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Research Article

Adverse Events of Immunization

Adverse events following immunization associated with the ChAdOx1nCoV-19 and BBV152 vaccine - a cross-sectional study

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Abstract: COVID-19, an infectious disease, has become a leading cause of death in many people. The rapid emergence of the pandemic prompted the development of a vaccine to mitigate the disease's harmful consequences. Vaccination is the only effective way to prevent infection from spreading and build immunity to the virus. However, developing adverse effects has become a major problem for vaccine reluctance. Accordingly, the interest has been shifted towards identifying the adverse effects developed following immunization. The current study objective is to assess and compare the intensity of adverse effects following 1st and 2nd dose of COVID-19 vaccination and the medication administered to relieve the symptoms associated with vaccination. A cross-sectional study was performed in a community over six months. A total of 836 participants were involved in the study. All the data regarding the vaccination were collected through a specially designed questionnaire form and analyzed in all the participants within the study group. According to the study, at least 1 AEFI was developed in about 90% of the study population. The most common systemic and local effect developed in the study population was fever (59.42%) and pain at the injection site (69.82%), respectively. With both vaccines (ChAdOx1 nCoV-19 and BBV152), the incidence and severity of AEFIs were lower after the second dose than after the first dose, and most of the symptoms associated with vaccination were alleviated by taking home remedies and symptomatic treatment. The adverse effects reported after receiving the ChAdOx1 nCoV-19 and BBV152 vaccines are typical of most vaccines, and the majority of them were tolerated, and most subsided in less than 24 hours.

Keywords: Corona Virus Disease-2019 (COVID-19), Adverse events following immunization (AEFI), ChAdOx1nCoV-19 (Covishield), BBV152 (Covaxin).

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1. INTRODUCTION

COVID-19 is an infectious disease that often affects the lungs and is characterized by decreased oxygen levels caused by SARS COV-2. The spikes on the virus identify the functional receptor[1], ACE-2 (Angiotensin Converting Enzyme-2), found in the nasopharynx, pharynx, and eye and expressed in numerous organs (heart, kidney, and lungs). [2,3] After the spike proteins bind to ACE-2 receptors, RNA internalizes and multiplies resulting in a cell burst. [4, 5] When the cells burst, viral particles infect the surrounding cells and quickly enter the lungs (Type II receptors) through the bronchus.[4] In the last two years, COVID-19 has risen to epidemic proportions, infecting many people. The rapid emergence of the pandemic prompted the creation of a vaccine to mitigate the disease's harmful consequences. Vaccination is the only effective way to prevent infection from spreading and build immunity against the virus. Several vaccines have been developed to combat COVID-19's harmful effects, including BNT162B2/Pfizer, ChAdOx1nCOV-19/AstraZeneca, BBV152/Bharat Biotech's Covaxin, mRNA-1273/ Moderna, Corona Vac, a vaccine from Sino Pharm and Wuhan Institute of Virology, Sputnik V, BBIBP-CorV and EpiVac Corona .[3, 6-8] However, Drugs Controller General of India has only authorized five vaccinations to date, including Covishield (ChAdOx1nCOV-19), Covaxin (BBV152), Sputnik, Johnson & Johnson, and Zycov D.[9-11] Among the current variable vaccinations, on 3 January 2021, India's top pharma authority granted emergency approval for two vaccines ChAdOx1nCOV-19 and BBV152 against COVID-19, even though phase III clinical studies for both vaccines were still underway in India.[7,12] Even though the vaccine is made available to everyone, vaccine reluctance has become a major barrier due to the poor transmission of medical information, worries about the Safety and effectiveness of hastily created new vaccines [13], the novelty of the vaccine, the notion that vaccine is not necessary[14], less dread of COVID-19 due to the perceptions that the disease is not severe and does not cause persistent medical concerns[15], the emergence of adverse effects after COVID-19 vaccination, having a COVID-19 test result that is positive even after immunization and the problem of determining which type of vaccine to be administered. Among all the factors, the emergence of adverse effects has become the most significant impediment to vaccine administration. Any medical episode after the vaccine administration is an adverse event following immunization (AEFIs) and has no causal association with vaccine use.[12,16,17] Despite randomized controlled trials demonstrating ChAdOx1nCOV-19 vaccine safety and efficacy[18,19], multiple severe AEs have been recorded[20]. In contrast, the phase I study of Covaxin revealed that 5% of participants reported local AEs, and 14% reported systemic AEs. However, other studies that evaluated the AEs of BBV152 were absent.[17]Many studies revealed that the most frequent AEs recorded with ChAdOx1nCOV-19 and BBV152 included injection site events (e.g., pain, redness, swelling, tenderness) and systemic effects (e.g., fatigue, headache, muscle or joint pain, fever with chills).[17,21]Occasionally, serious adverse events were reported.[22,23,24] Due to the restrained studies on the comparison of AEFI between ChAdOx1nCOV-19 and BBV152 adverse effects, this study was undertaken to emphasize the incidence, severity, and duration of adverse effects after administering any of the vaccines, ChAdOx1nCOV-19 or BBV152, as well as the home remedies and pharmacological treatment taken to alleviate the symptoms were also assessed.

