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A Study on Adverse events following vaccination with ChAdOx1 nCoV-19 vaccine (recombinant) among adults at a tertiary care center.

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Abstract

Background: Sudden advent of the Covid-19 pandemic called for safe and productive immunization techniques to combat the disease. India used two vaccines, Covishield and Covaxin, for emergency use. However, real-time data on vaccine safety and effectiveness haven't been established due to the rapid procurement of the vaccine.

Objective: This study aims to describe the adverse events following Immunization with the ChAdOx1 nCoV-19 vaccine.

Methods: This prospective cohort study included participants vaccinated in a private medical college; in Visakhapatnam from Jan to Sept 2021. Covishield vaccine IM in a double dose of 0.5 ml in a gap of 4 – 6-, 6-8-, and 8-12-weeks intervals was given to participants, monitored in the hospital for 30 minutes & then followed

till 28 days. Any Symptoms following vaccination were recorded.

Results: 42 .4% belonged to the age group of 31-40yrs & with 62% males. AEFI Post 1st dose had symptoms of Injection site pain (72%), fatigue (42%), myalgia (38.2%), fever (35%), headache (15%), and bleeding (0.004%).

AEFI Post 2nd dose was with symptoms like pain (4.2%), fatigue (8.0%), myalgia (4.0%), fever (2%), headache (1.0%), and dizziness (2%) with low frequency. The frequency of adverse effects seems to decrease as the vaccine interval increases.

Conclusion: Our study showed no significant adverse effects following Covishield immunization. Almost all the adverse effects weren't serious. Our study consisted mainly of the four weeks interval vaccinations; thereby, we noted a higher frequency of AEFI in this interval.

Keywords: Adverse Events Following Immunization (AEFI), Covid-19, Covishield.

Introduction

The Covid 19 pandemic caused severe distress to medical, economical, and social situations. Actions were taken to curtail the spread efficiently through increasing awareness, rapid diagnosis, and treatment due to which some improvement has been achieved. Scientists around the world have hastened the process to develop safe Immunization to halt the transmission and curb this pandemic. Vaccine safety is an important element in developing confidence among people. Quality vaccines with a higher degree of protection are required as they are given to people in good health. Though vaccines are closely observed and produced before license sanction, the occurrence of adverse events may not be excluded.[1] Emergency authorization was given to two Indian manufacturers Serum Institute of India- SII) ChAdOx1 CoV-19 VACCINE (Covishield) and Bharat Biotech Limited (Covaxin). On 16 January 2021, India started phase wise vaccination program with Covishield and Covaxin. Initially, in phase I health care workers (HCWs) were vaccinated followed by frontline workers, People aged 60 and 45 to 59 with comorbidities were targeted in phase II. [2]

Adenovirus vector ChAdOx1 with an optimized coding sequence for the spike protein that is a structural surface glycoprotein of SARS-CoV-2 is present in this ChAdOx1 nCoV-19 vaccine. It also has a tissue plasminogen activator leader sequence. [3] Symptoms like injection site tenderness, injection site pain, fever, chills, joint pains generalized weakness, headache, myalgia, and nausea may occur with Covishield. Rarely, events of demyelinating disorders were reported but without any causative evidence. [2] The validity and safety of the vaccine need to be examined as this bigger Immunization hasn't taken place.[4] An adverse event following Immunization (AEFI) is any untoward medical occurrence following vaccine administration, that may not have a causal relationship with the usage of the vaccine. It may be a symptom, disease, lab finding, or sign. AEFIs are grouped into five categories: Vaccine related reaction, Vaccine quality defect-related reaction, Immunization error-related reaction, and Immunization anxiety-related reaction and coincidental event. [5] The safety of the Covishield vaccine has not been confirmed. Post-large-scale administration, adverse events should be noted and adequate verification needs to be done as there are fewer data available now. The present study's objective is to report the AEFI's Post Covishield vaccination.

