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Assessment of safety and adverse events following COVID-19 vaccination and their predictors in first 30 days among healthcare workers of a tertiary care teaching hospital in North India

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ABSTRACT

Background: The COVID-19 vaccines were rolled out as an emergency measure, with an expedited approval to contain the pandemic. The objective of this study was to assess the incidence, pattern and severity of AEFIs reported following COVID-19 vaccination and their predictors among the healthcare workers.

Materials and methods: A prospective cohort study enrolling healthcare workers of a tertiary care Institute in North India receiving COVISHIELD™ from February to May 2021 was carried out to assess the incidence, pattern and severity of AEFI over the next 30 days. Both active and passive surveillance methods were used for AEFI recording. Bivariate analysis was performed to ascertain the predictors of AEFIs.

Results: A total of 836 healthcare workers who received the first dose of COVISHIELD™ were included in the study of which 201 (24.0 %) experienced one or more AEFIs. Majority of AEFIs were of minor grade (99.8 %) and resolved spontaneously. Majority (96.0 %) had onset of the AEFIs within 48 hrs of vaccination. Serious AEFIs, leading to hospitalization was noticed in 2(0.2 %) participants, both females, with suspicion of immunization stress related response (ISRR). Both of them recovered without any sequelae. No deaths were recorded. Factors found to be significantly associated with the occurrence of AEFIs in the participants were female gender ($p = 0.02$), monthly income > 20,000 INR ($p = 0.007$), presence of any chronic illness ($p < 0.0001$), history of allergic reaction to any drug/vaccine ($p = 0.01$), history of COVID-19 infection ($p < 0.00002$) and history of hospitalization due to COVID-19 ($p < 0.0002$).

Conclusion: Majority of the AEFIs observed were of minor grade with spontaneous resolution of the symptoms indicating safety and well tolerability of the vaccine. Female gender, higher income, history of allergy and co-morbidities, history of COVID-19 infection and history of hospitalization were found to be major predictors for the development of adverse events and require more watchful vaccination.

Introduction

The COVID-19 disease caused by severe acute respiratory syndrome – Corona virus 2 (SARS-CoV2) had spread rapidly with around 773 million confirmed cases of COVID-19 globally, including 6,991,842 deaths as on 31th December 2023 [1]. In India, there were around 45 million cases of COVID-19 with 533,346 deaths as reported to the World Health Organization [2]· As there is no specific treatment for COVID-19, preventive measures like COVID-appropriate behavior and vaccines remained the mainstay of containing the pandemic and preventing deaths. Currently, the strategy of vaccination against COVID-19 is being implemented all around the world to overcome this global catastrophe.

The development of a new vaccine generally takes an average of 10–15 years [3]. During the pandemic, vaccines against COVID-19 were developed at an unprecedented speed. These vaccines had different

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levels of effectiveness and were approved for emergency use. Vaccination against COVID-19 can help mitigate infection and transmission, decrease hospitalizations due to severe disease and deaths [4], establish herd immunity [5], and could ultimately conquer the pandemic.

In India, nine vaccines for COVID-19 were approved by the Drugs Controller General of India (DGCI). They are COVISHIELD (ChAdOx1 nCov9), Covaxin (BBV152), Sputnik V, Johnson & Johnson, Moderna's Spikevax, Zydus Cadila's Zycov-D, Corbevax, Covovax and Sputnik Light [6]. More recently, DCGI gave approval to the first intranasal COVID-19 vaccine, Bharat Biotech's BBV154 [7]. However, Covishield and Covaxin only have together contributed more than 99 % of all vaccine doses administered so far in the country [6].

Nation-wide COVID-19 vaccination drive in India was started on January 16, 2021, initially for the health care workers (HCWs) and frontline workers [8]. Later, the drive was extended for all elderly citizens aged 60 year and above on 1st March and for those aged 45–59 years on 1st April respectively. Finally, on 1st May 2021, it included all adults citizens aged 18 years and above [9]. Since then, more than 2.2 billon doses have been administered [2].

