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Adverse events following COVID-19 vaccination: first 90 days of experience from a tertiary care teaching hospital in South India

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Abstract

Background: The COVID-19 vaccination program was introduced in India on 16 January 2021. The Government-issued fact sheet was the only source of information regarding Adverse Events Following Immunizations (AEFIs) for these vaccines. The objective of this study was to assess the AEFIs reported following COVID-19 vaccination in a tertiary care teaching hospital.

Materials and methods: The spontaneous reporting method was used for data collection for a period of 3 months. A data collection form was designed to collect the data from the study population who reported adverse events. Collected data were analyzed and categorized by severity and seriousness. The causality assessment team performed causality assessment of the AEFIs using the World Health Organization's causality assessment algorithm.

Results: A total of 11,656 doses of COVID-19 vaccine were administered at the study site during the study period, of which 9292 doses were COVISHIELD™ and 2364 doses were COVAXIN™. In all, 445 AEFIs were reported from 269 subjects with an incidence rate of 3.48%. The majority of the subjects with AEFIs belonged to the age group of 18–45 years. Out of the total 445 AEFIs, 418 AEFIs were expected as per the fact sheets, 409 with COVISHIELD™ and 9 with COVAXIN™. Most of the AEFIs [62.02% ($n = 276$)] were observed at the system organ class of 'General disorders and administration site conditions'. After the causality assessment, out of 433 AEFIs to COVISHIELD™ vaccine, 94.22% ($n = 408$) of events were categorized to have 'consistent causal association with immunization'. Out of 12 adverse events following COVAXIN™, 8 (66.66%) events were categorized as 'consistent causal association with immunization'. All of them recovered from their adverse events without any sequelae.

Conclusion: Spontaneous reporting is one of the cheapest methods that can be used for the reporting of AEFI. This method helps health care professionals to identify rare events and potential signals.

Keywords: AEFIs of COVID-19 vaccine, COVAXIN™, COVID-19 vaccination, COVISHIELD™

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Background

In December 2019, a cluster of cases of pneumonia without an identifiable cause was reported from the cultural and economic hub of China, Wuhan City, home to 11 million people.[1,2] The causative organism was isolated as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). On 11 March 2020, the World Health Organization (WHO) declared the novel coronavirus disease (COVID-19) outbreak as a global pandemic.[3]

More than one-third of the global population underwent some form of lockdown and curfew because of this pandemic. The Government of India also took steps toward controlling the pandemic by a nationwide lockdown from 25 March 2020, restricting the movement of its 1.3 billion citizens. The lockdown was extended until the end of May. Subsequently, unlocking was initiated in a phased manner from 1 June 2020.[4] On 30 January 2020, India's first novel coronavirus patient was identified in South India, and by April 2021, more than 1.35 crore COVID-19-confirmed cases have been reported.[5]

The development of a vaccine generally takes an average of 10–15 years.[6] However, different public organizations, regulatory agencies, and pharmaceutical companies worked together to develop COVID-19 vaccines rapidly by a scientific approach. Knowledge gained through the past research on other diseases such as severe acute respiratory syndrome (SARS) and Middle East Respiratory Syndrome (MERS) caused by viruses of the same Corona family helped scientists to accelerate the development of new vaccines for the current COVID-19 pandemic. During the development process of vaccines, no clinical trial phases were skipped, but the phases were overlapped to speed up the process so that the vaccines could be made available to the public as soon as possible.[7,8]

The Government of India constituted the National Expert Group on Vaccine Administration for COVID-19 (NEGVAC) to oversee all aspects of the introduction of the COVID-19 vaccine in India. Two vaccines that were approved for restricted use in an emergency situation by the Central Drugs Standard Control Organisation (CDSCO) in India are COVISHIELD™ (AstraZeneca's vaccine manufactured by Serum Institute of India) and COVAXIN™ (manufactured by Bharat Biotech Limited).[9–11] Comparison of both COVISHIELD™ and COVAXIN™ is given in Table 1.

