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A study on adverse event following immunization of Covid -19 at tertiary care teaching hospital

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ABSTRACT:The coronavirus disease 2019 (COVID-19) vaccine is being distributed worldwide to prevent infection caused by the coronavirus. Adverse event following immunisation (AEFI) refers to an unanticipated medical emergency that happens after vaccination but is unrelated to the vaccination. Anything could be the cause, including an unanticipated unexpected test finding. The absence of post-vaccination follow-up time, as well as the quick speed of research and development, has aroused broad public concern regarding the safety profile of COVID-19 vaccine candidates. COVISHIELD (Serum Institute of India (SII)) and COVAXIN (Bharat Biotech) were the first emergency vaccines to be licenced in India.

This study was a prospective observational study that was carried out at tertiary care teaching Hospital at Mysuru to determine the AEFI and out of 1807 subjects received either of vaccine (Covisheild or Covaxin) 1686(93.3%) individuals experienced AEFI.

A total of 6222 AEFI reported out of which Covisheild had higher rate of AEFI incidence than Covaxin i.e. 4605(74.01%) and 1617(25.99%) respectively. Among the 1174 study subjects who reported AEFI had pain at the injection site (64.97%) was a very common AEFI followed by Fever (n=1022, 56.60%) and Myalgia (n= 935, 51.74%).This study data had showed that those who received the Covisheild vaccine experienced significantly more adverse responses than those who received the Covaxin vaccine and there is a need of multiple similar studies at multicentre to have a national AEFI data to reduce the incidence of AEFI and to increase the safety and efficacy of vaccination

KEYWORDS: Adverse Event Following Immunization(AEFI), Covisheild, Covaxin, SARS CoV-2,

I. INTRODUCTION

Adverse event following immunization (AEFI) is essentially an unexpected medical emergency that occurs after vaccination on immunization with no causal relationship to vaccination. It could be anything, including an unintended, abnormal laboratory finding[1]. The rapid pace of research and development, as well as the lack of post-vaccination follow-up time, sparked widespread public concern about the safety profile of COVID-19 vaccine candidates[2]. Vaccination against coronavirus disease 2019 (COVID-19) is underway worldwide to prevent infection caused by the coronavirus[3]. However, adverse events that are extremely rare cannot be observed during pre-licensure testing and can only be observed during marketing surveillance when the product is used on a large scale[1].

The establishment of AEFI as a result of any vaccination programme necessitates a careful assessment of a few factors such as laboratory handling, clinical factors, and epidemiological factors. Its cause and effect can be improved by determining the rate of illness following immunization that is greater than the rate of illness in the absence of vaccination. As a result, significant care must be taken when interpreting adverse event reports that are temporarily linked to vaccination causality[1].

COVISHIELD (Serum Institute of India (SII)) and COVAXIN (Bharat Biotech) were the first to be approved for emergency use in India.

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COVISHIELD is based on a replication-deficient simian adenoviral vector encoding the SARS-CoV-2 whole-length spike glycoprotein (S), whereas COVAXIN is based on an inactivated SARS-CoV-2 platform. The vaccines have been rolled out across India and are being administered to all individuals 18 years of age and older, with the exception of those who have a history of allergy to one of its components. The first vaccination phase was aimed at health-care workers, front-line workers (police, sanitary workers, and so on) who are at risk who were at risk of contracting COVID-19 and who agreed to receive the vaccines. Pre-approval COVID-19 vaccine trials have largely been conducted in healthy populations under controlled conditions, with limited inclusion of diverse ethnicities and a short duration of follow-up due to the merging of various phases of clinical trials. As a result, such studies may not detect all safety-related issues that arise when vaccines are intended for general population marketing. The primary goal of this observational study is to conduct AEFI in post immunization of covid 19 in the Indian population, i.e., use of COVISHIELD vs COVAXIN. We present the first interim AEFI in COVISHIELD vs COVAXIN in health care workers, front-line workers and the general population in two vaccination centers in Mysore, Karnataka. COVISHIELD and COVAXIN were the designated vaccines at these centers, and thus the focus of our research[5].

