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STUDY OF ADVERSE EVENTS AND BREAKTHROUGH INFECTION FOLLOWING COVID-19 VACCINATION

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ABSTRACT

Background: Covid-19 pandemic which started in China in 2019 created a chaos worldwide. Since COVID-19 has no known cure, vaccinations and preventive measures like COVID-19 appropriate conduct continue to be the mainstay of security. **Methods:** This is a retrospective observational study where in a total of 579 individuals of either gender, above 18 years of age who had received at least one dose of any of the two COVID-19 vaccines (Covishield or Covaxin) were studied. Information was gathered using a self-designed, pretested, semi-structured questionnaire using a Google Form which was shared via WhatsApp and electronic mail to participants meeting the selection criteria. **Results:** Around 579 participants were studied, 87% (501) participants received covishield and 13% (78) participants received covaxin. Number of participants taking 2 doses were 85% (491). Around 79.6% (461) participants experienced adverse events after 1st dose of vaccination out of which 80.2% participants experienced after covishield and 77% participants experienced after covaxin. Around 48.06% (236) participants experienced adverse events after 2nd dose of vaccination out of which 48.9% participants experienced after covishield and 40% of participants experienced after covaxin. More number of participants experienced adverse events after 1st dose than compared to the 2nd dose and this difference was statistically significant ($p \leq 0.0001$). Breakthrough infection were seen in 3.59% and 4.75% participants after 1st and 2nd dose of covishield respectively and 11.53% and 5.76% participants after 1st and 2nd dose of covaxin respectively. However, they were mild and none of them had to be hospitalized.

KEYWORDS: COVID-19, vaccination, Adverse-events, Breakthrough infection.

INTRODUCTION

In the world's fight against the COVID-19 pandemic, vaccines emerged as the greatest saviour of mankind. Many vaccine candidates were developed and entered clinical trials in early 2020. Many of these vaccines obtained emergency approval and governments around the world-initiated vaccination campaigns against COVID-19.[1,2]

COVID-appropriate behavior and vaccines remain the mainstay of protection. During the pandemic, vaccines against COVID-19 were developed at an unprecedented speed. These vaccines had a different level of effectiveness and were approved for emergency use. In India, five vaccines were approved by the Drugs Controller General of India till date they being Covishield (ChAdOx1), COVID-19 vaccine (Covaxin) (BBV152), SputnikV, Johnson &Johnson, and Zycov-D.[3,4,5]

Nation-wide COVID-19 vaccination was started on January 16, 2021, initially for the health care workers (HCWs). On March 1st and April 1st, vaccination drive was extended for those aged more than 60 years and 45–59 years, respectively. After May 1, 2021, it was extended to the 18–44 years age group extending its accessibility.[6]

COVAXIN®, India's indigenous ***COVID-19 vaccine*** by Bharat Biotech was developed in collaboration with the Indian Council of Medical Research (ICMR) - National Institute of Virology (NIV) in ***BSL-3 (Bio-Safety Level 3)*** high containment facility. The vaccine was developed using ***Whole-Virion Inactivated Vero Cell*** derived platform technology and they don't replicate and are therefore unlikely to revert and cause pathological effects. It is a 2-dose (0.5ml) vaccination regimen given 28 days apart. It is administered as an injection into the deltoid muscle of the upper arm. It is a vaccine with no sub-zero storage, no reconstitution requirement, and

ready to use liquid presentation in multi-dose vials, stable at 2-8°C.[7]

Covishield is developed by "Viral Vector Platform Technology". Recombinant, replication-deficient chimpanzee adenovirus vector encoding the SARS-CoV-2 Spike (S) glycoprotein. Produced in genetically modified human embryonic kidney (HEK) 293 cells. This genetically modified virus can very well command the immune system to prepare a mechanism against such viruses and consists of two different doses of 0.5 mL each. The 2nd dose should be administered between 28 to 42 days after the 1st dose. However, there is data available that suggests the administration of the 2nd dose up to 84 days (12 weeks) or more, has a better efficacy. It is administered as an injection into the deltoid muscle of the upper arm.[8]

COVAXIN demonstrated **77.8%** vaccine efficacy against symptomatic COVID-19 disease, **93.4%** against severe symptomatic COVID-19 disease and **63.6%** against asymptomatic COVID-19.[9] However, covishield vaccine had a protective efficacy of **67%** for preventing symptomatic and laboratory-proven Covid-19 and of nearly **100%** (72–100%) for preventing hospitalization and severe infection.[10]

There have been few studies related to AEFI (adverse events following immunization) after COVID-19 vaccination in recent times. The majority of the studies were on Covishield (ChAdOx1) and Covaxin. This study was done to record and compare the adverse events following covishield and covaxin vaccination and also to record breakthrough infection after covid vaccination.

