Active surveillance of adverse events following ChAdOx1 nCoV-19 immunization in geriatric population: a prospective multi-centric study from Jaipur, Rajasthan, India

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Abstract

India launched its coronavirus disease 2019 (COVID-19) vaccination drive starting with healthcare workers. The aim of the study was to evaluate adverse events following immunization (AEFI) amongst the Geriatric population associated with two doses of ChAdOx1 nCoV-19 vaccine. We also evaluated association of AEFI according to gender and elderly age groups.

An observational study, conducted among 437 individuals vaccinated at multiple community healthcare centers in Jaipur, of AEFIs associated with both doses of ChAdOx1 nCoV-19 vaccine, via telephonic interviews on the day of vaccination-Day 0, Day 7 and Day 15 from vaccination.

463 vaccinated individuals who responded for first dose AEFIs, and 437 (94.3% 437/463) responded to the telephone interview regarding the second dose. Of these, 5.5% (24/437) reported AEFIs for the second dose. Among 60 respondents who reported AEFI (both doses) fever (26) and fatigue (22) were the most reported systemic AEFI. Local AEFIs were injection site soreness (23). The AEFIs (both systemic and local) in respondents mostly lasted for 1-2 days. AEFI reported by respondents in the age group 60-70 years was higher than those above 70 years. Female respondents were associated with higher AEFI than the males.

The AEFIs of both the doses were observed in the first 2 days predominantly. Symptoms were minor, short lived and self-limiting. No serious adverse events attributable to vaccines were reported in our study. Adverse event following immunization is independent of gender and age distribution for both the doses.

Introduction

On 11 March 2020, the World Health Organization (WHO) declared the novel coronavirus disease 2019 (COVID-19) outbreak as a global pandemic.1 Till September 27, 2021, India recorded more than 33.8 million cases and 448,000 deaths from the day the coronavirus pandemic hit in December 2019.2 India rolled out its mass vaccine campaign against COVID-19 on January 16, 2021, with the most used vaccine i.e., ChAdOx1nCoV-19. Manufactured by Serum Institute of India in partnership with Oxford-AstraZeneca, it consists of a replication-deficient chimpanzee adenoviral vector ChAdOx1, containing the SARS-CoV-2 structural surface glycoprotein antigen (spike protein; nCoV-19) gene. ChAdOx1 nCoV-19 vaccination course consists of two separate doses of 0.5 ml each. Initially the gap between the two doses of ChAdOx1 nCoV-19 was 28 days. This gap was increased to 6-8 weeks in March 2021, which was further increased to 12-16 weeks in May 2021. As of 1 October 2021, over 89 million COVID-19 vaccination, which represents approximately 64% of the population.3

When people began to feel some hope in summer 2021 that the pandemic could recede to the background, the Delta variant emerged. First identified in India in late 2020, Delta swept rapidly and accounting for more than 99% of COVID-19 cases and leading to an upsetting increase in hospitalizations.4 R0 value (Indicates how contagious an infectious disease is) of Delta variant was found to be higher (R0 of 5.08) of the any ancestral strains (R0 of 2.79) of SARS-CoV-2.5 Hence, the people who were reluctant from vaccination were more in danger and would form a basis for ensuring safety during the future national vaccination against Covid-19 and to get over the vaccine hesitancy.

Objective

The objective was to draw a comparison between the AEFIs associated with the first and second dose of ChAdOx1 nCoV-19 vaccine among vaccinated individuals above 60 years of age.

Materials and Methods

Study design and population

An observational study was conducted at multiple community vaccination centers in
However, we were not able to report some phone interview regarding the second dose. (94.3% 437/463) responded to the tele-
responded for first dose AEFI, and 437 for the survey data.

Deviation and percentage were calculated AEFI. The respective mean, mode, standard
deviation and percentage were calculated for the survey data.

Out of 463 vaccinated individuals who
responded for first dose AEFIs, and 437 (94.3% 437/463) responded to the tele-
phone interview regarding the second dose. However, we were not able to report some

Statistical analysis

Data was analyzed using Microsoft Excel, Minitab (a statistical software) and
online statistical tool was used for performing the chi-square test, to test the associa-
tion between the gender and AEFI status and between the age group and respondent’s
AEFI. The respective mean, mode, standard deviation and percentage were calculated for the survey data.

Results

Out of 463 vaccinated individuals who responded for first dose AEFIs, and 437 (94.3% 437/463) responded to the tele-
phone interview regarding the second dose. However, we were not able to report some

Table 1. Adverse events following ChAdOx1 nCoV-19 immunization reported by the study population.

| Symptoms                          | Frequency (n=463) | Percentage% | Frequency (n=437) | Percentage% |
|-----------------------------------|------------------|-------------|------------------|-------------|
|                                   | Systemic symptoms with first dose | Systemic symptoms with second dose |
| Fatigue                           | 14               | 3.02%       | 8                | 1.83%       |
| Fever                             | 17               | 3.67%       | 9                | 2.05%       |
| Dizziness                         | 2                | 0.43%       | 0                | 0%          |
| Diarrhoea                         | 1                | 0.21%       | 0                | 0%          |
| Injection site soreness           | 10               | 2.15%       | 13               | 2.97%       |
| Itching and rash                  | 1                | 0.21%       | 0                | 0%          |

In most of the respondents, symptoms lasted for more than 24 hours. The AEFIs (both systemic and local) in respondents mostly lasted for 1-2 days (66.7%; 40/60) from the day of vaccination (Figure 2) AEFI reported by respondents in the age group 60-70 years (44) was higher than those above 70 years (16) (Tables 2 and 3) (Figure 3). The P value for the association between Age group and respondent AEFI is 0.196. Female respondents (35) were associated with higher AEFI than the males (25).