2. MATERIALS AND METHODS

2.1. Study design and population

A cross-sectional study was conducted in the community for six months. The study subjects were the general population greater than or equal to 18 years who had received at least one dose of ChAdOx1 nCoV-19 or BBV152 vaccine and the pregnant women, pediatrics, persons who were unwilling to participate in the study, and participants who received other than Covishield and Covaxin vaccines were excluded. The study was conducted after obtaining permission from the Institutional ethics committee (IEC number-SPSP/2021-2022/PD01).

2.2. Data collection and consent

After obtaining permission from the institutional review board, the data was obtained through direct participant interaction and obtain the participant's willingness in the study. During the interaction, the participant was asked to fill out a specially designed questionnaire form, including demographic details, awareness about the COVID-19 vaccine, vaccination details, and post-vaccination details. All the participants (n=836) were given brief details of the study, and consent was collected. Participants were assured that the data collected was kept anonymous and confidential.

2.3. Data management and analysis

Based on the data obtained, the awareness about the COVID-19 vaccine among the population, vaccination details, reason for vaccine hesitancy, type of AEFIs developed, the intensity of adverse effects following 1st and 2nd dose of vaccination, home remedies and pharmacological treatment taken to treat AEs were assessed. All the data obtained was subsequently segregated using Microsoft Excel-2010, and the relevant calculations were made.

3. RESULTS AND DISCUSSION

3.1. Results

Most participants (98%) reported an intention to receive the COVID-19 vaccine; only 2% reported no intention to vaccinate. The reasons provided by the participants who stated they had no desire to get vaccinated included: lack of interest (33.33%); poor health (20%); Fear/Panic (20%); Believing that the vaccine is not enough to fight against the disease (6.66%); Psoriasis (6.6%); Urticaria (6.6%) and Vaccine reluctance (6.6%). Among those who received vaccination (n=821), 630 (77.58%) received Covishield, 182 (22.41%) received Covaxin, and 9 (1.09%) received other types of vaccine. Of the 812 subjects, 759 (92.44%) experienced adverse events following immunization, while 53(6.45%) have not experienced any adverse events following immunization. Among 759 subjects, 588 (77.4%) experienced AEs due to Covishield, and 171(22.5%) experienced AEs due to Covaxin administration. (Fig.1)