Aims and Objectives

1. To evaluate the occurrence of adverse events following immunization (AEFI) amongst Health Care Workers with either one or two doses of Covishield and Covaxin.
2. To study the breakthrough infections after covid vaccination.

MATERIAL AND METHODS

This is a retrospective observational study conducted in a rural tertiary care hospital in Karnataka. It is a questionnaire-based study carried out to evaluate the occurrence of adverse events following immunization (AEFI) amongst health care workers of either gender who had received at least one dose of any of the two COVID-19 vaccines (Covishield or Covaxin) and also to study the breakthrough infections after vaccination. Information was gathered using a self-designed, pretested, semi-structured questionnaire using a Google Form which was shared via the social media platform (WhatsApp) and electronic mail to participants meeting the selection criteria. Institute Ethical committee approval was obtained before starting the study.

Definition

Adverse event following immunization is any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine.

When someone who is vaccinated with either a primary series or a primary series plus a booster dose gets infected with the virus that causes COVID-19, it is referred to as a **"vaccine breakthrough infection."**

Inclusion criteria

Age >18 years, who had received either one or two doses of covid vaccine.

Exclusion criteria

1. Age <18 years.
2. Pregnant and lactating women.
3. Those with prior history of reaction to vaccine of any kind.

Statistical analysis

The data were entered in Microsoft Excel and analysed using SPSS version 20.00. Descriptive Statistics were used to assess the baseline data. All quantitative variables were presented in frequency and percentages and mean. Continuous variables were expressed as mean (standard deviation) and categorical variables were expressed frequency and percentage. The difference in adverse effects based on the type of vaccine and doses were compared using the chi-square test. p value < 0.05 was considered statistically significant.

RESULTS

The study population consisted of 579 participants. Majority, 412 (71.15%) of participants, belonged to the age group of 20-30 years. Majority were female participants (357, 62%). 501(87%) participants received covishield and 78(13%) received covaxin. 491 (85%) participants received 2 doses of vaccine, whereas 88(15%) received only 1 dose.

Table 1: Demographic profile of participants of covid-19 vaccination (n=579).

Demographic profile	Number of participants, n (%)
Age group	
18-20 years	64(11%)
21-30 years	412(71.15%)
31-40 years	50(8.63%)
41-50 years	30(5.18%)
51-60 years	14(2.41%)
61-70 years	7(1.2%)

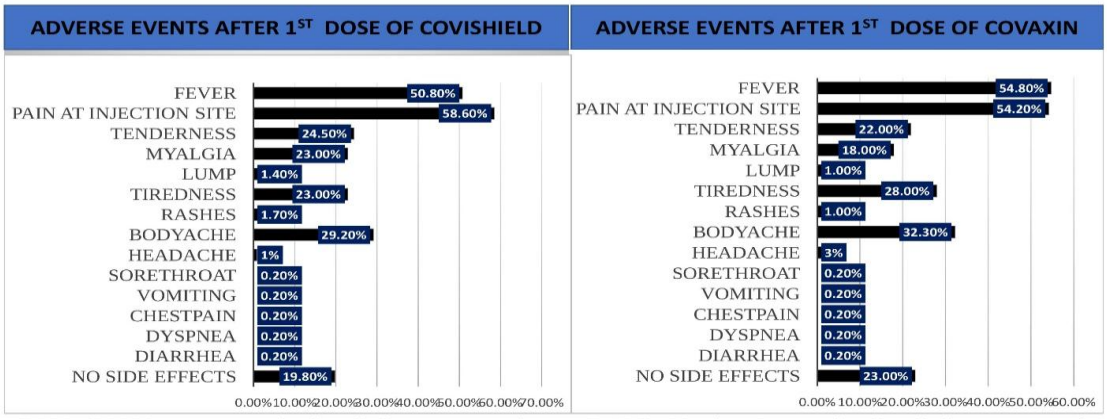
71-75 years	2(0.34%)
Mean age	28.05
Sd (standard deviation) age	8.75
Gender	
Male	222(38%)
Female	357(62%)

Around 461(79.6%) participants experienced adverse events after 1st dose of which 401/501(80.2%) after covishield and 60/78 (77%) after covaxin.