Vaccination campaigns for COVISHIELD™ and COVAXIN™ were started in India on 16 January 2021 for all health care professionals and frontline workers. Vaccination drive for citizens aged above 60 years started on 1 March 2021 and later included citizens aged above 45 years with comorbidities. By 1 April 2021, the program was expanded to include all those aged 45 years and above even without comorbidities.[12–15] Vaccination program with COVISHIELD™ was started on 16 January 2021 itself at the study site and COVAXIN™ was subsequently added to the vaccination program from 13 March 2021.

An Adverse Event Following Immunization (AEFI) is any untoward medical occurrence that follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine. Operational guidelines of COVID-19 vaccines clearly specify everything including the process of monitoring, reporting, and management of AEFIs. The possible AEFIs following both the vaccines are given in the vaccine fact sheet (Table 1).[10,11]

As per the operational guidelines, each beneficiary needs to be observed at the immunization center for a minimum of 30 min for AEFIs or adverse events (AEs) of special interest (AESIs). After 30 min, the beneficiaries are free to report the development of any AEs to the vaccination center whenever they develop any.[16] This study was conducted with an objective to assess the AEs following COVID-19 vaccinations at the study site.

Methodology

Study site

The study site is a tertiary care teaching hospital having an adverse drug reaction–monitoring center (AMC) under the Pharmacovigilance Program of India (PvPI). Both active and passive surveillance for AEFIs have been instituted in this site for the past 9 years.

Study type: Prospective Observational Study.

Study duration: 90 days (16 January 2021 to 16 April 2021)

Study participants: The study enrolled the vaccination beneficiaries who reported any AEs.

Study process: The study population was observed for a period of 30 min following vaccination at the Immunization center. Posters of the possible AEFIs were made available in the

Table 1. Comparison between COVISHIELD™ and COVAXIN™.[9,10]

	COVISHIELD™	COVAXIN™
Developer	The Oxford-AstraZeneca and is being manufactured by the Serum Institute of India (SII)	Hyderabad-based Bharat Biotech International Ltd in association with the Indian Council of Medical Research (ICMR) and the National Institute of Virology (NIV)
Type of vaccine	The viral vector platform A chimpanzee adenovirus, ChAdOx1, has been modified to enable it to carry the COVID-19 spike protein into the cells of humans	Inactivated vaccine Developed with whole virion inactivated vero cell–derived technology
Ingredients	L-histidine, L-histidine hydrochloride monohydrate, magnesium chloride hexahydrate, polysorbate 80, ethanol, sucrose, sodium chloride, disodium edetate dihydrate (EDTA), water for injection	Contains 6 µg of whole virion inactivated SARS-CoV-2 antigen (Strain: NIV-2020-770) and other inactive ingredients such as aluminum hydroxide gel (250 µg), TLR 7/8 agonist (imidazoquinolinone) 15 µg, 2-phenoxyethanol 2.5 mg, and phosphate ® buffered saline up to 0.5 ml. The vaccine thus has been developed by using inactivated/killed virus along with the aforementioned chemicals
Doses	Vaccination course consists of two separate doses of 0.5 ml, each given 4–6 weeks apart	Vaccination series is two doses given 4 weeks apart with a dose of 0.5 ml each
Site of administration	The vaccine will be given as an intramuscular (IM) injection only, preferably in the deltoid muscle	The vaccine will be given as an injection into the deltoid muscle of the upper arm
Age limit	Approved for restricted use in emergency situation in individuals aged 18 years and above	
Storage guidelines	Stored at 2°C–8°C, which is a household refrigerator temperature	Stored at 2°C–8°C, which is a household refrigerator temperature.
Efficacy	Efficacy of 70.4%	Efficacy of 81%
Possible AEFIs	*Very common (may affect more than 1 in 10 people)* Tenderness, pain, warmth, redness, itching, swelling, or bruising where the injection is given Generally feeling unwell, feeling tired (fatigue), chills or feeling feverish, headache, feeling sick (nausea), joint pain, or muscle ache *Common (may affect up to 1 in 10 people)* A lump at the injection site, fever, being sick (vomiting), and flu-like symptoms, such as high temperature, sore throat, runny nose, cough, and chills *Uncommon (may affect up to 1 in 100 people)* Feeling dizzy, decreased appetite, abdominal pain, enlarged lymph nodes, excessive sweating, itchy skin, or rash	Injection site pain/swelling/redness/itching Headache Fever Malaise/body ache Nausea Vomiting Rashes