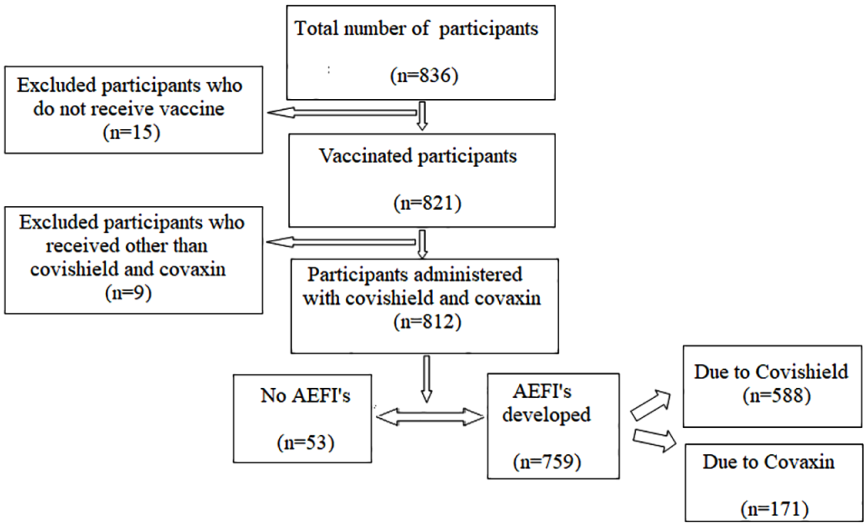


Fig 1. Schematic diagram of assessment of AEs developed with COVID-19 vaccines (ChAdOx1 nCoV-19 and BBV152)

AE=Adverse events; ChAdOx1 nCoV-19 = Covishield; BBV152=Covaxin; n=number of participant's; N=Total adverse effects. A total of 2,133 AEFIs with 1,390 systemic AEs and 743 local AEs were recorded from 759 subjects (an average of 2.81 AEs per person). The most common systemic adverse effects included fever (59.42), followed by tiredness (44.13%), headache (38.47%), muscle or joint soreness (36.62%), nausea (2.63%), and diarrhea (1.84%). In contrast, the most common local adverse effects included pain at the injection site (69.82%), followed by swelling at the injection site (15.15%), redness at the injection site (7.64%), itching at the injection site (3.55%), allergic reactions (0.79%) and swollen armpit (0.79%). (Fig.2) The distribution of systemic and local AEs between two vaccinations is shown in Table.1. When systemic and local AEs from ChAdOx1nCoV-19 and BBV152 were evaluated, the probability of AEs developed after ChAdOx1nCoV-19 administration was found to be relatively lower when compared to the AEs developed after BBV152 administration. However, diet, social habits, and co-morbid conditions do not affect the development of AEs.

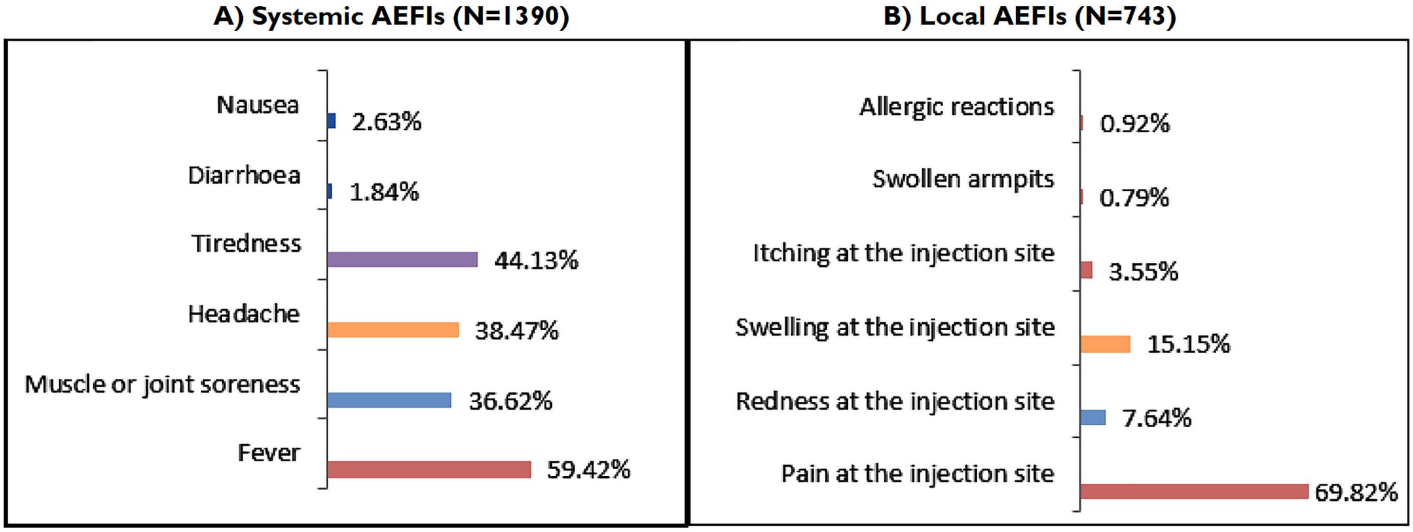


Fig 2: AEs developed after administering ChAdOx1 nCoV-19 and BBV152. N=Total adverse effects