Materials and methods

This is a Prospective cohort study done in a private medical college, Visakhapatnam from Jan 2021- Sept 2021. Participants included doctors, nurses, para-medical

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staff, sanitary workers, and also the common public who got vaccinated at our center. Taking population size 6200, estimation error (d) = .05, estimated proportion (p) = 0.5, alpha (α) = 0.02, minimum sample size was calculated to be 498. To round it off 500 convenience sample size was taken by randomization. 20-80-year-old males and females who received two doses of the Covishield vaccine were included. All those who did not receive both the doses of the Covishield vaccine and those who received Covaxin and Pregnant women were excluded. Covaxin wasn't given at our center, only a minority got Covaxin vaccination, thus excluded from the study. People aged below 20 years and above 80 years are not included. 0.5 ml vaccine is given intramuscularly in the deltoid region. Doses were given at an interval of 4-6 weeks, 6-8 weeks, and now 8-12 weeks. As a part of Central Government operational rules, all subjects are observed for half an hour post-vaccine, AEFI was recorded from a dose of vaccination to post 28 days. A standard questionnaire wasn't available at that time. So, all the participants were given a questionnaire to collect data about Age, sex, profession, Vaccination dates, Type of vaccination, Duration between vaccinations, and symptoms following vaccinations. Data will be entered in MS Excel and analyzed in SPSS V22. Descriptive statistics are represented with Mean, Median with IQR, Percentages, and with SD.

Results

Among 500 participants, 42 .4% were of age 31-40yrs. 69 years was the eldest person who participated in the study.

Table 1: Age and Sex distribution

Age group	Males	Females
22-30	54	38
31-40	149	123
41-50	60	29
51-60	22	11
61-70	25	39
Total	310	240

(Table No: 1). 62% of males participated in this study compared to females with 48 %. AEFI Post 1st dose showed symptoms of Injection site pain (72%) with high frequency followed by fatigue (42%), myalgia (38.2%), fever (35%), headache (15%), and bleeding (0.004%). AEFI Post 2nd dose was minimal with symptoms like pain (4.2%), fatigue (8.0%), myalgia (4.0%), fever (2%), headache (1.0%), and dizziness (2%) with low frequency. (Table No: 2)

Table 2: AEFI post 1st dose and 2nd dose

AEFI	Frequency post 1st Dose	Percent	Frequency Post 2nd dose	Percent
Pain	360	72	21	4.2
Fatigue	210	42	40	8.0
Myalgia	191	38.2	20	4.0
Fever	175	35	10	2
Headache	75	15	5	1
Bleeding	2	0.004	10	2

Table 3: Distribution of No: of persons vaccinated according to time interval along with no of AEFI in that interval.

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Time Interval in weeks	Vaccines given	Frequency of AEFI	Percent
4 to 6	380	400	91.4
6 to 8	90	20	4.5
8 to 12	30	18	4.1
Total	500	438	100.0

In our study, 76% were given vaccination within an interval of 4 weeks mostly following the initial guidelines from ICMR, followed by 18 % in 6-8 weeks and very less i.e. 6 % with 8-12 weeks interval between the two vaccines. (Table No: 3). frequency of adverse effects seems to decrease as the interval between vaccines increases. Our study constituted mostly of the 4 weeks interval vaccinations; thereby we noted (400) higher frequency of AEFI in this interval. (Table No: 3). The Time of onset of AEFI with vaccine1 is relatively more in the 1- 12 hours period and then decreased within 7 days. The time of onset of AEFI post vaccine 2 is less pronounced than vaccine 1. (Table No:4) We also observed that few who did not show any symptoms after vaccine1 showed symptoms after vaccine 2, however, the percentage is less.

Table 4: Time of onset of AEFI post 1st and 2nd doses

Time of onset of AEFI	<1 hour	1-12 hours	12-24 hours	24-48 hours	48-72 hours	72 hours - 7 days
Vaccine 1	48	290	30	12	2	0
Vaccine 2	22	30	4	0	0	0

Discussion

Safe vaccination strategy and impartial distribution are important in ending the COVID-19 pandemic. It is heartening to see many vaccines being developed. [6]

Prior testing of COVID-19 vaccines included only few subjects belonging to a few races with less follow-up time in the optimal environment only. So prior licensing studies do not eliminate all the issues of protection considering the large-scale distribution among people from all the communities [7] calling for the need for more research in this area. This study is thus undertaken to weigh the adverse events following Post covishield immunization.