FIGURE 1 shows that pain at injection site, fever were the most predominant adverse event after 1st dose of both covishield and covaxin vaccination.

Around 236(48.06%) participants experienced adverse events after 2nd dose of vaccination out of which 215/439 (48.9%) after covishield and 21/52 (40%) after covaxin.

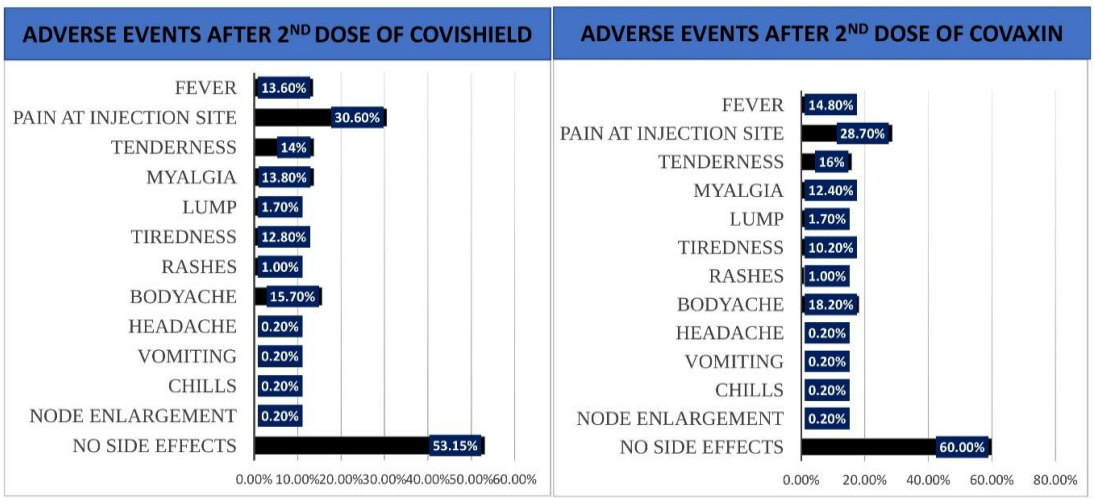
FIGURE 2 shows that pain at injection site, body ache were predominant adverse events seen after 2nd dose of both covishield and covaxin vaccination.



401/501(80.2%) participants developed adverse events after 1st dose. Predominant adverse events were Pain at injection site (293/501 ;58.6%), Fever (284/501 ;50.8%), Body ache (146/501 ;29.2%).

60/78 (77%) of participants developed adverse events after 1st dose. Predominant adverse events were Pain at injection site (42/78 ;54.2%), Fever (43/78 ;54.8%), Body ache (25/78 ;32.3%).

Figure 1: Comparison of adverse events after 1st dose of covid vaccine.



215/439 (48.9%) participants developed adverse events after 2nd dose. Predominant adverse events were Pain at injection site (135/439 ;30.5%), Body ache (69/439 ;15.6%), Fever (60/439 ;13.5%).

21/52 (40%) of participants developed adverse events after 2nd dose. Predominant adverse events were Pain at injection site (16/52 ;30.6%), Body ache (8/52 ;15.7%), Fever (7/52;13.6%).

Figure 2: Comparison of adverse events after 2nd dose of covid vaccine.

Adverse events were predominantly seen after one to four hours post vaccination and lasted for 2 -3days. Adverse events following vaccination were similar in covishield and covaxin.

Participants who received the first dose of Covaxin, 60 (77%) participants out of 72 participants reported experiencing adverse events while 21(40%) participants out of the 51 participants who had received the second dose of vaccine reported experiencing adverse events and this difference was statistically significant ($p \leq 0.0001$).

Participants who received the first dose of Covishield vaccine, 401(77%) participants out of 501 participants reported experiencing adverse events while 215(48%) participants out of the 439 participants who had received the second dose of vaccine reported experiencing adverse events and this difference was statistically significant ($p \leq 0.0001$).

Large number of participants experienced adverse events after first dose compared to second dose of vaccine. However, adverse events following covid vaccination were mild. No serious adverse events (embolic, thrombotic events, myocarditis) had been reported during this survey.

Figure 3 shows Breakthrough infection after covid vaccination.