Discussion

In this prospective, community-based study conducted at multiple community healthcare center in Jaipur, we have investiga-
ted adverse events following immunization (AEFIs) associated with first and sec-
dose of ChAdOx1 nCoV-19 vaccine. In
our study, overall common adverse events after the first and second dose of the ChAdOx1 nCoV-19 vaccine were fever, fatigue, injection site soreness. No serious AEFI attributable to vaccines were reported and all respondents who developed AEFIs, improved within 2 days (66.7% 40/60) of vaccination. The rate of adverse events showed a declining trend after 2 days of vaccination. Symptoms were mild in severity and short-lived. ChAdOx1 nCoV-19, thus have minor, self-limiting, and tolerable AEFIs associated with both, the first and the second dose. This supports the findings of phase 1 and phase 2/3 trial of ChAdOx1 nCoV-19 vaccines wherein most recipients reported with non-serious AEFI.

In our study, 7.8% of the study population reported AEFIs with first dose and 5.5% with the second dose. These findings are in agreement with the findings of Phase 2/3 Safety trial of ChAdOx1 nCoV-19 where fewer adverse events were reported after the boost vaccination than after the prime vaccination. Also, we found that for respondents in the age group 60-70 years, AEFIs reported were 8.7% with the first dose and 6.4% with the second dose, and in those above 70 was 6.2% with the first dose and 3.9% with the second dose, which concur findings of phase 2/3 safety trial of ChAdOx1 nCoV-19 where reactogenicity reduced with increasing age. However, in our study the adverse events were reported at much lower frequencies in comparison to the Phase 2/3 trial of the ChAdOx1 nCoV19 vaccine where 73% in 56-69 year group and 61% in the 70 years and older group, reported adverse events. Higher number of minor AEFI were reported by female respondents than the males, irrespective of the age group. However, we did not find any supporting evidence of high reactogenicity in females, but this might be due to the influence of various sociodemographic variables in our survey data.

The Ministry of Health and Family Welfare noted that as of, 30th November 2021 1,240,157,719 vaccine doses had been administered. Of these, 788,635,410 were first doses and 451,522,309 second dose. As on 15th June 2021, the number of deaths reported following COVID-19 vaccination was 0.0002% of 235 million doses administered. AEFI data in India showed that there is a very minuscule but definitive risk of thromboembolic events. However, no such serious and thromboembolic event was reported by respondents in our study group.

### Limitation

The major limitation of our study is the relatively small sample size to assess serious/rare AEFI which could be attributed to the location of the multiple healthcare center which were remote and had a relatively less inflow of population. Since, the study was conducted only on specific age group, reporting bias is possible. Other limitations of our study could be recall bias as follow up interviews were carried out via telephone.

### Conclusions

Only 7.7% respondents experienced adverse effect after the first and 5.5% after the second dose of ChAdOx1 nCoV-19 vaccine. Though all were mild and short-lived.

| Age group | Respondents with AEFI with first dose | Respondents with no AEFI with first dose | Respondents with AEFI with second dose | Respondents with no AEFI with second dose |
|-----------|--------------------------------------|-----------------------------------------|--------------------------------------|------------------------------------------|
| 60-65     | 18                                   | 155                                     | 12                                   | 154                                      |
| 65-70     | 8                                    | 116                                     | 6                                    | 110                                      |
| 70-75     | 7                                    | 93                                      | 4                                    | 90                                       |
| 75-80     | 3                                    | 36                                      | 1                                    | 34                                       |
| 80-85     | 0                                    | 16                                      | 1                                    | 15                                       |
| 85-90     | 0                                    | 8                                       | 0                                    | 8                                        |
| 90-95     | 0                                    | 3                                       | 0                                    | 2                                        |
|           | 36                                   | 427                                     | 24                                   | 413                                      |

AEFI, adverse events following ChAdOx1 nCoV-19 immunization.
On applying Chi-Square test we conclude that there is no existence of evidence that depicts association between gender and AEFI status. Also, no evidence exists regarding association between age group and response of AEFI status for both the doses of the vaccine as the P value is greater than 0.05. Thus, it could be concluded that adverse event following immunization is independent of gender and age distribution at the time of first and second dose.

We also found a relation between the data of ‘first and second dose’ with respect to the different symptoms, which indicates that the same symptoms will be observed after the second dose also. Since the P value is 0.039, we conclude that the relationship exists for the population also.

The AEFIs of both the doses were observed in the first 2 days predominantly. Symptoms were minor, self-limiting, and had a lower reactogenicity profile with both doses of ChAdOx1 nCoV-19. No serious adverse events attributable to vaccines were reported in our study.

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