vaccination and observation area to educate the beneficiaries on possible AEFIs. Also, the vaccination team informed the beneficiaries to report back if they develop any kind of AEs. Information such as demographic details (age, gender, contact details) of the beneficiary, date and time of vaccination, vaccine details (name, batch number, and dose number), details of pre-existing medical condition, and details of AE was collected in the suitably designed data collection form after taking informed consent from each beneficiary. All the reported events were categorized to its system organ classification (SOC) as per the Medical Dictionary for

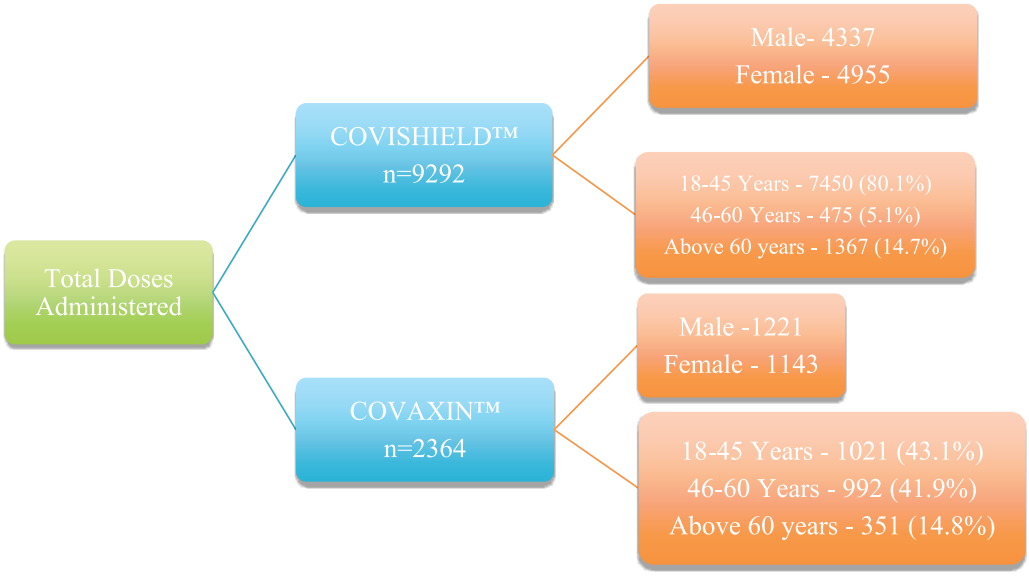

Figure 1. Details of total vaccinations at the study site.

Regulatory Activities (MedDRA) SOC classification. The reported events were subjected to causality assessment as per the new algorithm developed by the safety and vigilance department of the WHO.[17] Also, reported events were categorized by severity, seriousness, type of medical intervention for the AEs, and the outcome of the event.

Definitions used

1. *Health Care Workers (HCWs)*: Health care providers and workers in health care settings (public and private), including integrated child development service (ICDS) workers.[16]
2. *Frontline Workers*: Personnel from State and Central Police department, Armed Forces, Home, Guard, prison staff, disaster management volunteers and Civil Defense Organization, and Municipal Workers and Revenue officials engaged in COVID-19 containment, surveillance, and associated activities.[16]

Ethical clearance

Ethical clearance for the study was obtained from the Institutional Human Ethics Committee (IHEC) of JSS Medical College, JSS Academy of Higher Education and Research, Mysuru. (Ref. No.: JSSMC/ IEC/220121/18/2020-21).

Results

The total number of COVID-19 vaccine doses administered at the study site was 11,656, of which the COVISHIELD™ vaccine constituted 9292 doses. A total of 5986 beneficiaries received COVISHIELD™ and 1749 beneficiaries received COVAXIN™. A total of 9062 (77.74%) doses were administered to HCWs and 852 (7.30%) doses were administered to frontline workers. About 3306 beneficiaries of the COVISHIELD™ vaccine completed their vaccination schedule (2 doses) and 2680 have partially completed (one dose) their schedule. Among the beneficiaries of COVAXIN™, only 26.01% (n = 615) completed their vaccination schedule (2 doses) and 1134 have partially completed (one dose) their schedule. The number of doses of COVISHIELD™ and COVAXIN™ delivered among the age groups of the study population is provided in Figure 1.