Table.1 Distribution of systemic and local AEFIs per the vaccine, diet, social habits, and co-morbid condition. N=Total adverse effects

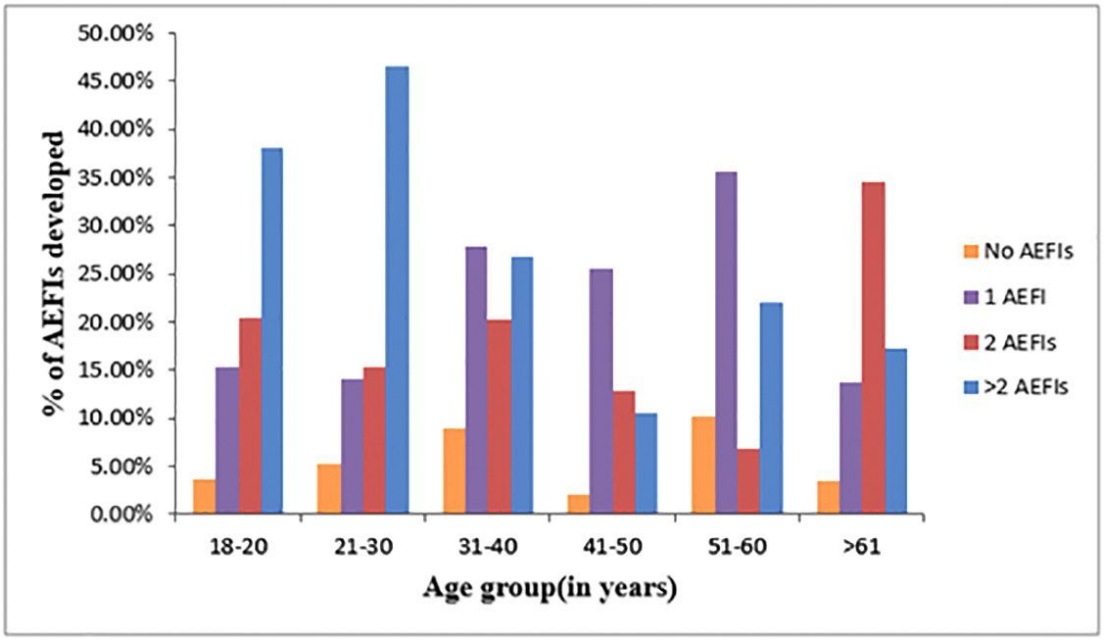
Parameter		Systemic AEFIs (N=1390)	Local AEFIs (N=743)	Total
Vaccine name (N=2133)	ChAdOx1 nCoV-19	1075 (68.16%)	502(31.84%)	1577
	BBV152 (n=171)	315 (56.65%)	241 (43.35%)	556
Gender (N=2133)	Male (n=324)	595 (63.8%)	337 (36.2%)	932
	Female (n=435)	795 (66.2%)	406 (33.8%)	1201
Diet (N=2133)	Veg (n=120)	219 (67%)	108(33%)	327
	Non-veg (n=43)	65 (60.7%)	42(39.3%)	107
	Mixed (n=596)	1106 (65.1%)	593(34.9%)	1699

Social habits (N=2133)	Non-alcoholic (n=697)	1276 (65.50%)	672 (34.5%)	1948
	Alcoholic(Daily) (n=17)	52 (73.24%)	19 (26.76%)	71
	Alcoholic(Occasional) (n=45)	62 (54.4%)	52 (45.6%)	114
	Non-Smoker (n=742)	1358 (63.35%)	720 (34.65%)	2078
	Smoker(Daily) (n=9)	18 (64.28%)	10 (35.72%)	28
	Smoker(Occasional) (n=8)	14 (51.85%)	13 (48.15%)	27
Co-morbidities (N=2133)	Nil (n=682)	1248 (65.23%)	665 (34.77%)	1913
	Single (n=52)	106 (64.24%)	59 (35.76%)	165
	Multiple (n=25)	36 (65.45%)	19 (34.55%)	55

