RESEARCH ARTICLE

A participant centered surveillance of adverse events following coronavirus disease immunization phase 1 at a tertiary care teaching hospital

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ABSTRACT

Background: Coronavirus disease (COVID-19) pandemic is caused by severe acute respiratory syndrome coronavirus. Vaccines could play an important role in increasing population immunity. Adverse events following immunization (AEFI) is a recent development to improve the speed and transparency of vaccine safety post-marketing.

Aim and Objective: To describe adverse events following COVID-19 immunization phase 1.

Materials and Methods: An observational primary questionnaire-based study was conducted regarding AEFI after getting approval from Institutional Ethics Committee. Total 241 health care providers were sent pretested and validated questionnaires through SMS containing online Google form link, data were collected. AEFI was classified and percentage value calculated, association between age and gender difference established by Chi-square test.

Results: Among 241 health care providers 103 were voluntarily participated. Following 1st dose of vaccination, out of 103 healthcare provider 45 (44%) experienced local as well as systemic kind of reactions. Most common local and systemic reaction were pain at injection site and fever respectively. Following 2nd dose of vaccination, out of 103 healthcare providers, 29 (28.40%) experienced local as well as systemic reaction. Most common local and systemic reaction were pain at injection site and headache respectively. NSAIDS were most commonly used medication to resolve AEFI after 1st and 2nd dose of vaccine.

Conclusion: Vaccine have side effects, but none of them are as severe as the disease itself. Active surveillance for adverse events to vaccine is a good method for detecting and quantifying mild adverse events.

KEY WORDS: Coronavirus disease immunization; Adverse events following immunization; Active surveillance

INTRODUCTION

The coronavirus disease (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has caused widespread impact on health, including higher rate of mortality among older adults and those with pre-existing health conditions and, various preventive measures such as social distancing, covering nose and mouth with mask are taken across the world to prevent spread of pandemic.

Vaccines could play an important role in increasing population immunity, preventing severe disease, and reducing the ongoing health crisis. In response, rapid global efforts to develop and test vaccines against SARS-CoV-2 have led to an unprecedented number of candidate vaccines starting clinical trials during 2020.[1] Active participant-centered monitoring of adverse events following immunization (AEFI) is a recent development to improve the speed and transparency of vaccine safety post-marketing.[2]

Vaccines are a unique pharmaceutical product because they are recommended for nearly everyone in the community.[3]
Local side effects, such as swelling, redness, and pain at the injection site are commonly occur recipients. Fever, tiredness, and myalgia are also commonly seen AEFI.[4]

In India, nationwide vaccination for covid-19 was started on January 16, 2021, in which COVISHIELD™ was given to front line health care workers in phase 1 of immunization.[5]

AEFI is defined as “any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the use of the vaccine.”[6]

The COVISHIELD™ vaccine is a recombinant, replication-deficient chimpanzee adenovirus vector vaccine encoding the SARS COV-2 spike glycoprotein. This vaccine contains genetically modified organisms produced in genetically modified human embryonic kidney 293 cells.[7]

COVISHIELD™ vaccine manufactured by Serum Institute of India Pvt Ltd is similar to the COVID-19 Vaccine AstraZeneca (manufactured by AstraZeneca), a ChAdOx1 nCoV-19 Corona Virus Vaccines and requires two separate doses of 0.5 ml intramuscular (IM) injection, 2nd dose administered between 4 and 6 weeks apart.[7,8]

In animal studies and clinical trial COVISHIELD™ has shown safe profile. They have shown that the adenovirus-vectored vaccine ChAdOx1 nCoV-19, encoding the spike protein of SARS CoV-2, is immunogenic in mice, eliciting a robust humoral and cell-mediated response.[9]

Post-marketing surveillance is crucial to study the safety of vaccines recently marketed, for which the safety pattern could be not clearly defined in the registration studies.[10] Post-marketing surveillance has traditionally relied on passive (or spontaneous) reporting from consumers and health providers.[11] The surveillance of vaccine safety is an essential requirement in vaccination programmes.[12]

However, post-marketing vigilance of AEFI is equally essential to prove its short and long-term safety in general population. Very few studies have been conducted on AEFI following covid-19 vaccination in India so we conducted this study for surveillance of AEFI of covid-19 vaccination carried out at our tertiary care teaching hospital.

**MATERIALS AND METHODS**

The study was carried out at our tertiary care teaching hospital after obtaining written permission from the Institutional Ethics Committee with a number of CUSMC/IEC(HR)/RP-02/2021/Approval-RP-02/1578.

It was an observational, primary, questionnaire-based study involving health care providers vaccinated with 1st dose of COVISHIELD™ vaccine between 16th and 26th January 2021 and 2nd dose of between 15th and 26th February 2021 at the tertiary care teaching hospital. Study was conducted in two parts, same participants were included in the study following 1st and 2nd dose of vaccination.

At the vaccination site, the AEFI monitoring room was established to observe and inform regarding the development of AEFI post-vaccination, all healthcare providers were observed for 30 min.

Total 241, healthcare providers were given information about the study telephonically, then SMS containing link of pretested and validated questionnaires based online Google form was sent and responses were analyzed. Which is shown in flow chart in Figure 1.

Participants were asked to fill Google form-based questionnaires divided into five sections, 1st section comprised participants informed consent. Second section comprised socio-demographic data i.e., age, gender, education qualification. The 3rd and 4th sections comprised 10 questions regarding the AEFI after vaccination and the 5th section comprised of thanking message regarding participation in the study.

Data were analyzed in Microsoft excel sheet 2013. And the association between age and gender difference was established by Chi-square test where P-value < 0.05 is significant.