The number of subjects who reported AE was 269 and the calculated incidence rate of AEs following COVID-19 vaccination was 3.48% (total number of subjects who developed AEFIs/total number of beneficiaries × 100). The incidence rate of AEs

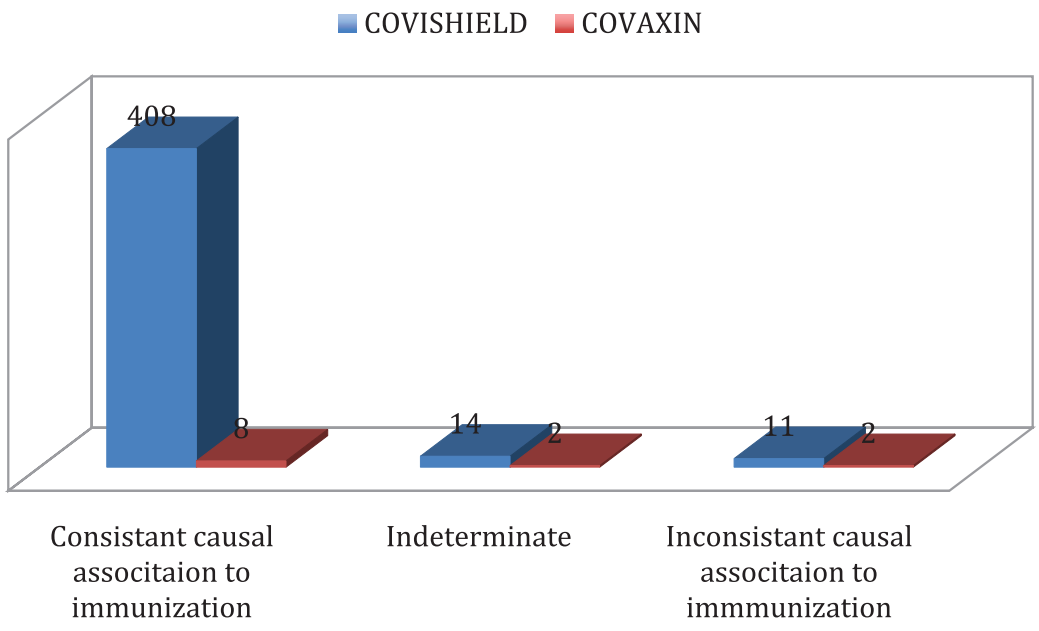

Figure 2. The causality assessment category.

following COVISHIELD™ was 4.32% and following COVAXIN™ was 0.57%. Females (n = 198) developed more AEFIs when compared with males (n = 71). In all, 22.67% of the study population developed AEFIs during the observation period following the vaccination, of which 53 AEFIs were to COVISHIELD™ and 8 to COVAXIN™. The majority of the study population with AEFIs belong to the age group of 18–45 years (82.53%, n = 222) followed by 46–60 years (6.32%, n = 17) and above 60 years (11.15%, n = 30). The incidence of AEFI occurrence in the age group of 18–45 years was 2.62% (222 AEFIs in 8467 beneficiaries), including 2.97% AEFIs among COVISHIELD™ beneficiaries (222 of AEFIs in 7450 beneficiaries) and none in COVAXIN™ beneficiaries. The incidence of AEFIs in the age group of 46–60 years was 1.17% (17 AEFIs in 1447 beneficiaries), including 2.79% in COVISHIELD™ beneficiaries (13 AEFIs in 465 beneficiaries) and 0.40% in COVAXIN™ beneficiaries (4 AEFIs in 982 beneficiaries). Similarly, the incidence of AEFIs in the age group of above 60 years was 1.72% (30 AEFIs in 1742 beneficiaries), including 1.74% in the COVISHIELD™ beneficiaries (24 AEFIs in 1377 beneficiaries) and 1.6% in the COVAXIN™ beneficiaries (6 AEFIs in 365 beneficiaries). A total of 243 subjects developed AEFIs within 24 h, 17 between 24 and 48 h, 6 between 48 and 72 h, 2 between 72 and 96 h, and 1 after 4 days. A detailed description of time temporal relationship of vaccine with AEFIs is given in Tables 2 and 3.

