows number of recipients developed adverse events following immunization to booster dose (Precautionary dose) of COVID-19 vaccine

Total 157 health-care professionals received vaccine, among them 120 recipients developed ADRs, and 37 recipients did not experience any ADRs.

Majority of the health-care professionals experienced pain at the injection site (n=63, 52.5%) and generalized weakness (n=63.52.5%), followed by fever (n=58, 48.6%), headache (n=52, 43.3%), body aches, chills, cough (n=50, 41.6%), cold (n=40, 33.3%), and swelling at the injection site (n=20, 16.6%) (Figure 3).

Fischer exact test applied and statistically significant (Table 1) 6 (n) (4.1%) recipients tested positive for COVID-19 virus with Covishield and developed symptoms such as fever, chills, cold, and cough. 3 (n) (27.2%) recipients were tested positive for COVID-19 virus with Covaxin. There was a statistically significant difference between these two groups with P=0.01 using Fischer exact test.

Symptoms were mild that maximum number of recipients required paracetamol tablet only that is 85 (70.8%) recipients, 9 (7.5%) of recipients received combination of paracetamol and montelukast tablets, 21 (17.5%) recipients taken paracetamol tablet with azithromycin tablet, and 5 (4.16%) recipients taken combination of fabiflu, doxycycline, augmentin, and montelukast (Figure 4).

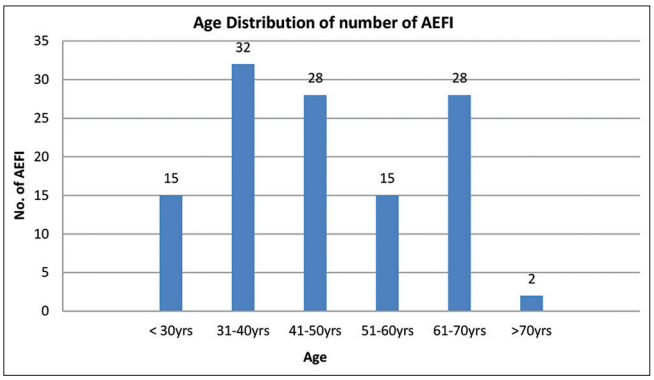


Figure 1: Age distribution of number of adverse events following precautionary dose of COVID-19 vaccine

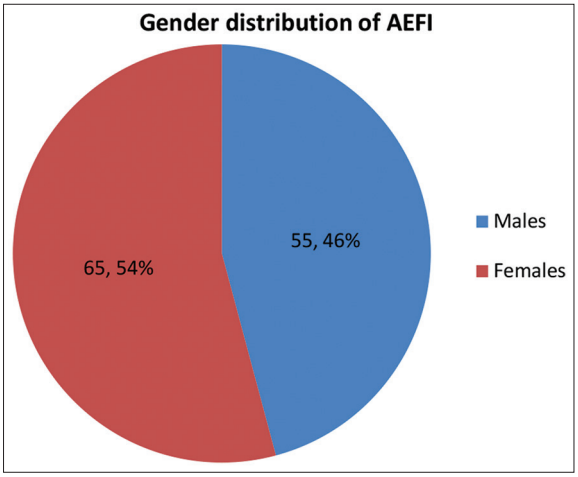
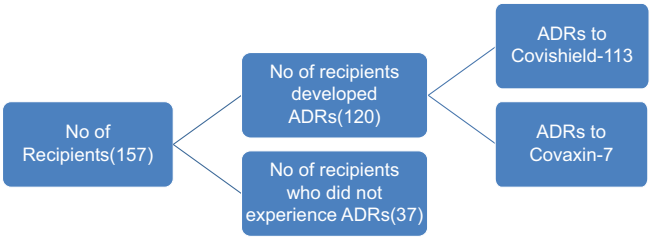


Figure 2: Gender distribution of number of adverse events following precautionary dose of COVID-19 vaccine



Flow chart 1: No of recipients developed adverse events following immunization to booster dose (Precautionary dose) of COVID-19 vaccine.