Adverse events following immunization (AEFI) are defined as any untoward medical occurrence that follows immunization and that does not necessarily have a causal relationship with the usage of a vaccine. The adverse event may be any unfavorable or unintended sign, abnormal laboratory finding, symptom, or disease [10].The guideline document released by the Government of India mentions management plans for AEFI and recording of the same through the COVID Vaccine Intelligence Network (Co-WIN) application [11]. Co-WIN is a web-based application developed for management of COVID-19 vaccination process including AEFI reporting. As of December 15, 2022, the incidence of adverse events following COVID-19 vaccinations among the beneficiaries in India as reported by Co-WIN portal was 0.006 % [12]. However, this figure is grossly underestimated as the mechanism of adverse event following immunization (AEFI) reporting is not known to all beneficiaries and reporting by the vaccination centres and the district immunization officers (DIO) is not uniform round the country.

The WHO COVID vaccine safety surveillance manual recommends active and various passive systems to monitor AEFIs. This is to ensure vaccine safety and generate data on the overall short-term and long-term effect [13]. A systematic review on adverse events reported from COVID-19 vaccine trials reported that COVID-19 vaccines are relatively safe but stressed the need for long-term post-marketing surveillance data, particularly in high-risk vulnerable populations such as elderly and those with co-morbidities to ensure the safety of COVID-19 vaccines [14]. This is due to the intrinsic limitation of randomized clinical trials (RCTs), which usually involve a limited number of homogeneous participants for a limited duration of time. Actual, real-world roll out differs significantly from RCTs in terms of widely heterogeneous populations, vaccine supply, willingness for vaccination, accessibility to vaccines, etc.

Similarly, a systematic review and *meta*-analysis assessing the safety of COVID-19 vaccines in 26 real world studies revealed an incidence rate of 1.5 % (1.4–1.6 %) for adverse events, 0.4 (0.2–0.5) per 10, 000 for severe adverse events, and 0.1 (0.1–0.2) per 10,000 for death after vaccination [15].

It is, therefore, critical to keep a vigilant eye on the emerging adverse effects of the COVID-19 vaccines and to identify their predictors in order to take appropriate measures. The current study was conducted with the objective to assess the incidence, pattern and severity of AEFI following vaccination with ChAdOx1 nCov9 Corona virus vaccine (Recombinant) (COVISHIELD) among the healthcare workers and to evaluate their predictors.

Material & methods

Study design, settings and population

A prospective, single-center observational study was conducted at the COVID-19 Vaccination Centre at SSL Hospital, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India from 1st February to 31st may 2021.The hospital is a 700-bed tertiary care teaching institute situated in Eastern part of India and caters to patients from 4 states of India and adjoining country of Nepal.

The study subjects were Health Care Workers (HWCs) getting vaccinated with the first dose of the ChAdOx1 nCov-19 vaccine i.e. COVISHIELD™. The healthcare Workers consisted of doctors, nurses, technicians, ward attendants, housekeeping staffs and security guards.

As per government policy, adult HCWs of any age were eligible for COVID-19 vaccination. HWCs who didn't receive vaccination and among those who received the vaccination, HCWs who did not give consent for participation in the study were excluded.

The study age group included 18–44 years and more than 45 years age-group both and they were selected proportionately.

Sample size and sampling strategy

The minimum sample size required for the study was estimated to be 322, taking 29.8 % prevalence (p) of AEFI from the study by Parida et al. [16], absolute precision (d) as 5 %, and confidence interval of 95 %. The sample size was calculated using Openepi software using the formula $Z_{\alpha}\, 2p(1-p)/d^2$. However, we intended to include everyone who received COVID-19 during the study period. Consecutive sampling was employed to enrol participants in the study.