A total of 445 AEFIs occurred among 269 subjects, that is, 1.6 AEFIs per person with a range of 1–7 AEFIs. Out of the total AEFIs, 433 AEFIs occurred with COVISHIELD™ and 12 with COVAXIN™. A total of 50.9% (n = 137) of beneficiaries reported single AE, 34.9% (n = 94) of beneficiaries reported 2 AEs, 8.6% (n = 23) of beneficiaries reported 3 AEs, 3.7% (n = 10) of beneficiaries reported 4 AEs, 0.7% (n = 2) of beneficiaries each reported 5 and 6 AEs, and 1 beneficiary (0.4%) reported 7 AEs.

Out of the total 445 AEFIs, 418 AEFIs were expected as per the fact sheets, 409 with COVISHIELD™ and 9 with COVAXIN™. Out of the AEFIs specified in the fact sheet, 402 AEFIs were reported with the first dose of COVISHIELD™ and 7 with the second dose of COVISHIELD™. Also, 8 AEFIs were reported with the first dose of COVAXIN™ and 1 with the second dose of COVAXIN™. A detailed description of reported AEFIs is presented in Table 4.

A total of 20 beneficiaries who developed AEFIs had comorbid conditions and all of them received the COVISHIELD™ vaccine. The comorbid conditions observed were diabetes + hypertension (n = 10), hypothyroidism

Table 2. Time temporal relationship of COVISHIELD™ vaccine and AEFI.

Time (h)	COVISHIELD™ (n = 259)									
	1st dose (n = 252)					2nd dose (n = 07)				
	Subjects who developed AEFIs		Number of AEFIs (n = 426)[a]		Total no. of AEFIs after 1st dose (n = 426)[a]	Subjects who developed AEFIs		Number of AEFIs (n = 07)[b]		Total no. of AEFIs after 2nd dose (n = 07)[b]
	Male (n = 63)	Female (n = 189)	Male (n = 95)	Female (n = 331)		Male (n = 3)	Female (n = 4)	Male (n = 3)	Female (n = 4)	
⩽30 min	9 (3.3%)	37 (13.8%)	13	46	59	3 (1.1%)	4 (1.5%)	3	4	7
⩾30 min to 24 h	46 (17.1%)	135 (50.2%)	75	247	322	–	–	–	–	–
25–48 h	5 (1.9%)	12 (4.5%)	5	29	34	–	–	–	–	–
49–72 h	1 (0.4%)	4 (1.5%)	-	7	7	–	–	–	–	–
73–96 h	2 (0.7%)	–	2	–	2	–	–	–	–	–
⩾97 h	–	1 (0.4%)	–	2	2	–	–	–	–	–

AEFI, Adverse Events Following Immunization.
[a]AEFI reaction that occurred from fact sheet for COVISHIELD™ (1st dose) = 402, AEFI reaction that occurred from other than fact sheet for COVISHIELD™ (1st dose) = 24; Total = 426 AEFIs.
[b]AEFI reaction that occurred from fact sheet for COVISHIELD™ (2nd dose) = 7, AEFI reaction that occurred from other than fact sheet for COVISHIELD™ (2nd dose) = 0, Total = 7 AEFIs.

Table 3. Time temporal relationship of COVAXIN™ vaccine and AEFI.