The Incidence of AEFI in our study is 87.6% (n=500) and 62 people did not develop any AEFI after the vaccination. Compared to Silvery et al [8] with 61.02% AEFI (n=299); 191 were without any AEFI. This difference may be due to the number of people undertaken for study and of different age groups. All AEFI reported in this study were within 1week of vaccination similar to our study though. Severe AEFI'S after 2nd dose was seen in 6 persons of which, 2 persons had only after 2nd dose in a study. However, No serious AEFIs were noted in our study.

The incidence of AEFI following the first dose of Covishield vaccination in our study was found to be 91.4% similar to Silvery et al with 58. 36%, Deep Kamal [9] with 57%. A study by Prativa Subedhi[10] showed 79.1%, MVAERS Korean study[11] with 98.1 % incidence of AEFI. Other studies showed decreased frequency, which may be due to active follow-up problems post-vaccination.

Two critical effects i.e subjects with altered sensorium and 1020 non-critical AEFI were reported within 48 hours of first dose in a prospective study by DeepKamal,[9] Within 48 hours of second dose, two hundred and twenty non-critcal AEFI were reported. After 15 days for both the doses no AEFI was reported. This is similar to our study with almost all AEFIs occurring mostly in the first 24 hours and No AEFIs at all after 15 days.

In a Study by Pedro M Folegatti,[12] ChAdOx1 nCoV-19 group had more local and systemic reactions; those

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including pain, feeling feverish, chills, muscle ache, headache, and malaise which got reduced by use of paracetamol when used as prophylactic, medication. No critical illnes related to ChAdOx1 nCoV-19 was noted.

In a study By Upender Kaur,[13] majority of AEFIs resolved quickly and were of mild to moderate nature. No deaths were recorded.

AEFI post 1st dose of vaccination shows injection site pain as most common minor AEFI reported followed by fatigue and myalgia, similar to a study by Prativa Subedhi[10]. Injection site pain mustve caused by the technique used by the HCW and also the apprehension of the patient towards vaccination. However, a study by Mengistu Hagazi Tequare [14] and Deep Kamal [9] showed higher frequency of myalgia and fatigue than pain. Other study by Vijaya Chandra reddy[15] also showed fever and general pain as most common symptoms. A study by Deep Kamal [9] showed head ache as the most common minor AEFI. This is similar to other studies though the incidence of occurrence of AEFI is more with current study.

In our study, AEFI Post 2nd dose was minimal and with lower incidence than 1st dose.

Injection site pain was 2nd most common symptom observed and is similar to a study by Md. Musab Khalil [16]. Fatigue constituted the most common side effect in our study followed by myalgia similar to Vijay Chndra's study [15] and Study by Deep Kamal [9]. Dizziness was o minimal in our study similar to Deep Kamal study [9] and also Md. Musab Khalil [16]

In a study of 294 patients, aged 18 to 79 years, underwent evaluation, among them, 50 VITT suspected cases and 170 definite VITT (Vaccine induced immune thrombotic thrombocytopenia) were identified. These patients received first dose of ChAdOx1 nCoV-19 vaccine and were symptomatic post 5 to 48 days (median, 14) after vaccination.[17]

In contrast to this, VITT were not observed in our study at all. This may be because of the ethnic differences in the study population.

AEFI in our study presented with symptoms common to any vaccine, also common to all COVID-19 vaccines and especially, ChAdOx1 nCoV-19. [18]

The symptoms were self-limiting and those who reported AEFIs took right off the shelves drugs. There was no report of critical illness leading to disability, mortality or others requiring hospitalization, which is similar to results from other studies. [19, 20] Frequency of adverse effects seems to decrease as the interval between vaccines increased.

Keeping track of the ongoing and ever evolving research is essential for us to retain control over the pandemic and return to normality. This work thus can give an insight into the vaccination safety in this new phase of the pandemic preparation.

The study was done by convenience sampling and only on the subjects vaccinated at our centre, calling for a larger population study. Also, at the time of study a standard questionnaire was not available to limit the bias. And, as with new emerging variants, use of vaccines and their safety implications may vary. Also, vaccine enhanced covid-19 disease needs to be ruled out in case of wild strains.

Conclusion

Covishield Vaccine in our study has been well tolerated with no significant or serious adverse effects. All Symptoms were less severe and resolved spontaneously. However, adequate monitoring and follow up on larger scale is required to establish the safety profile of these vaccines.

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