Study procedure

As per the operational guidelines, each vaccine recipient was observed for a minimum of 30 min for AEFI at the vaccination centre [11]. An onsite medical team consisting of a physician and 2 nurses was deployed at the centre for detection and stabilization of immediate adverse events during the observation period. In addition, education on AEFI was provided by a trained medical staffs to the beneficiaries at the time of exit. The rapid response preparedness included availability of critical care physicians on site with emergency medicine consultations, designated observation area and emergency medical equipment such as crash carts. After 30 min, the beneficiaries were free to report the development of any AEFI to the surveillance team by calling on the mobile number displayed at the vaccination centre whenever they develop any. Posters of the possible AEFI were made available in the vaccination and observation areas to educate the beneficiaries on possible AEFI. Also, the surveillance team informed the beneficiaries to report back if they develop any kind of AEs on the WhatsApp group formed for each day vaccine beneficiaries. 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 AEFIs was collected in the suitably designed data collection form after taking informed consent from each beneficiary immediately after vaccination. A telephonic follow-up was then conducted on the 8th, 15th, 22nd and 30th day of vaccination. Solicited local adverse events like pain at the injection site, tenderness/soreness, erythema, swelling/induration, pruritus associated with injection, and solicited systemic adverse events like pain, fever, nausea/vomiting, headache, fatigue, myalgia, acute allergic reaction/rash, and joint pain were assessed. All the unsolicited adverse events reported by the study participants were also recorded. Also, reported events were categorized by severity, seriousness, type of medical intervention for the AEs, and the outcome of the event.

The adverse events were graded as minor, severe, and serious based on the operational guidelines on COVID-19 vaccines issued by Ministry

of Health and Family Welfare, Government of India [11]. Minor AEFIs were ccommon, self-limiting reactions such as pain, swelling at the injection site. Severe AEFIs were those which can be disabling and rarely life threatening but do not lead to long-term problems. Examples of severe reactions include non-hospitalized cases of anaphylaxis that has recovered, high fever (>102-degree F), etc. Serious AEFIs were those which results in death or requires inpatient hospitalization or results in persistent significant disability or a AEFI cluster or evokes significant parental/ community concern [11].

Statistical analysis

The data were entered into excel sheets and analyses were performed using SPSS software (version 25.0; IBM Corp., Armonk The, NY, USA). Data were checked for consistency and completeness before entry and analysis. The descriptive data were presented using frequencies and proportions. Bivariate analysis using the chi-square test was performed to find out the association between outcome and predictor variables. Outcome variable was incidence of AEFI and the predictor variables consisted of various socio-demographic and medical characteristics of the participants. A $p < 0.05$ was considered significant.

Ethics statement

This study was approved by the Institutional Review Board of Institute of Medical Sciences (Approval letter No. Dean/2021/EC/2524). Written informed consent was taken from all the participants before inclusion in the study.

Results

A total of 1256 healthcare workers(HWCs) were listed for vaccination of which 836(67.6 %) who received the first dose of COVISHIELD^{TM} vaccine during the study period were included and monitored for AEFI for a period of 30 days. Their background characteristics are as mentioned in Table 1.

Around one-fifth of the study participants gave history of suffering from any chronic illness.A total of 125 (14.9 %) gave a history of laboratory confirmed COVID-19 infection in past of which 31(3.7 %) were hospitalized due to the COVID-19 infection. Only 6(0.3 %) had a history of allergic reaction to any drug/vaccine. Around 11 % gave a history of alcohol consumption whereas history of smoking was given by around 12 % of the participants (Table 2).

A total of 201 (24.0 %) participants reported to experience one or more AEFIs during the observation period i.e. within 30 min of vaccination till 30 days (Fig. 1). Among these, only 2 (0.2 %), both being females having co-morbidities of hypothyroidism and hypertension, reported to experience severe symptoms requiring hospitalization, and the rest 199 (23.8 %) were having mild symptoms only with spontaneous resolution. Of the 2 participants experiencing severe symptoms, one had vertigo with altered sensorium and another one had dizziness with malaise, anxiety and palpitation with onset within 15 min of vaccination. Both were discharged within 24 h of admission. Of the rest 199 participants having mild symptoms, 102(51.2 %) took paracetamol tablets and rest 97(48.8 %) had spontaneous resolution..