Time (h)	COVAXIN™ (n = 10)									
	1st dose (n = 09)					2nd dose (n = 01)				
	Subjects who developed AEFIs		Number of AEFIs (n = 11)[a]		Total no. of AEFIs after 1st dose (n = 11)	Subjects who developed AEFIs		Number of AEFIs (n = 01)[b]		Total no. of AEFIs after 2nd dose (n = 01)
	Male (n = 03)	Female (n = 06)	Male (n = 05)	Female (n = 06)		Male (n = 01)	Female (n = 00)	Male (n = 01)	Female (n = 00)	
⩽30 min	1 (0.4%)	6 (2.2%)	3	6	9	1 (0.4%)	–	1	–	1
⩾30 min to 24 h	1 (0.4%)	–	1	–	1	–	–	–	–	–
25–48 h	–	–	–	–	–	–	–	–	–	–
49–72 h	1 (0.4%)	–	1	–	1	–	–	–	–	–
73–96 h	–	–	–	–	–	–	–	–	–	–
⩾97 h	–	–	–	–	–	–	–	–	–	–

AEFI, Adverse Events Following Immunization.
[a]AEFI reaction that occurred from fact sheet for COVAXIN™ (1st dose) = 8, AEFI reaction that occurred from other than fact sheet for COVAXIN™ (1st dose) = 3, Total = 11 AEFIs.
[b]AEFI reaction that occurred from fact sheet for COVAXIN™ (2nd dose) = 1, AEFI reaction that occurred from other than fact sheet for COVAXIN™ (2nd dose) = 0, Total = 1 AEFI.

Table 4. Reported AEFIs.

Reported AEFIs	1st dose	2nd dose
AEs following COVISHIELD™ vaccine (AEs specified in fact sheet)		
	(n = 426)[a]	(n = 07)[b]
Tenderness, pain, warmth, redness, itching, swelling, or bruising where the injection is given	78	7
Generally feeling unwell	10	–
Feeling tired (fatigue)	4	–
Chills or feeling feverish	29	–
Headache	29	–
Feeling sick (nausea)	5	–
Joint pain or muscle ache	66	–
Fever[c]	125	–
Being sick (vomiting)	8	–
Flu-like symptoms, such as high temperature, sore throat, runny nose, cough, and chills	7	–
Feeling dizzy	32	–
Abdominal pain	3	–
Enlarged lymph nodes	1	–
Excessive sweating, itchy skin, or rash	5	–
AEs following COVISHIELD™ vaccine (AEs not specified in fact sheet)		
Tachycardia	2	–
Tremors	1	–
Lip swelling	1	–
Insomnia	1	–
Eye burning sensation	3	–
Tingling/numbness on digits	3	–
Chest tightness	3	–
Edema of upper/lower limbs	1	–
Edema of face	1	–
Loose stools	3	–
Stomatitis	1	–
Puffy eyes	2	–

(Continued)

Table 4. (Continued)

Reported AEFIs	1st dose	2nd dose
Pricking pain in leg	1	–
Sneezing	1	–
AEs following COVAXIN™ Vaccine (AEs specified in fact sheet)		
	(n = 11)[d]	(n = 01)[e]
Injection site pain/swelling /redness/itching	3	1
Headache	1	–
Fever[c]	2	–
Malaise/body ache	0	–
Nausea	1	–
Vomiting	0	–
Rashes	1	–
AEs following COVAXIN™ Vaccine (AEs not specified in fact sheet)		
Giddiness	3	–

[a]Out of 252 subjects who reported AEFIs, 426 (402 from fact sheet + 24 other than fact sheet) AEFIs occurred with first dose of COVISHIELD™.
[b]Out of 7 subjects who reported AEFIs, 7 (7 from fact sheet + 0 other than fact sheet) AEFIs occurred with second dose of COVISHIELD™.
[c]Feverish is a self-reported feeling of feverishness, whereas fever is an objective fever measurement (mild: 100.4°F to 101.2°F, moderate: 101.3°F to 102.2 °F, severe: more than 102.2°F.
[d]Out of 9 subjects who reported AEFIs, 11 (8 from fact sheet + 3 other than fact sheet) AEFIs occurred with first dose of COVAXIN™.
[e]Out of 1 subject who reported AEFIs, 1 (1 from fact sheet + 0 other than fact sheet) AEFI occurred with second dose of COVAXIN™.

(n = 3), hypertension (n = 2), gastroesophageal reflux disease (2), hyperthyroidism + hypertension (n = 1), diabetes mellitus (n = 1), and bronchial asthma (n = 1). Most of the AEFIs [62.02% (n = 276)] were observed at the SOC of 'general disorders and administration site conditions' and the least affected SOC was 'blood and lymphatic system disorders' (n = 1). The details of the SOC implicated in AEFIs are presented in Table 5.