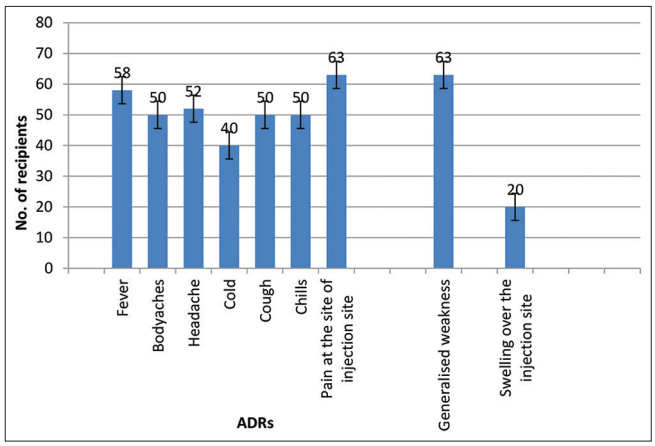


Figure 3: Adverse events following immunization to COVID-19 vaccine

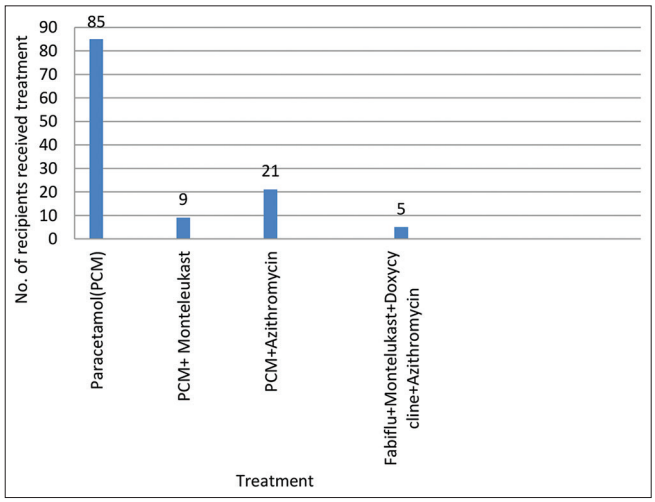


Figure 4: Treatment of adverse events following immunization to booster dose (precautionary dose)

Table 1: Comparison between booster doses of Covishield and Covaxin

Number of Recipients	Group 1 (Covishield)	Group 2 (Covaxin)
Number of recipients received vaccine	146	11
Number of recipients positive for COVID virus	6 (4.1)	3 (27.2)
Number of recipients negative for COVID virus	140 (95)	8 (72.7)
P-value	0.01	

DISCUSSION

In the present study, totally 113 recipients developed adverse events to Covishield and 7 recipients developed adverse events to Covaxin.

Considering the age of the vaccine recipients, in the present study, majority of recipients who developed adverse events following immunization were in the age group of 31–40 years (n=32, 26.6%) and only 1.6% (n=2) of health-care professionals were above 70 years of age. Similar findings were observed in a study done by Konda et al.,[13] whose findings were ages of 18–30 years reported 178 (34.9%) adverse events following immunization and other age groups, 82 (27.4%) recipients between 31 and 45 years of age reported 149 (29.3%) events. This study is also in accordance with the interim analysis of clinical trials data for Covishield that showed that adverse reactions were generally milder and reported less frequently in older adults, that is, 65 years.[14] Polack et al.,[15] observed similar findings in the study on safety and efficacy of BNT162b2 mRNA COVID-19 vaccine, which showed a relatively larger people in the age group of 16–55 years reporting more local reactions (such as pain at injection site, redness, and swelling) and systemic events (such as fatigue, fever, headache, muscle pain, chills, and joint pains) compared to people aged more than 55 years.

In this present study, majority of health-care professionals who developed adverse events following immunization were females (54%) more than males (46%). Similar findings were observed in a study done by Konda et al.,[13] which showed that AEFIs reported more in females (53%) than males (42%). A study done by Kadali et al.,[16] on side effects of BNT162b2 mRNA COVID-19 vaccine in healthcare workers after vaccination, showed that responses to online questionnaire was higher in females (86.55%) compared to males.