Out of the 201 participants reporting any AEFI, 88(43.8 %) reported to experience an AEFI within 30 min of direct observation, 51(25.4 %) reported to experience between 30 min and 24 h, 32(15.9 %) between 24 h and 48 h, 8(4.0 %) reported any AEFI between 48 h and 14 days with no participant reporting any AEFI after 14 days of vaccination. More than one AEFI was reported by 124 (61.7 %) participants, and rest 77 (38.3 %) participants had reported only one AEFI.

Pain/tenderness at the injection site (35.3 %) was the most common AEFI reported followed by fever (26.9 %), headache (20.9 %) and myalgia/bodyaches (16.4 %) (Table 3).

In bivariate analysis, factors found to be significantly associated with the occurrence of AEFIs among the participants were female gender ($p = 0.02$), monthly income > 20,000 INR ($p = 0.007$), presence of any chronic illness ($p < 0.0001$), history of allergic reaction to any drug/vaccine ($p = 0.01$), history of COVID-19 infection ($p < 0.00002$) and history of hospitalization due to COVID-19($p < 0.0002$) (Table 4).

Table 1
Background characteristics of the Healthcare Workers participants receiving COVISHIELD vaccine (N = 836).

Variables	Frequency N (%)	Percentage (%)
Mean age in years ± SD	35.75 ± 9.52	
Age-groups		
18–44	684	81.8
45–59	137	16.4
≥ 60 years	15	1.8
Sex		
Male	573	61.2
Female	263	38.8
Religion		
Hindu	783	83.6
Muslim	16	1.7
Sikh	02	0.2
Christian	35	3.7
Marital status		
Unmarried	197	23.6
Married	636	76.1
Widowed/Divorced/Separated	03	0.4
Level of Education		
Up to matriculation	38	45.4
Intermediate or Diploma	189	22.6
Graduation	356	42.6
Post-graduation & Above	243	29.1
Occupation		
Doctor	230	27.5
Nursing Officer/Technician/Other paramedics Attendant/Housekeeping staff/Security guard	404	48.3
Monthly income(in INR)	202	24.2
Up to 20,000	114	13.6
20001–50,000	141	16.9
50,001–1,00,000	441	52.8
>1,00,000	340	40.7
Dietary habit		
Vegetarian	348	41.6
Non-vegetarian	488	58.4

Discussion

In the current study, we investigated the incidence, pattern and severity of AEFIs among the healthcare workers (HCWs) receiving first dose of ChAdOx1 nCoV-19 Corona virus vaccine (recombinant) i.e. COVISHIED^{TM}. The mean age of the participants was 35.75 ± 9.52 years with majority being males (61.2 %) and belonging to the age-group of 18–44 years (81.8 %). The incidence of AEFIs among them within 30 days of receiving the first dose of vaccine was found to be 24.0 %. Studies by Kushwaha et al. [17] from North India and Kujur et al. [18] from Eastern India assessing AEFI with 1st dose of COVISHIELD and Parida et al. [16] from Eastern India assessing AEFI with Covaxin reported similar figures of 30.4 %, 33.6 % and 29.8 % respectively. However, studies by Kaur U et al. [19], Kaur S et al. [20] and Jha et al. [21] from North India reported the incidence of AEFI as 40.0 %, 46.0 % and 73.9 % respectively with 1st dose of COVISHIELD^{TM} whereas studies by Kamal et al. [22], Jose M et al. [23], Jose D et al. [24] and Manda et al. [25] from Southern India and study by Velhal et al.[26] from Western India reported the incidence of AEFI as 57 %, 50.4 %, 54.3 %, 49.9 % and 94.4 % respectively, much higher than our finding. However, Joshi et al. [27] from Northern India and Basavaraja et al.[28] from Southern India reported the incidence of AEFI as 6.4 % and 4.3 % respectively after 1st dose of COVISHIELD, much lower than our figure. Similarly, studies across the globe also reported the incidence of AEFI following COVID-19 vaccination to be highly variable. A study by

Table 2
Medical conditions including history of COVID-19 among study participants (N = 836).