**RESULTS**

Among 241 healthcare providers, 103 voluntarily participated in the study. After the 1st dose of vaccination 58 (56%), healthcare providers did not experience any kind of reaction whereas 45 (44%) healthcare providers experienced local (pain/swelling/redness at injection site) as well as systemic (fever, muscle pain, headache, nausea, vomiting) reaction, while after 2nd dose of vaccination 74 (71.60%) healthcare providers did not experience any kind of reaction whereas...
29 (28.40%) healthcare providers did experience a local as well systemic reaction. Socio demographic classification of data was done according to age and gender, among participants 67 (65%) were male and 36 (35%) were female, out of 67 males 23 (34%) and among 36 females 22 (61%) had experienced AEFI. In 2nd dose there were 68 (66%) male and 35 (34%) female, among which 16 (24%) male and among 13 (38%) female had experienced reactions. On application of Chi-square test, it was observed that difference in gender is statistically significant in 1st dose ($\chi^2 = 6.82$, $P = 0.0008$, Df = 1), while it is not significant in 2nd dose ($\chi^2 = 2.11$, $P = 0.14$, Df = 1). Participants were divided into 3 groups, 18–38, 38–58, and 58–78. After 1st and 2nd dose of vaccination most common AEFI was seen in 18–38 years of age groups, they are shown in Figure 2. It was observed that difference in age is statistically significant in 1st dose ($\chi^2 = 23.66$, $P = 0.0000073$, Df = 1), while it is not significant in 2nd dose ($\chi^2 = 2.639$, $P = 0.269$, Df = 1).

Adverse events were categorized as local and systemic reactions. Most common local reaction following 1st and 2nd dose of vaccination was pain at injection site 42 (93.33%) and 22 (75.86%), respectively, they are shown in Figure 3. Most common systemic reaction following 1st dose of vaccination was fever 26 (57.78%) and the following 2nd dose of vaccination was headache 18 (62.06%), they are shown in Figure 4. Other reactions experienced are shown in Figures 5 and 6 respectively following 1st and 2nd dose of vaccination.

33 (73.33%) participants took medication to resolve AEFI among them non-steroidal anti-inflammatory drugs (NSAIDS) 30 (69.77%) were the most commonly used medication, after 2nd dose 19 (65.51%) participants did take

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medication to resolve the reactions same as the 1st dose most commonly used class of medication was NSAIDS 17 (58.60%), followed by other class of medication was I (3.4%) steroids. These results are shown in Figure 7.

Reactions were resolved in 96% of participants in 1st dose, whereas 97% participants in 2nd dose following medication.

Post 1st dose of vaccination, 11% participant and post 2nd dose 3% participant reported to the pharmacovigilance authority about adverse events.

**DISCUSSION**

In India biggest vaccination drive started from January 16, 2021, for COVID-19 immunization. The objective of the study was to describe AEFI. In this study, AEFI was seen in 45 (44%) after 1st dose and 29 (28.40%) after 2nd dose of vaccination. Females were experienced more AEFI in both doses of vaccination. 58–78 years of age group experienced less AEFI. The most common local reaction was pain at injection site following both doses of vaccination, whereas after 1st dose and 2nd dose most common systemic reaction was fever and headache respectively. The most common medication used to resolve reaction were NSAIDS.

We have observed that the incidence of AEFI was relatively higher among females compared with males in study populations which is contradictory to findings reported by Sebastian et al.[13] our findings are statistically significant after 1st dose while not after 2nd dose, which may be due to prophylactically measure taken by individuals. About 58–78 years of age group did not experience any kind of AEFI after 1st dose of vaccination. Furthermore, the most common reactions were observed in 18–38 years of age group in both doses. There were less reactions observed in older individuals compared to younger individuals similar findings were observed in a study conducted by Ramasamy et al.[6] Our findings are statistically significant after 1st dose. These findings were encouraging because older individuals are at disproportionate risk of severe COVID-19.[10] Most common AEFI observed in local reaction was pain at injection site, while the most common systemic reaction observed after 1st dose of vaccine was fever followed by muscle pain and headache. These results match with the study conducted by Folegatti et al.[1] Whereas after 2nd dose of vaccination most common systemic reaction was headache followed by fever and muscle pain. The common AEFIs observed in our study and the frequency of occurrence were comparable to the data from the interim analysis of pooled data on adenoviral vector COVID-19 vaccine (Oxford/AZ-ChAdOx1 nCov-19) from four clinical trials conducted in the United Kingdom, Brazil, and South Africa.[11] Most of our participants had mild symptoms and the symptoms resolved within a few days which is similar to the finding in the interim analysis of the pooled data.[14] The COVISHIELD™ was found safe and well-tolerated in phase II/III clinical trial in India and in an interim analysis adverse events after the first dose were comparable to the Oxford/AZ-ChAdOx1 nCov-19 vaccine.[15] Most common used medication to resolve the AEFI was NSAIDS after both the doses of vaccine and the reactions were symptomatically treated, and no any serious adverse reactions were noted. Anaphylactic or acute hypersensitivity reactions may be life-threatening, one must look for such sudden onset reaction and all emergency medicine should kept ready before hand.[4] Through such any anaphylactic reactions were not reported in this study. In our study, we did not receive any AEFI related to pulmonary embolism and deep venous thrombosis.

The present study shows that there were no serious AEFI reported after vaccination, which describes the safety of the vaccine. Limitation of the study is sample size was very less, more data can be generated from a study with larger sample size, long-term safety can not evaluated cause short-time study.

**CONCLUSION**

The study revealed that all adverse events were mild to moderate in nature, at present we can conclude that COVID-19 vaccine COVISHIELD™ is safer. Vaccine have side effects, but none of them are as severe as the disease itself. An active search system for adverse events to vaccine is a good method for detecting and quantifying mild adverse events.

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