In the study by Polack et al.,[15] it was observed that there was slight male predominance in the trial compared to female (50.6 vs. 49.4%). Interim analysis of pooled data from four clinical trials conducted in the United Kingdom, Brazil, and South Africa that aimed at studying the safety and efficacy of ChAdOx1 nCoV-19 vaccine (covishield) also showed more females participants (55.8% vs. 44.2%).[17]

In this study, most frequently reported adverse events were pain at the injection site and generalized weakness, fever, headache, body aches, chills, cough, cold, and swelling at the injection site. Goldlin et al.,[18] and Konda et al.,[13] also observed similar adverse events like mentioned above in their studies. A study done by Aye et al.,[19] showed a potential association between first and second dose of COVID-19 vaccination and cardiac manifestations such as myocarditis and acute MI, but, in the present study, none of the recipients complained of cardiac manifestations. Polack et al.,[15] observed similar findings in the study on safety and efficacy of BNT162b2 mRNA COVID-19 vaccine reporting more local reactions (such as pain at injection site, redness, and swelling) and systemic events (such as fatigue, fever, headache, muscle pain, chills, and joint pains).

In the present study, booster dose (Precautionary dose) Covishield was taken by 146 recipients, whereas only 11 recipients received Covaxin booster dose (Precautionary dose). Six recipients were tested positive for COVID-19 virus with Covishield and developed all symptoms such as fever, chills, cold, and cough. Three recipients were tested positive for COVID-19 virus with Covaxin. There was a statistically significant difference between these two groups (P=0.01).

In the present study, recipients who developed ADRs to booster dose received treatment, symptoms were mild that maximum number of recipients required paracetamol tablet only that is 70.30% recipients, 7.40% of recipients needed combination of paracetamol and montelukast tablets, 18.30% recipients needed paracetamol tablet with azithromycin tablet, and 3.70% recipients required combination of fabiflu, doxycycline, augmentin, and montelukast.

Limitations of the study

Strength of the study is prospective design of the study and limitations of the study include; it is a single centered study. Limitations can be overcome by conducting in multiple centers over long-term period.

CONCLUSION

This study concludes that all the reported adverse events to booster dose of COVID-19 vaccine were non-serious and were mild to moderate, which have subsided with treatment. Even though few studies on adverse events following immunization to first and second dose of COVID-19 vaccine have evaluated cardiac manifestations, these findings are not evident in the present study. Hence, long-term follow-up studies are required to understand the safety of these vaccines in multiple age groups and with comorbidities.

ACKNOWLEDGMENT

We would like to Acknowledge Principal, Vice Principal, and the Management of Gandhi medical college and hospital for giving permission to conduct the study in this institution.