Variables	Frequency(n)	Percentage (%)
History of any chronic illness/co-morbidity		
Present	160	19.1
Absent	676	81.9
*Pattern of chronic illness/co-morbidity**		
Hypertension	67	8.0
Diabetes Mellitus	53	6.3
Bronchial Asthma	23	2.8
CAD/Heart disease	07	0.8
Musculoskeletal disease	03	0.4
Epilepsy	03	0.4
Received any vaccine in past 4 weeks		
Yes	02	0.2
No	834	99.8
Tested positive for COVID-19 in past		
Yes	125	14.9
No	711	85.1
History of hospitalization due to COVID-19		
Present	31	3.7
Absent	805	96.3
History of allergic reaction to any drug/vaccine		
Present	06	0.7
Absent	830	99.3
History of alcohol consumption		
Present	94	11.2
Absent	742	88.8
History of alcohol consumption within 24 h		
Present	15	1.8
Absent	821	98.2
History of Smoking/smokeless tobacco products		
Present	102	12.2
Absent	734	87.8

*Multiple co-morbidities possible.

Kadaki et al. [29] from USA assessing side effects of BNT162b2 mRNA vaccine among the HCWs reported 100 % of them experiencing any AEFI. Similarly, Marfo et al. [30] from Ghana reporting AEFI with COVISHIELD^{TM} among the HWCs reported the incidence rate of 706 per 1000 doses of vaccine whereas Asefa et al. [31] from Ethiopia reported the incidence rate of AEFI with the Oxford AstraZeneca vaccine as 51.3 %. This wide variation in incidence of AEFI across these studies is mainly due to varied type of COVID-19 vaccine used, method of reporting the AEFI (active v/s passive), differences in age-groups and education level of the participants and differences in the period of follow ups.

Among those participants experiencing any AEFI in our study, majority (119, 99.0 %) experienced only mild/minor grade AEFI with only 2(1.0 %) experiencing a severe AEFI requiring hospitalization but without any sequelae or long-term complication. Similar results were reports by other studies from various parts of India [16–28] and across the globe [29–33]. In the study by Kamal et al. [22], two serious AEFI (altered sensorium) were reported within 48 h after the 1st dose of COVISHIELD^{TM} vaccine. In our study too, two cases of serious AEFI, both

Table 3
AEFI types/pattern observed among the participants experiencing any AEFI (*N* = 201).

Sl. No.	AEFI observed*	No. (%)
	Pain/tenderness at injection site	71(35.3)
	Fever/Chills	54(26.9)
	Headache	42(20.9)
	Myalgia/bodyaches	33(16.4)
	Malaise/weakness	21(10.4)
	Dizziness/Vertigo	18(8.9)
	Itching/redness/rash at the injection site	16(8.0)
	Nausea/Vomiting	5(2.5)
	Cold/flu-like symptoms	3(1.5)
	Tingling sensation in fingers	2(1.0)
	Anxiety/Palpitation	2(1.0)
	Chest Pain	1(0.5)
	Burning sensation in legs	1(0.5)
	Loose stools	1(0.5)
	Joint pain	1(0.5)
	Increased Lacrimation	1(0.5)
	Altered sensorium/psychosis	1(0.5)
	Breathlessness	1(0.5)

*Multiple responses possible.