After the causality assessment, out of 433 AEFIs to COVISHIELD™ vaccine, 94.22% (n = 408) of events were categorized to have 'consistent causal association with immunization', which included 342 (78.98%) events of 'vaccine product–related reaction' and 66 (15.24%) events of 'immunization anxiety-related reaction'. Out of 12 AEs following COVAXIN™, 8 (66.66%) events were categorized as 'consistent causal association with immunization' and all of the reactions were 'immunization anxiety-related reactions'. Eleven events following COVISHIELD™ and two events following COVAXIN™ were categorized as having an 'inconsistent causal association with immunization'. The casuality assessment categories are depicted in Figure 2.

In all, 94.52% of the AEFIs were mild, three events were moderate, and one event was severe. None of the events were categorized as serious in nature. More than half of the study population (57.99%) sought medical attention due to AEs, and among them the majority [91.66%, n = 143)] had telephonic contact with the doctor and the rest (8.44%, n = 13) visited their doctor. None of the events fulfilled the criteria to become a serious event. Data on medical attention were

Table 5. System organ classification associated with AEFIs.

System organ classification	COVISHIELD™		COVAXIN™		Total *N* (%)
	1st dose	2nd dose	1st dose	2nd dose	
Blood and lymphatic system disorders	1	–	–	–	1 (0.22)
Cardiac disorders	1	–	–	–	1(0.22)
Eye disorders	5	–	–	–	5 (1.12)
Gastrointestinal disorders	23	–	1	–	24 (5.39)
General disorders and administration site conditions	260	7	8	1	276 (62.02)
Psychiatric disorders	2	–	–	–	2 (0.45)
Skin and subcutaneous tissue disorders	5	–	1	–	6 (1.35)
Nervous system disorders	62	–	1	–	63 (14.16)
Musculoskeletal and connective tissue disorders	66	–	–	–	66 (14.83)
Respiratory, thoracic, and mediastinal disorders	1	–	–	–	1 (0.22)
Total	426	7	11	1	445 (100)

collected, while the AEFI was reported spontaneously, and all of them voluntarily decided to obtain medical attention for their AEFIs. All the study population recovered from their AEs without any sequelae.

Discussion

Both the vaccines introduced in India had undergone the rigorous, multistage testing process, including phase III clinical trials that involved thousands of subjects to ensure the safety of the vaccines.[8] A total of 14,53,03,350 doses of COVID-19 vaccines were administered in India (includes first dose:12,14,85,043; second dose: 2,38,18,307) through 52,785 vaccination sites. A total of 19,544 AEFIs were reported in the Co-WIN portal.[18] A total of 602,990 individual case safety reports of AEs to COVID-19 vaccines were recorded by VigiFlow of the Uppsala Monitoring Centre (WHO collaborating center for international drug monitoring).[19] Europe reported the majority of the AEFIs to the global database, contributing to 73% of the total reports followed by 17% from America and 6% from Asia.[19]

We observed more AEFIs in the age group of 18–45 years, and an incidence of AEFI occurrence in this age group was 2.62%. We also observed 40% of events following COVID-19 vaccines, in line with that reported in VigiAccess for the age group of 18–44 years.[19] This might be due to the fact that the first groups who received vaccination were health care professionals and frontline workers who majorly belonged to this age group. In total, 71% of females developed AEFIs in this study comparable to 73% of females globally.[19]Also, there were a larger number of reports in the first half of the study duration ($n = 159$) and fewer reports in the second half ($n = 110$).

We observed an incidence rate of 3.48% of AEFIs among the study population, whereas the national incidence rate reported was 0.016%.[18] This difference in the incidence rate might be due to the fact that most vaccinators across the country give more preference to vaccinate their beneficiaries and educate them about mild or moderate AEFIs. And health care workers/consumers may not spend their time to report any mild or moderate AEFIs, which were already known. Underreporting is one of the major concerns in the spontaneous reporting method of safety surveillance. However, the study site is a recognized AMC under the Pharmacovigilance Program of India, and the HCWs are aware of the importance of Pharmacovigilance activities.