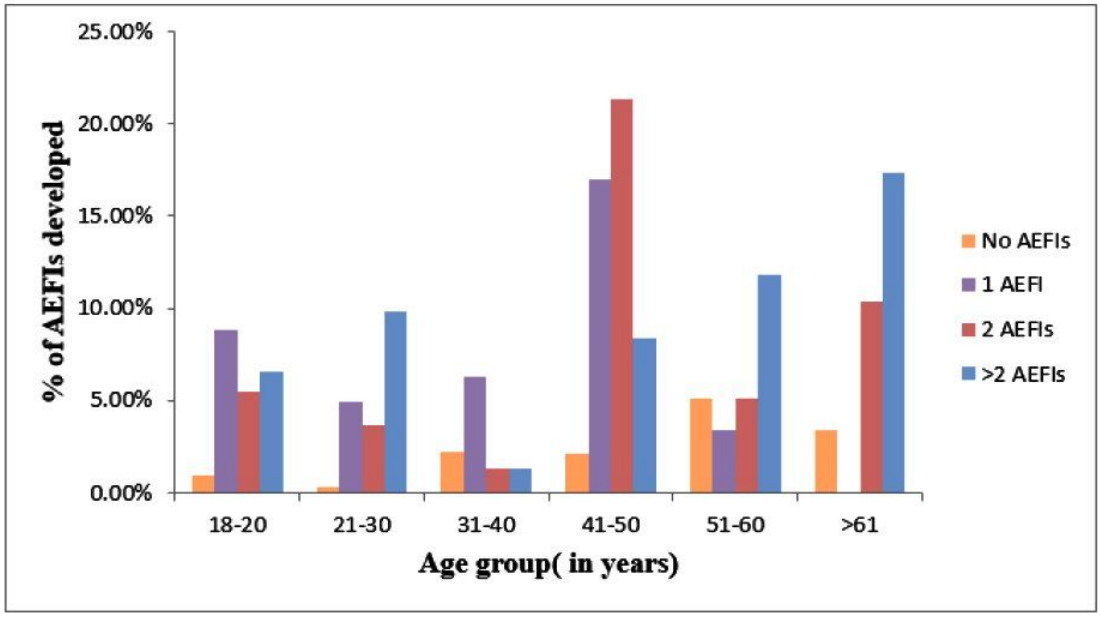
Table 1 The distribution of systemic and local AEFIs per the vaccine, diet, social habits, and co-morbid condition. N=Total adverse effects Upon analysis, AEs experienced among Covishield-administered participants (n=588) have developed 1 AEFI in 147 (25%), 2 AEFIs in 142 (24.2%), and >2 AEFIs in 299 (50.8%) subjects. In contrast, AEs experienced among Covaxin-administered participants (n=171) have developed 1 AEFI in 55 (32.2%), 2 AEFIs in 48 (28.1%), and >2 AEFIs in 68 (39.7%) subjects (Table.2). The greatest proportion of people who have administered the vaccine among the various age groups was 21-30 (40.51%), followed by 18-20 (34.85%), 31-40 (9.85%), 51-60 (7.26%), 41-50 (5.78%) and >61 (3.5%). Among 759 participants, 507 (66.8%) developed AEs on Day 1, 210 (27.7%) developed AEs on Day 2, and 42 (5.5%) developed AEs on Day 3. The duration of symptoms following immunization varied from person to person. In 345 participants (45.5%), symptoms associated with AEFIs have subsided in <24 hours, and in 414 participants (54.5%), symptoms associated with AEFI have persisted for >24 hours. In the vast majority of participants, 630 (83%) had more intensity of adverse effects after administering dose-1. In comparison, only 129 (17%) had more intensity of adverse effects after administering dose-2(Table. 3) (Fig.3). Some people have utilized home remedies, some have used pharmacological treatment, and only a small number of people used both. Of the 759 participants, 362 (47.7%) treated their AEFI using home remedies, and 464 (61.10%) have taken medication to relieve AEFI. Among 362 participants, 153 (42.2%) have taken plenty of water, 141 (38.9%) have moved their arm gently, 98 (27.07%) have taken plenty of sleep, 62 (17.12%) have applied ice pack, 44 (12.15%) have dressed lightly to reduce the symptoms associated with AEFI. (Fig.4) Among 464 participants, the majority of the people 95.86% have administered Paracetamol, whereas few have administered aceclofenac (0.64%), tramadol (0.2%), ibuprofen (0.2%) and others (1%). (Table.4).