Breakthrough infection after 1st dose occurred in 18/501(3.59%) after covishield and 9/78(11.53%) after covaxin. 21/439 (4.75%) after covishield and 3/52(5.76%) after covaxin contracted breakthrough infection after 2nd dose. Breakthrough infection after covid vaccine were more commonly seen after covaxin. However, breakthrough infections after vaccination were mild and none of them had to be hospitalized.

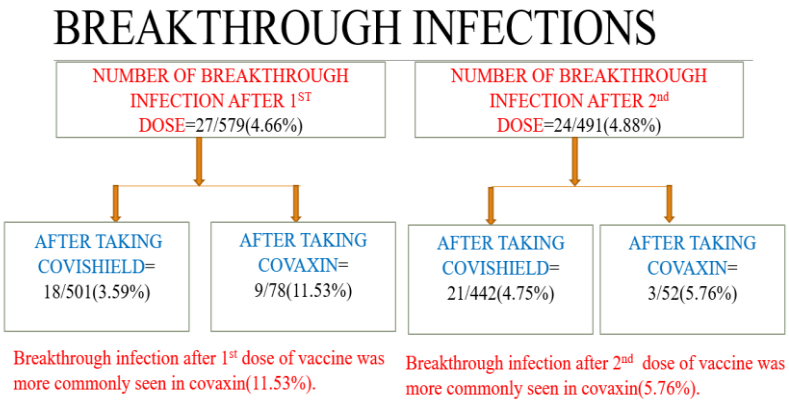


Figure 3: Breakthrough infection after covid vaccine.

DISCUSSION

In this study, we have studied AEFI among Covaxin and Covishield beneficiaries. Higher AEFI was reported among the beneficiaries who took the first dose when compared to the second dose. The majority of the AEFI was mild in nature. Pain at the injection site was the most common AEFI, followed by fever and body ache. Similarly, in a study conducted by Parida et al.[11] injection site pain, tenderness, fever, headache, fatigue, and myalgia were reported as the AEFI following vaccination.

The mean age of the people vaccinated in this study was 28.05 years. The cross-sectional study done by Kotiwale V A *et al* reported that the mean age of the participants was 38.54 years.[12]

Majority of participants in this study were female. Females reported higher AEFI than males in our study. Similarly, in a cross-sectional study conducted in Malaysia it was reported females experienced more adverse events than males.[13]

The AEFI following covishield was 77% after the first dose and 48% after the second dose. Similarly, in a study done by *M. N. Alam et al*[14] it was 100% and 20% after first and second-dose respectively.

The AEFI following covaxin was 77% after the first dose and 40% after the second dose. Similarly, in a study done by Parida et al[11] in a tertiary center it was reported 38.1% and 26.4% after first and second-dose respectively.

AEFI data in India showed that there is a very miniscule but definitive risk of thromboembolic events. The reporting rate of these events in India is around 0.61/million doses.[15] No serious adverse events (embolic and thrombotic events) were found in our study.

The proportion of breakthrough infection after the 1st dose of vaccination was 3.5% (18/501) after covishield and 11.53% (9/75) after covaxin. The proportion of breakthrough infection after the 2nd dose of vaccination was 4.75% (18/501) after covishield and 5.76% (3/52)

after covaxin. Breakthrough infection after covid vaccination was more common after covaxin. Similarly, in a study done by Krishna et al found that breakthrough infection prevalence was less with Covishield™ (21.41%) when compared to Covaxin® (31.84%).[16]

Limitations of the study

Small sample size to assess serious/rare AEFI. The study was conducted only on health care workers. Hence, there is possibility of reporting bias as reporting of adverse events might be different from the general population. Results of the study might not be a true representation of the incidence of adverse events and bigger metacentric studies are required to generalize the results to the universal population. We did not include the data according to existing common medical conditions of recipients, hence could have altered the incidence of adverse events. Also, we evaluated only short-term adverse effects, and long-term surveillance in the global population will be required to investigate possible future effects.

CONCLUSION

To conclude higher number of participants who received Covishield experienced adverse events compared to those who received Covaxin. A greater number of participants experienced adverse events after first dose compared to second dose of the covid vaccine which was statistically significant. However adverse events were mild and similar after both covishield and covaxin. Higher number of participants who received Covaxin contracted breakthrough infection. Covid-19 vaccination did not prevent break through infection but break through infection after vaccination was not severe and none of them needed hospitalization. Hence, the need of the hour is to acknowledge the importance of covid-19 vaccination and its role in preventing severe infection and minimizing ICU admission.

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Conflicts of interest

There are no conflicts of interest.

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