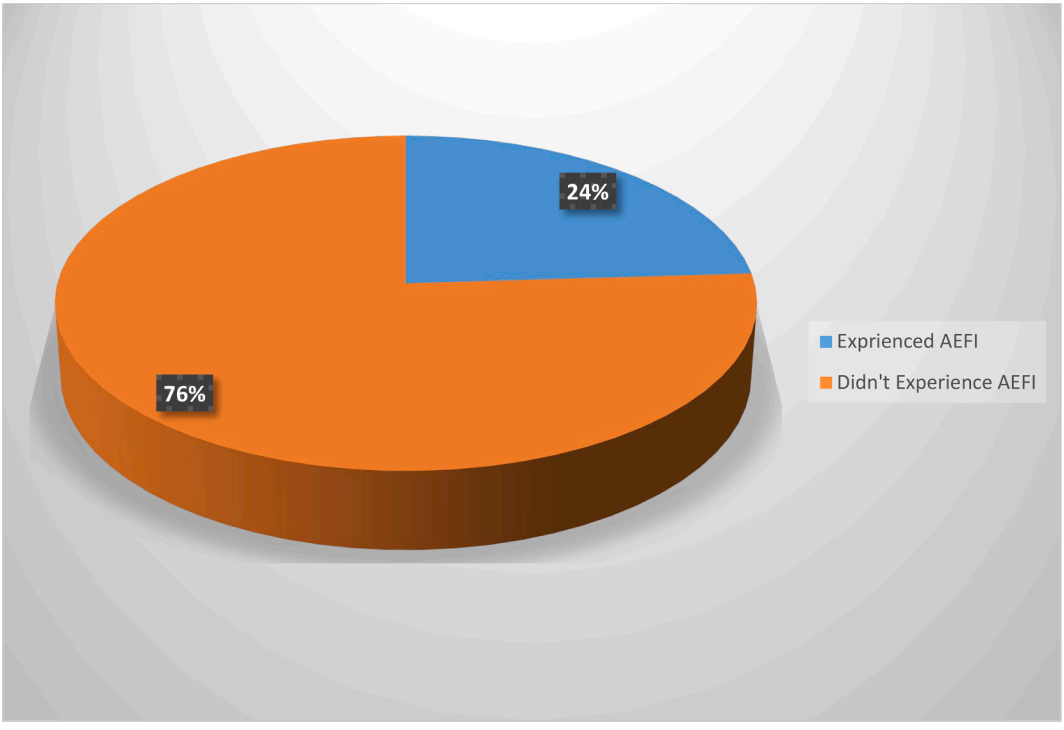

Fig. 1. Incidence of AEFI among the healthcare workers receiving 1st dose of COVISHIELD^{TM} (N = 836).

Table 4
Association of Socio-demographic & Medical characteristics with occurrence of AEFIs among the participants (n = 836).

Variables	Reported AEFI(n = 201) n(%)	Didn't report AEFI (n = 635) n(%)	X^{2*}-value	p-value
Age-groups(in years)				
18–44	170(24.8)	514(75.2)	2.52	0.11
45–59	30(21.9)	107(78.1)		
≥ 60	01(6.7)	14(93.3)		
Sex				
Male	125(21.8)	448(78.2)	4.95	0.02**
Female	76(28.9)	187(71.1)		
Religion				
Hindu	185(23.6)	598(76.4)	1.17	0.27
Others	16(30.2)	37(69.8)		
Level of Education				
Below Graduate	58(25.4)	170(74.6)	1.12	0.28
Graduate & Above	143(23.5)	465(76.5)		
Occupation				
Doctor	51(22.1)	179(77.9)	0.60	0.43
Nurse/other paramedics	150(24.7)	456(75.3)		
Monthly income(in INR)				
≤ 20,000/-	16(14.0)	98(86.0)	7.24	0.007**
> 20,000/-	185(25.6)	537(74.4)		
Presence of any chronic illness				
Yes	64(40.0)	96(60.0)	27.58	< 0.00001**
No	137(20.3)	539(79.7)		
History of allergy to drug/vaccine				
Yes	3(50.0)	3(50.0)		
No	198(23.8)	632(76.2)	6.01	0.01**
History of COVID-19 infection				
Yes	50(40.0)	75(60.0)	18.49	0.00002**
No	151(21.2)	460(78.8)		
History of hospitalization due to COVID-19				
Yes	16(51.6)	15(48.4)	13.39	0.0002**
No	185(23.0)	620(77.0)		
Current alcohol use				
Yes	25(26.6)	69(73.4)	0.32	0.90
No	177(23.8)	565(76.2)		
Current tobacco use (smoke/smokeless)				
Yes	21(20.6)	81(79.4)		0.38
No	180(24.5)	554(75.5)		