Table 2: Age-wise AEs developed among ChAdOxI nCoV-19 and BBV152 administered participants—AEs=Adverse events; AEFI's=Adverse events following immunization.

	COVISHIELD (n=630)				COVAXIN (n=182)					
Age	**No AEFIs**	**1AEFI**	**2 AEFIs**	**>2 AEFIs**	**No AEFIs**	**1 AEFI**	**2 AEFIs**	**>2 AEFIs**	**Total**	**Percentage**
18-20	10 (3.7%)	42 (15.4%)	56 (20.5%)	104 (38.1%)	3 (1%)	24 (8.8%)	15 (5.5%)	19 (6.6%)	273	100%
21-30	17 (5.2%)	46 (14.15%)	50 (15.4%)	151 (46.5%)	1 (0.3%)	16 (4.9%)	12 (3.7%)	32 (9.85%)	325	100%
31-40	7 (8.9%)	22 (27.8%)	16 (20.2%)	21 (26.7%)	2 (2.5%)	5 (6.3%)	5 (1.3%)	1 (1.3%)	79	100%
41-50	1 (2.12%)	12 (25.51%)	6 (12.8%)	5 (10.63%)	1 (2.12%)	8 (17.02%)	10 (21.3%)	4 (8.4%)	47	100%
51-60	6 (10.2%)	21 (35.6%)	4 (6.8%)	13 (22%)	3(5.08%)	2 (3.38%)	3 (5.08%)	7 (11.86%)	59	100%
>61	1 (3.58%)	4 (13.7%)	10 (34.4%)	5 (17.24%)	1 (3.44%)	0 (0%)	3 (10.34%)	5 (17.3%)	29	100%
Total	42	147	142	299	11	55	48	68	812	



i) Age-wise AEFIs developed in ChAdOx1 nCoV-19 administered participants



ii) Age-wise AEFIs developed in BBV152-administered participants

Fig 3: Adverse effects developed among different age groups following immunization of ChAdOx1 nCoV-19 and BBV152 vaccines.

Table 3: Characteristics of AEFIs (2130 AEFIs reported from 759 individuals) reported for ChAdOx1 nCoV-19 and BBV152 vaccines.

Parameter		Frequency (%)(n=759)
Onset of AEFIs	Day-1	507 (66.8%)
	Day-2	210 (27.7%)
	Day-3	42 (5.55)
Duration of symptoms	<24 hours	345 (45.5%)
	>24 hours	414 (54.5%)
Intensity of AEFIs	Dose-1	630 (83%)
	Dose-2	129 (17%)