II. NEED OF STUDY:

Adverse Event Following Immunization (AEFI) data from India revealed the risk of thromboembolic events following the AstraZeneca-Oxford vaccine (Covishield in India) and covaxin. According to a study given to the Health Ministry by the National AEFI, the number of cases of bleeding and clotting following COVID vaccination in India is miniscule and in accordance with the projected frequency of diagnosis of these illnesses in the country. On March 11, 2021, in view of global concerns about “embolic and thrombotic events,” specifically with AstraZeneca-Oxford vaccine [Covishield in India], a decision was made to perform an urgent, in-depth examination of the adverse events (AE) in India. The Ministry of Health has issued separate advisories to healthcare workers and vaccine recipients to encourage people to be aware of suspected thromboembolic symptoms occurring within 20 days of receiving any COVID-19 vaccine and to report them to the health facility where the vaccine was given. Covishield, the COVID-19 vaccine, continues to have a solid, positive benefit risk profile, according to the Ministry, with significant potential to prevent infections and reduce mortality due to COVID-19 around the world, including in India[6]. As a result, we wanted to track down those who had been vaccinated with covishield and covaxin during the first and second doses to see if they had developed an AEFI.

III. METHODS

Research Ethic

The study protocol was approved by the Institutional Ethical Committee with approval numberECR/134/Inst/KA/2013/RR-19. The research has been carried out in compliance with the ethical principles outlined in the Declaration of Helsinki of 1964 and its subsequent modifications.

Study Site:

The study was conducted on the Trauma Care center and Krishna Rajendra Hospital attached to Mysore Medical College and Research Institute(MMCRI). The study site was selected based on the vaccination drive arranged by District Administration of Mysuru along with Ministry of Health and Family Welfare, Government of India

Study Design

The study was a Prospective observational study and was carried out from January until July 2021.

Study Population and Sample Size Determination

The study was carried out among population residing in Mysuru taluk with an estimated population of 30,01,127(as per 2011 census). A total of 2010 people were included in the study. The telephonic interview was not completed by 203 subjects, and others did not show up for the second dose. As a result, they were deemed ineligible for the study due to the study's requirements. The study enlisted 1807 people in order to look at the side effects of the covid 19 vaccine. 901 subjects were given covaxin and 906 were given covishield.All of the participants in the current study are healthcare workers, front line workers and general population of >18yrs

Inclusion criteria:

1. Subjects who are enrolled and receiving Vaccination.
2. Subjects who have received both the dose of Vaccination.

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Exclusion criteria:
1. Subjects whose data is incomplete.
2. Subjects who are not enrolled or not receiving Vaccination at tertiary care.
3. Subjects who are not ready to cooperate to the study conducted.
4. Subjects who haven't responded for telephonic interview

Instrument for data collection

Data collection was carried out in two phases. In first phase close monitoring of the subjects were carried out for AEFI observation (if any) soon after immunization with either of one vaccine. The observations were recorded in both paper CRF as well as electronic-CRF(Excel) and AEFI were classified into Very common (>1 in people), Common (up to 1 in 10 people) and Uncommon (up to 1 in 100 people). In second phase subjects were assessed for their post vaccine health status telephonically within 24-48hrs.The same phases will be continued for second dose of vaccination

Study protocol and Informed consent

Each subject soon after vaccination was approached and the purpose of the study was explained. The consent of the subject was taken for their inclusion in the study and subjects cooperation and
participation was overwhelming.

Data Analysis

Age data and AEFI distribution of the study participants were expressed as Mean and Standard deviation. Gender and AEFI categorical variables were expressed in terms of Frequency distribution and percentage.Statistical analysis was carried out using Chi-Square for distribution analysis to compare observed results and ANOVA statistical test used to determine the means of two immunization groups by using IBM SPSS Software for Windows version 22. The data were analysed on consideration of significant value at $p < 0.05$

IV. RESULTS

Socio-demographic factors of the vaccinated subjects

The total number of the study participants who satisfied inclusion criteria and gave their consent for the study in two sites were 1807 and were included as study participant. Among the 1807 subjects Covishield was received by 901 subjects represents 49.9% response rate and covaxin was received by 906 subjects which makes 50.1% of study participants, the mean age of the study participants was 56.26±19.04 (range 18-96years) and 65.81±08.94 (range 45-96years) for Covisheild and Covaxin respectively.

Among the study population, men were 471(52.3%) for Covisheild and 527(58.2%) for Covaxin women were 430(47.7%) and 379(41.8%) respectively The gender distribution showed a marginal superiority of men over women. Table 1 shows the mean and standard deviation for AEFI frequency distribution using ANOVA statistical test, which was found to be 5.11 ± 1.799 and 1.78 ± 1.157 among the study participants receiving Covisheild and Covaxin respectively.