*Chi-square/Fischer exact test.
** Statistically significant.

in females having co-morbidities of hypothyroidism and hypertension, with similar presentation having onset within 15 min of vaccination were recorded. However, both the cases had symptom resolution within 24 h with no sequelae and were mostly due to immunization stress related response (ISSR) [34]. Stress responses to vaccination are manifested immediately before, during, or after vaccination. This may include acute stress responses including vasovagal reactions (e.g., fainting, palpitations, hyperventilation, and dizziness). They usually occur in the immediate time period surrounding a vaccine administered by the injectable route. An acute stress response or vasovagal reaction is usually transient and resolves spontaneously. This was consistent with our findings.

The common AEFIs reported in our study were pain/tenderness at the injection site, fever, headache, myalgia and malaise. These are also the common adverse events reported in the Phase 2/3 trial of ChAdOx1 nCoV-19 vaccine [34]. Similar pattern of AEFI was observed in the most of other Indian studies [18–28]. However, Kushwaha et al. [17] in their study reported fever (69.6 %) and feeling unwell (52 %) to be more commoner AEFIs than pain/swelling at the injection site (36.8 %) subsequent to the first dose of COVISHIELD^{TM}vaccine. Kadali et al.[29] assessing the side effects of BNT162b2 mRNA COVID-19 vaccine reported soreness, fatigue, myalgia, headache, chills, fever and joint pain as the most commonly reported symptoms. In the study by Beccia et al. [33] from Italy three clusters of adverse effects defined by the presence/absence of fatigue, malaise, localized pain, chills, pyrexia, insomnia, nausea and injection site pain, were frequently reported together.

Young adults reported AEFIs more frequently than the elderly beneficiaries in our study; however, the difference was not statistically significant (p = 0.11).However, some studies found age to be significantly associated with AEFI. Kamal et al. [22] in their study found significant association of AEFI with age with the incidence being higher in the age group of > 50 years. In contrast, Parida et al. [16]' Kaur U et al. [19], Kaur S et al. [20], Jose M et al. [23] and Jose D et al. [24] reported higher AEFI among the younger participants. In a study by Sathyapalan et al. [36] from Southern India assessing adverse events after first dose of COVISHIELD^{TM} vaccine, the prevalence of systemic and allergic symptoms were observed to be significantly high among respondents aged < 25 years. Vaccine reactogenicity, the reason behind the occurrence of AEFI, has also been reported to be higher among the younger individuals compared to the older ones in the phase 2/3 clinical trials of ChAdOx1 nCoV-19 Coronavirus Vaccine (Recombinant) i.e. COVISHIELD^{TM} in India [37].

The proportion of females reporting AEFI was significantly higher as compared to males in our study (p = 0.002). This finding is similar to that of some other studies from India [16,18–21,25–28,36] and abroad [31,32,38]. In contrast to this, no gender difference was reported in the studies by Kushwaha et al. [17], Kamal et al. [22] and Marfoh et al. [30]. Previous studies conducted for assessing the gender differences in responses to influenza vaccine [39,40,41] had also documented higher incidence of AEFI among females compared to males. The reasons for this can be the genetic factors as well as the sex hormones which are known to influence cytokine levels and immune response to vaccination. It has been observed that women tend to produce higher titers of neutralizing antibodies post vaccination as compared with men [41].