n= number of participants

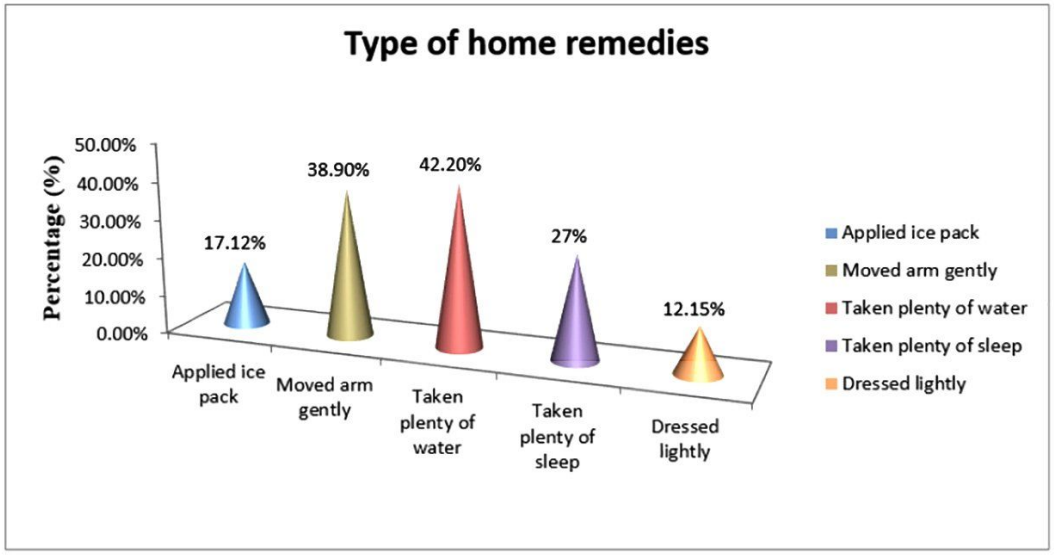


Fig 4: Types of home remedies followed for treating AEFIs

Table 4: Medication administered to treat AEFIs

Type of Medication	Frequency (%)
Paracetamol 650mg	195(42%)
Paracetamol 500mg	245(53%)
Paracetamol+ Ibuprofen	2 (0.43%)
Paracetamol 500mg+Caffeine	2 (0.43%)
Aceclofenac	3 (0.64%)
Ibuprofen	1 (0.2%)
Tramadol	1 (0.2%)
Cetirizine	10 (2.1%)
Others	5 (1%)
Total	464(100%)

4. DISCUSSION

The rapid emergence of the pandemic prompted the development of a vaccine to mitigate the disease's harmful consequences. However, given the rapid development of COVID-19 vaccines, it is difficult to determine their efficacy and Safety. As a result, steps should be taken to identify any potential AEFIs. The efficacy and safety profile of COVID-19 vaccines should therefore be enhanced through ongoing monitoring and data collection. Accordingly, the current study was designed to evaluate the adverse events caused by administering two different COVID-19 vaccines, ChAdOx1nCoV-19 (Covishield) and BBV152 (Covaxin), the use of which is currently widespread throughout the world, and the remedies are taken to treat AEs. Even though several published studies have been on the AEs linked to the ChAdOx1nCoV-19 and BBV152 vaccines, these studies only included participants who had received the ChAdOx1nCoV-19 or BBV152 vaccine. To the author's knowledge, this is the first study to compare and assess the AEs associated with the ChAdOx1nCoV-19 and BBV152 vaccines. Therefore, the current study findings added more data to comparing the AEs linked to the ChAdOx1nCoV-19 and BBV152 vaccines. In the current study, most AEs were observed between the ages of 21 and 30. Furthermore, a sizable portion of AEs was observed more among ChAdOx1nCoV-19 administered vaccine population. ChAdOx1 nCoV-19 was administered by the greatest number of participants, while comparably fewer participants were administered BBV152 during the study period. Consequently, it is conspicuous to observe maximal AE with ChAdOx1nCoV-19. The greatest proportion of people who have administered the vaccine among the various age groups was 21-30 (40.51%). While assessing the influence of age, gender, diet, social habits, and co-morbidities in the development of AEs reporting with two vaccines (ChAdOx1nCoV-19 and BBV152) administered in India. During the six-month study period, it was asserted that diet, social habits, and co-morbidities do not influence the development of adverse effects. However, age and gender have shown variations in the development of AEs. The incidence of AEFIs tended to decline with advancing age after the first dose of both vaccinations (ChAdOx1nCoV-19 and BBV152), which is evident in several studies conducted by Soumya Mahapatra et al., Jeon M et al., Ossato A et al. and Riad. A et al.[12,13,16,25]; nevertheless, when analyzed by gender, AEs were more common in females than males, which agrees with Soumya M et al. study.[12] However, the data reveals that females outnumber males in the study population; hence more females received the vaccine, resulting in more AEs in females. Due to the widespread vaccination campaigns, AEFIs linked to ChAdOx1, nCoV-19, and BBV152 have been documented in several nations with varying incidences. Kaur RJ et al., a double-blinded randomized controlled Phase I clinical trial on the BBV152 vaccine, revealed that pain at the injection site and headache were the most common local and systemic adverse effects, respectively. Only one serious adverse effect was observed, and multicentric trials on the ChAdOx1 nCoV-19 vaccine revealed that about 168 serious adverse events were observed.[22] However, in the current study, neither the ChAdOx1 nCoV-19 nor the BBV152 vaccines were associated with serious adverse events. In the current analysis, the ratio of systemic and local AEs was