Pattern of AEFI Distribution among study participants

The incidence of AEFI is split into four groups depending on their distribution, and it was discovered that the study sample had several AEFI, with just 6.69 % reporting none. Table 2 demonstrates that participants who got Covaxin had a 79.8% incidence of 1-3 AEFI, while Covisheild had a 4-6 AEFI rate 540(59.93 %). In participants vaccinated with Covisheild, a higher number of AEFI (> 6) was recorded.

Table 1. Demographic Details for AEFI Distribution

Variable		Covisheild (N=901)	Covaxin (N=906)
Age	(Mean±S.D)	56.26 ± 19.04	65.81 ± 08.94
Gender	Men [Frequency(%)]	471 (52.3%)	527 (58.2%)
	Women [Frequency(%)]	430 (47.7%)	379 (41.8%)
AEFI distribution	(Mean±S.D)	5.11 ± 1.799	1.78 ± 1.157

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Table 2. Total Number of AEFI Distribution

AEFI distribution Group	Covisheild (N=901)	Covaxin (N=906)	Total
0	02 (0.2%)	119 (13.1%)	121 (06.69%)
1-3	117(18.9%)	723 (79.80%)	894 (49.47%)
4-6	540 (59.93%)	64 (07.06%)	604 (33.42%)
>6	188 (20.86%)	00 (00.00%)	188 (10.40%)

AEFI frequency distribution of Covisheild Vs Covaxin

Of a total sample of 1807 subjects, ranging in age from 18 to 96 years, 3614 vaccine doses were given. Each subject received 2 vaccine dose on an average. Out of 1807 subjects, 901 subjects (49.9%) received Covisheild and suffered 4605(74.01%) AEFI and 906 subjects received Covaxin(50.1%) with 1617(25.99%) AEFI reported.Covisheild showed majority of very common AEFI, The most frequent types of adverse reactions to Covisheild vaccine were Pain at Injection site (17.35%), Tenderness at injection site (15.09%) and Myalgia (14.02%) and The most frequent types of adverse reactions to Covaxin reported were, fever(27.6%) Pain at Injection site (23.2%) and Myalgia (17.8%).

Uncommon AEFI contributed a very low rate of incidence, with 7.4% in Covisheild and 5.8% in Covaxin, with dizziness (2.9%) and sweating (2.5%) coming in first respectively.

Figure 1&2 represents the data for AEFI reported from Covisheild and Covaxin, were AEFI classified into three domains of Very common (affect> 1 in 10 people), Common (affect up to 1 in 10 people) and Uncommon (affect up to 1 in 100 people) as per incidence