Other than female gender, other significant predictors for AEFI in our study were higher income, presence of any chronic illness/co-morbidity, history of drug/vaccine allergy, history of COVID-19 infection, and history of hospitalization due to COVID-19. These results are similar with the results reported by Parida et al. [16], Kaur U et al. [19] and Jha et al. [21]. Presence of any co-morbidity was also significantly associated with AEFI in the studies by Khalil et al. [42] from Bangladesh, and Meni et al.[38] from United Kingdom. Similarly, a higher incidence of reactogenicity was reported in participants with previous SARS-CoV-2 infection by some other studies [27,43]. Higher income being one of the predictors of AEFI is a unique finding of our study which requires further investigation.

In our study, 24.0 % of the study participants had reported at least one or more adverse after the first dose. The adverse events reported in our study were in much lower frequencies in comparison to the Phase 2/3 trial of ChAdOx1 nCoV19 vaccine wherein 88 % of participants in the age-group of 18–55 years reported local reactions and 86 % of them reported systemic reactions [35]. The trial reported better tolerability of the vaccine in older adults than in younger adults which was also evident through our study. In the phase 2/3 clinical trial assessing immunogenicity and safety of SII-ChAdOx1 nCoV-19 i.e. COVISHIELD^{TM} in India, a total of 26.2 % participants reported unsolicited adverse events (AEs) after the first dose [37] which is similar to our finding.

Some of least common AEFI reported in our study were tingling sensation in fingers and anxiety/palpitation, each reported only by 2 (1.0 %) participants and chest Pain, burning sensation in legs, loose stools, Joint pain, increased Lacrimation, altered sensorium and breathlessness, each observed in 1(0.5 %) participant only. Study by Velhal et al. [26] also reported tingling sensation in hands, acidity and

burning sensation in eyes as the least common AEFIs observed. However, they reported dysguesia and ageusia to be present in 4.9 % of the participants which was not observed in any of our study participants. This emphasizes the importance of AEFI surveillance, both active and passive, at each vaccination site to report the rare and unknown adverse events.

Limitations.

Being a single Centre study, the findings may not be generalizable to other regions of the state and country. AEFI reporting was completely symptoms based and no further laboratory investigations could be carried out due to lack of resources. As only health workers were included in the study, it may not represent the findings in the general population. During the study period, only COVISHIELD vaccine was supplied by the district health authorities and available at our vaccination centre. Hence, direct comparison between COVAXIN and COVISHIELD was not possible in the same population.

Conclusion & recommendations

COVID vaccination has been observed to be safe and well tolerated with more systemic symptoms than local symptoms. Our study demonstrated that AEFI post vaccination with the first dose of COVISHILED™ is very common as 1 in 4 participants reported one or more AEFI. However, majority (99.0 %) of the participants who experienced any AEFI had mild symptoms only which resolved spontaneously in 2–3 days without any sequelae. COVID vaccination has been observed to be safe and well tolerated with more systemic symptoms than local symptoms. The factors found to be significantly associated with AEFI occurrence were female gender, higher monthly income (≥20,000), presence of any chronic illness, history of allergy to any drug/vaccine, previous COVID-19 infection and history of hospitalization due to COVID-19.

Active surveillance at fixed intervals coupled with passive surveillance for AEFI in the vaccine recipients would enable robust monitoring and reporting of AEFI with very little chances of under-reporting of the non-serious adverse events. The institution where vaccination is being conducted should have both active as well as passive surveillance systems with community participation to monitor AEFI and further be reported to district and state health authorities for the purpose of necessitating any relevant intervention.

CRediT authorship contribution statement

Abu Bashar: . Bhushan Kamble: . Sampath Kumar: Data curation, Investigation, Methodology, Project administration, Resources, Validation, Visualization, Writing – review & editing. **Sanket V. Nandekar:** Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Visualization, Writing – review & editing. **Sharad Kumar Mathur:** Conceptualization, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Author contributions

MAB, BK and SKM were involved in designing the research and getting the necessary approvals required for the study. MAB, BK, SK and SVN were involved in the data collection and data entry. MAB, SK and SVN performed data analysis and preparation of the manuscript. MAB and BK were also involved in the monitoring of the research and finalization of the manuscript. All the authors approved the final manuscript for publication.

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