similar among both vaccines (ChAdOx1nCoV-19 and BBV152). Additionally, during the study period following the first and second dose vaccinations, no significant AEFIs necessitating hospitalization or fatalities were documented. Several studies conducted by Dutta S et al., Soumya M et al., Jeon M et al., and Parida SP et al. stated regarding the most common systemic and local adverse effects; the current study also indicated that the most frequent systemic and local AEs with both vaccines (ChAdOx1nCoV-19 and BBV152) were found to be fever with chills, headache, fatigue, myalgia, malaise, diarrhea, nausea and pain, redness, swelling, itching at injection, swollen armpits, and allergic reactions respectively.[7,12,13,17] On comparison between the two vaccines, both the incidence of overall AEFIs after the administration of ChAdOx1 nCoV-19 and BBV152 had a greater proportion of >2AEFIs (47.4%, 37.3 %), followed by 1 AEFI (23.3%, 30.2%) and 2 AEFI's (22.5%, 26.3%) respectively. In this study, at least 1 AEFI was reported in more than 90% of the participants who have received the ChAdOx1nCoV-19 and BBV152 with 93.3% and 93.9%, respectively. These findings were also evident in the study conducted by Jeon M et al.[13]. However, in terms of individual categories, a greater proportion of AEFIs was observed among ChAdOx1 nCoV-19 administered participants. This study confirms that the duration of symptoms following immunization varied from person to person. In 45.5% of participants, symptoms have subsided in <24 hours; in 54.5%, symptoms have lasted for >24 hours. In agreement with Jeon M et al., stating that the systemic and local AEFIs were lower following the administration of the second dose than that of the first dose, the authors also found that the incidence and severity of AEFIs were lower after the second dose with both vaccines (ChAdOx1 nCoV-19 and BBV152).[13] Most of the side effects from ChAdOx1 nCoV-19 and BBV152 vaccination were alleviated by using home remedies and symptomatic treatment. Despite these findings, the study has several limitations. First, the adverse effects following the first and second doses were not individually compared. Second, the results might not be extrapolated since the sample size was relatively small. In the future, there will be a need for extensive, long-term safety monitoring studies. Lastly, the study population has not received both vaccines in equal numbers, thus preventing a clear pronouncement of the outcome. Reviewing other vaccines could yield dependable safety findings.

5. CONCLUSION

In conclusion, short-term adverse effects reported after receiving the ChAdOx1nCoV-19 and BBV152 vaccines are typical of most vaccines, including systemic adverse effects (fever, muscle or joint soreness, headache, tiredness, diarrhea, and nausea). In contrast, some others have developed local adverse effects (pain, redness, swelling, itching at the injection site, swollen armpit, and allergic reactions). In comparison, the incidence and severity of AEFIs after the second dose were lower than those of the first dose, the majority of them were tolerated, and most of them were relieved by taking the home remedies, and symptomatic treatment to the adverse effects and most of them were subsided in less than 24 hours. However, further studies are required to confirm the effectiveness of immunization.

6. ACKNOWLEDGEMENT

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7. AUTHORS CONTRIBUTION STATEMENT

All the authors had full access to all the data in the study. Dr. Durga Prasad T.S: Methodology, Supervision, Accuracy of data analysis and interpretation, Review-original and final draft before submission. Guna Gouru: Conceptualization, Documentation, Methodology, Collection of the data, Analysis, and interpretation of the data, Writing, Review, and editing the original draft and final version of the manuscript. S.Vasuprada: Conceptualization, Design, Collection of the data, Analysis, and interpretation of the data, Review. B. Sandhya: Collection of the data, Analysis, and interpretation of the data, Review. Kavipriya D.S: Collection of the data, Analysis, and interpretation of the data, Review. T.Sudhakar: Collection of the data, Review.

8. CONFLICT OF INTEREST

Conflict of interest declared none.

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