Also, we observed that the incidence rate of COVISHIELD™ is higher when compared with COVAXIN™. This large difference might be due to the change in the population who received both these vaccines. COVISHIELD™ was received by healthcare workers/frontline workers who were working in the hospital set up, and the beneficiaries were aware of the reporting system of AEs and had taken initiatives to contact the study team, whereas COVAXIN™ was taken majorly by frontline workers who were working outside the hospital setup and citizens who were not aware of the importance of AEFI reporting. Also, the vaccination team explained all the beneficiaries, the possible AEFIs, and management strategies at home. Hence, the reporting rate was less for COVAXIN™. The incidence rate of AEFIs reported within 30 min was 0.66%, and a similar result of 0.9% incidence was observed in a recent Indian study.[20] However, the overall incidence in this study[20] was as high as 40%, which is much higher than the incidence observed in the current study (3.48%). This might be due to the difference in the study method as the refereed study had followed up their beneficiaries in fixed time intervals for identifying the AEs, and they enrolled a smaller study population compared with our study.

We observed AEFIs, which were not seen in the clinical trials of both COVISHIELD™ and COVAXIN™, and similar events were seen in the VigiAccess™. A very less number of the study population with comorbidities developed AEFIs, which shows that the vaccine is safe for beneficiaries with any kind of comorbidities. The SOC implicated majorly in the AEFIs was 'general disorders and administration site conditions', and the same is observed in the global database. We observed less number of events with the SOC of 'blood and lymphatic system disorders' and observed a total of 25,160 events in this SOC in the VigiAccess™. However, we have not reported any event of blood clots, a majorly discussed rare event globally.[21] Another majorly involved SOC observed in VigiAccess™ was musculoskeletal and connective tissue disorders (n = 209779), and 15.52% of the events were categorized under this SOC in the current study.[19]

In all, 94.22% and 66.66% of events, respectively, following COVISHIELD™ and COVAXIN™ were categorized as having a consistent causal association with immunization, out of which 342 (78.98%) events following COVISHIELD™ and all events following COVAXIN™ were classified as vaccine product–related reactions. A total of 3.23% (n = 14) of events following COVISHIELD™ and 16.66% (n = 2) of events following COVAXIN™ were categorized under 'indeterminate' as the temporal relationship was consistent, but there was insufficient definitive evidence for vaccine causing events. These events may be potential signals as these were not present in the fact sheets as well. A total of 13 events were categorized as coincidental as those were caused by something other than the vaccine product, immunization error, or immunization anxiety. In the new causality assessment scale, only reactions that have evidence in published peer-reviewed literature that this vaccine might cause the event if administered correctly are classified as a vaccine product–related reactions. Reactions observed for the first time during post-marketing surveillance were not considered as 'consistent with a causal association with vaccine'. All new serious AEs are labeled as coincidental events 'inconsistent with causal association' or 'unclassifiable', and the association with the vaccine is not acknowledged. This mandates the conduct of systematic post-marketing surveillance studies.[22]

Limitation of the Study

As the study followed a spontaneous reporting method, we could not collect the data of all beneficiaries who had comorbidities and did not develop AEFIs. Similarly, we could not calculate the proportion of AEFIs reported in HCWs, vaccine-wise and dose-wise, as complete information was not available with the study team. Both the vaccines described in the study were introduced in two different timelines, which led to the large difference in the number of beneficiaries receiving each of these vaccines.

Conclusion

This study observed a higher incidence rate of AEFIs than the country's overall incidence rate as the study site is an AMC and the HCWs were aware of the vaccine safety activities. None of the events reported were severe or serious, which reiterates that the vaccines used in India are safe and the events will last without any kind of sequelae. Studies of this nature reinforce the need for

vigilant monitoring and reporting of AEFIs especially for newly introduced vaccines, as to identify potential signals.

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Author contributions

JS and MDR were involved in designing the research and getting the necessary approvals required for the study. JS and SBJ were involved in the data collection, data analysis, and preparation of the manuscript. CKB provided the necessary clinical support for the study. CKB, JS, and MDR were also involved in the monitoring of the research and finalization of the manuscript.

Conflict of interest statement

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