REFERENCES

1. Alwan NA, Burgess RA, Ashworth S, Beale R, Bhadelia N, Bogaert D, et al. Scientific consensus on the COVID-19 pandemic: We need to act now. Lancet. 2020;396(10260):e71-e72.
   https://doi.org/10.1016/S0140-6736(20)32153-X
2. World Health Organization. Statement on the Second Meeting of the International Health Regulations (2005) Emergency Committee Regarding the Outbreak of Novel Coronavirus (2019-nCoV). Geneva: World Health Organization; 2020. Available from: https://www.who.int/news/item/27-04-2020-who-timeline---covid-19 [Last accessed on 2021 Feb 14].
3. WHO Coronavirus (COVID-19) Dashboard; 2022. Available from: https://covid19.who.int [Last accessed on 2022 Jun 06].
4. India Rolls out the World's Largest COVID19 Vaccination Drive, 2021. Available from: https://www.who.int/india/news/feature-stories/detail/india-rolls-out-the-world-s-largestcovid-19-vaccination-drive [Last accessed on 2021 Apr 25].
5. Fortune. Why India Just Might Pull Off 'the World's Largest Vaccination Program'. New York: Fortune; 2021. Available from: https://www.fortune.com/2021/01/15/india-covid-vaccine-registration-campaign [Last accessed on 2021 Apr 25].
6. Folegatti PM, Ewer KJ, Aley PK, Angus B, Becker S, BelijRammerstorfer S, 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):467-478.
   https://doi.org/10.1016/S0140-6736(20)31604-4
7. Tapia MD, Sow SO, Mbaye KD, Thiongane A, Ndiaye BP, Ndour CT, et al. Safety, reactogenicity, and immunogenicity of a chimpanzee adenovirus vectored Ebola vaccine in children in Africa: A randomised, observer-blind, placebo-controlled, phase 2 trial. Lancet Infect Dis. 2020;20(6):719-730.
   https://doi.org/10.1016/S1473-3099(20)30019-0
8. Voysey M, Clemens SA, Madhi SA, Weckx LY, Folegatti PM, Aley PK, et al. Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: A pooled analysis of four randomised trials. Lancet. 2021;397(10277):881-891.
   https://doi.org/10.1016/S0140-6736(21)00432-3
9. Tracking the Coronavirus Vaccinations around the World; 2022. Available from: https://www.nytimes.com/interactive/2021/world/covid-vaccinations-tracker.html [Last accessed on 2022 Jun 06].
10. Guidelines for COVID-19 Vaccination of Children between 15-18 Years and Precaution Dose to HCWs, FLWs and 60+ Population with Comorbidities; 2022. p. 6. Available from: https://www.mohfw.gov.in/pdf/guidelinesforcovid19vaccinationofchildrenbetween15to18yearsandprecautiondosetohcwsflws&6 [Last accessed on 2022 Jun 06].
11. Precaution Dose to be Available to 18+ from April 10: Key Points; 2022. Available from: https://www.timesofindia.indiatimes.com/india/precaution-dose-to-be-available-to-all-from-april-10-key-points/articleshow [Last accessed on 2022 Jun 06].
12. Chenchula S, Karunakaran P, Sharma S and Chavan M. Current evidence on efficacy of COVID-19 booster dose vaccination against the Omicron variant: A systematic review. J Med Virol. 2022;94(7):2969-2976.
    https://doi.org/10.1002/jmv.27697
13. Konda VC, Gokul T, Poojitha M and Rao KU. Adverse events following immunization to Covid-19 vaccines in a tertiary care hospital-a descriptive study. Biomed Pharmacol J. 2021;14(4):2149-2156.
    https://doi.org/10.13005/bpj/2312
14. Serum Institute of India. Coronavirus Disease (COVID-19) Vaccines. Maharashtra, India: Serum Institute of India; 2021. Available from: https://www.seruminstitute.com/product_covishield [Last accessed on 2021 Apr 19].
15. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med. 2020;383(27):2603-2615.
    https://doi.org/10.1056/NEJMoa2034577
16. Kadali RA, Janagama R, Peruru S and Malayala SV. Side effects of BNT162b2 mRNA COVID-19 vaccine: A randomized, cross-sectional study with detailed self-reported symptoms from healthcare workers. Int J Infect Dis. 2021;106:376-381.
    https://doi.org/10.1016/j.ijid.2021.04.047
17. 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(10269):99-111.
    https://doi.org/10.1016/S0140-6736(20)32661-1
18. Goldlin TJ, Kalyanaraman S, Ravichandran M and Ramya JE. A pharmacovigilance study of covishield in a tertiary care teaching hospital in Tamil Nadu. J Pharmacol Pharmacother. 2021;12(3):131-136.
    https://doi.org/10.4103/jpp.jpp_63_21
19. Aye YN, Mai AS, Zhang A, Lim OZ, Lin N, Ng CH, et al. Acute myocardial infarction and myocarditis following COVID-19 vaccination. QJM. 2021;hcab252.
    https://doi.org/10.1093/qjmed/hcab252

Authors Contribution:
KC- Definition of intellectual content, literature survey, prepared first draft of manuscript, implementation of study protocol, data collection, data analysis, manuscript preparation and submission of article; **MRP-** Concept, design, clinical protocol, manuscript preparation, editing, and design of study, statistical analysis and interpretation; **BG-** Coordination and manuscript revision; **PRO-** Data collection, prepared first draft of manuscript, implementation of study protocol; **ES-** Literature survey and preparation of figures.

Work attributed to:
Department of Pharmacology, Gandhi Medical College and Hospital, Secunderabad, Telangana, India.

Orcid ID:
Kandula Chaitanya - https://orcid.org/0009-0008-3713-2249
Mary Rohini P - https://orcid.org/0000-0001-8593-1637
Bhuvaneshwari G - https://orcid.org/0000-0002-2052-5301
Edavaluru Shravya - https://orcid.org/0009-0009-2118-2513
Praneeth Reddy O - https://orcid.org/0009-0004-6620-6332

Source of Funding: None, **Conflicts of Interest:** None.