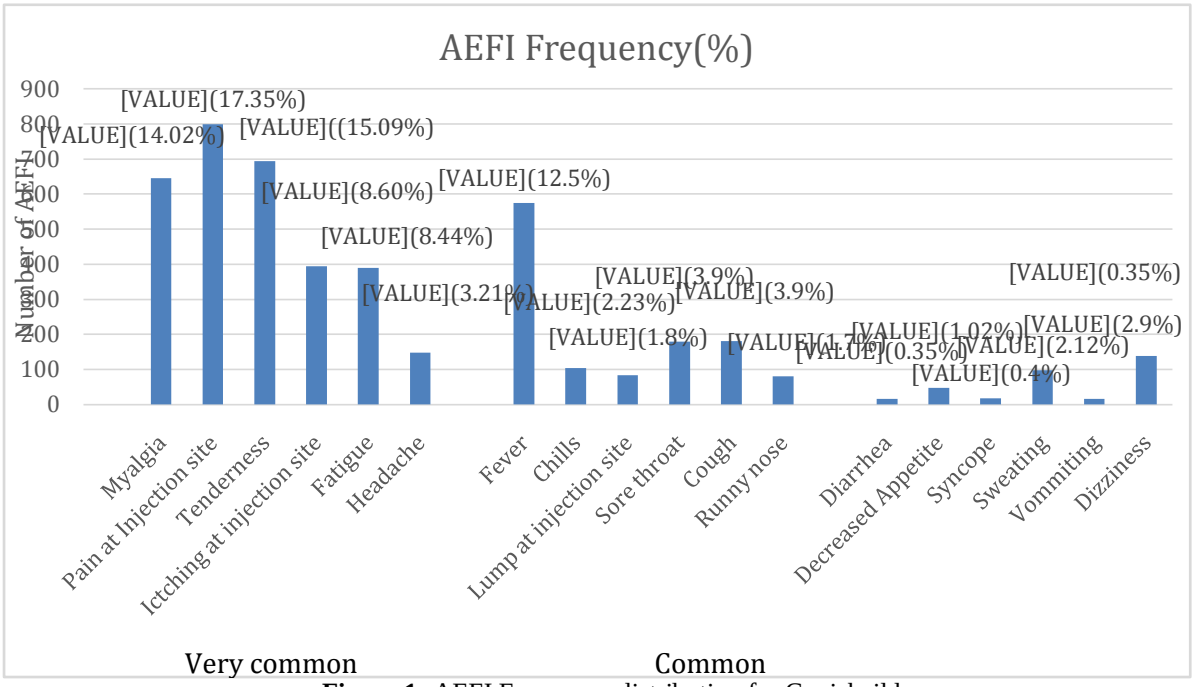

Figure 1: AEFI Frequency distribution for Covisheild

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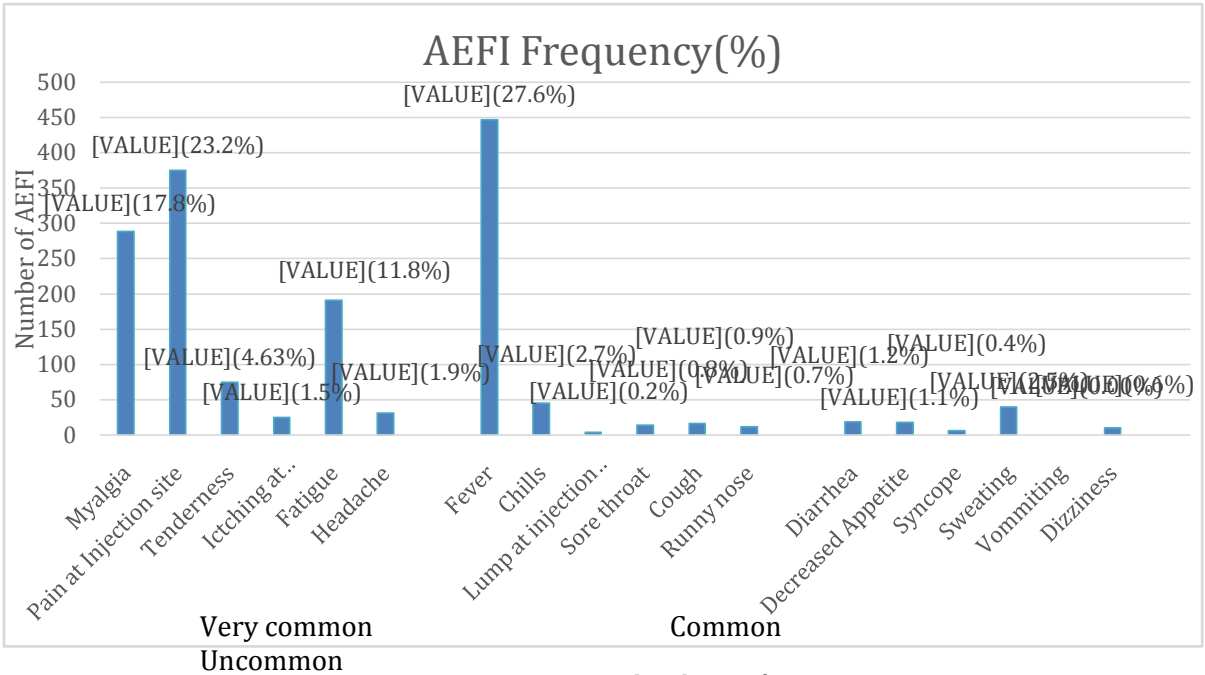

Figure 2. AEFI Frequency distribution for Covaxin

I. Incidence rate AEFI comparison of Covisheild Vs Covaxin

The total incidence rate of AEFI reported was 6222, among which 1174 subjects had pain at the injection site (64.97%) was a very common AEFI reported followed by Fever (n=1022, 56.60%) and Myalgia (n= 935, 51.74%) with statistical significant p value ($p < 0.05$)

Only 6.8% (n=424) subjects reported Uncommon AEFI (up to 1 in 100 subjects) among which the subjects who are vaccinated with Covisheild reported 78.5% (n=333) of total Uncommon AEFI. Dizziness (8.19%), sweating (7.64%), and decreased appetite (3.6%) being most commonly reported Uncommon AEFI.

CATEGORY	AEFI	COVISHEILD [Frequency (%)] 4605(74.01%)	COVAXIN [Frequency (%)] 1617(25.99%)	Total 6222(100%)	P-Value
VeryCommon(>1 in 10 People)	Myalgia	646(71.7%)	289(37.9%)	935(51.74%)	<0.001
	Pain at Injection Site	799(88.68%)	375(41.39%)	1174(64.97%)	<0.001
	Headache	148(16.43%)	31(03.42%)	179(09.90%)	<0.001
	Tenderness	695(77.14%)	75(08.28%)	770(42.61%)	<0.013
	Itching at Painsite	395(43.84%)	25(02.76%)	420(23.24%)	<0.001
	Fatigue	389(43.17%)	191(21.08%)	580(32.09%)	<0.600
Common(1 in 10 People)	Fever	575(63.82%)	447(49.34%)	1022(56.60%)	<0.001
	Chills	103(11.43%)	45(04.97%)	148(08.19%)	<0.001
	Lump at Injectionsite	83(09.21%)	04(0.44%)	87(04.81%)	<0.001

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up to 1in10people)	SoreThroat	179(19.87%)	14(01.55%)	193(10.68%)	<0.001
	Cough	180(19.28%)	16(01.77%)	196(10.84%)	<0.001
	RunnyNose	80(08.88%)	12(01.32%)	92(05.09%)	<0.001
Uncommon (up to 1in100 people)	Syncope	18(02.00%)	06(0.66%)	24(01.33%)	<0.001
	Diarrhea	16(01.78%)	19(02.10%)	35(01.93%)	<0.001
	Vomiting	16(01.78%)	00(0.00%)	16(00.88%)	<0.001
	DecreasedAppetite	47(05.22%)	18(01.99%)	63(03.60%)	<0.001
	Sweating	98(10.88%)	40(04.42%)	138(07.64%)	<0.001
	Dizziness	138(15.32%)	10(01.10%)	148(08.19%)	<0.001

Table 3. Incidence rate AEFI comparison of Covisheild Vs Covaxin

V. DISCUSSION

The overall adverse reaction rates in this prospective research of adverse effects following immunization linked with two types of COVID-19 vaccines were 74.01% in the Covisheild group and 24.99 % in the Covaxin group, respectively. AEFI was more common in the Covisheild subjects than in theCovaxin subjects when comparing the two types of vaccinations.

Our study population exhibited a significant incidence rate of AEFI when compared to previous published research. Pain at the injection site was the most prevalent AEFI observed in this study, followed by fever and myalgia, as in previous studies from India, China, and the United States[7,8]. Other studies from throughout the world indicated lump at the injection site as the most prevalent AEFI.Out of 6222 AEFI we found that adverse events after vaccination were more frequent in men (n=3316) than in women (n=2906).

COVID-19 vaccines are expected to be distributed on a wide scale in a short period of time with minimal training and field preparedness, resulting in a higher number of Immunization Error-Related Reactions. Staff members who are unfamiliar with immunization may also be requested to conduct immunization tasks this may contribute a bias in understanding AEFI with error caused during immunization. Due to a variety of reasons, including older age groups, different vaccinating circumstances, the novelty of the vaccination and their delivery methods, a higher incidence of Immunization anxiety-related reactions like vomiting and syncope is anticipated.

Because many vaccines have real or potential underlying comorbidities, it will be difficult to distinguish true coincidental incidents from COVID-19 vaccine product related responses, pharmacological reactions, or interactions.

When it comes to novel vaccination platforms, knowledge of potential Vaccine quality faults may be insufficient at the time of COVID-19 vaccine licensure, and more information will be required, necessitating the strengthening of AEFI surveillance. Furthermore, the quick scaling up of vaccine production raises extra hazards, necessitating the identification of the particular ingredient responsible for the incident.

VI. CONCLUSION

In conclusion, those who received the Covisheild vaccine experienced significantly more adverse responses than those who received the Covaxin vaccine. Men were more frequently experienced negative side effects. The vaccines used are safe, and the AEFIs that were discovered were minor. As this study shows, when mass immunizing, the frequency and severity of adverse events linked with the Covisheild vaccination is anticipated.

A similar ongoing multi-centric studies around the country will aid in the collection of further safety data, particularly for newly launched vaccines. The training and experience of healthcare professionals involved in immunization programmes are significant in avoiding immunization error-related reactions. This type of studies involving national AEFI database will help in understanding vaccine safety issues in the country and this provides feedback to Healthcare professionals on public vaccine safety concerns.This study facilitatesauthoritiesto communicate effectively with general public and helps to sustain public faith in vaccines.

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Conflict of Interest
None

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