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Reporting adverse events of ChAdOx1 nCoV-19 coronavirus vaccine (Recombinant) among the vaccinated healthcare professionals: A cross-sectional survey

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***Background & objectives*: The safety of the ChAdOx1 nCoV-19 vaccine is a cause of concern for many who have been vaccinated. The people have multiple concerns and fear regarding the adverse events of the vaccine. Thus, this study was undertaken to establish the safety profile of ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombinant) among the healthcare professionals.**

***Methods*: This was a descriptive cross-sectional survey. After taking clearance from the institutional ethics committee 1500 healthcare professionals, who had their vaccination in the past two weeks were selected. They were provided with an online survey proforma regarding adverse events following immunization (AEFIs) of COVID-19 vaccine developed using google forms with an informed consent form affixed to it.**

***Results*: A total of 1036 individuals participated in the study. The mean and median (inter quartile range) age of the participants was 37.7 ±11.25 and 35 (29-46) yr, respectively. Of these, 52.1 per cent were female, 29.3 per cent were doctors, 33.4 per cent were nurses and 9.5 per cent were paramedical staff. Forty six per cent participants experienced one or more minor AEFIs such as pain, tenderness, redness, *etc.* at the injection site. Fatigue (31.75%), generalized feeling of unwell (28.57%), muscle pain (23.16%) and fever (21.71%) were the most commonly reported systemic AEFIs followed by headache (20.07%), dizziness (10.03%) and joint pains (15.25%). Most of them experienced these AEFIs within 24 h of the first dose of administration. About 42 per cent of the participants took oral antipyretics/analgesics for managing the AEFIs.**

***Interpretation & conclusions*: ChAdOx1 nCoV-19 Corona Virus Vaccine was found to be associated with mild local and systemic AEFIs that were more common after the first dose as compared to the second dose. There adverse events could be dealt with oral over-the-counter medications, with no requirement of hospitalization.**

Key words Adverse events - ChAdOx1 nCoV-19 - coronavirus disease 2019 - healthcare professionals - side effects - vaccination

*Equal contribution

The Government of India launched the COVID-19 mass vaccination programme on January 16, 2021 all over the country in a phased manner[1-3]. In the first phase, the healthcare and the frontline workers from various sectors were prioritized to receive the vaccine[2,3]. In the second phase, individuals above 60 yr, and individuals above 45 yr of age with certain co-morbidities, were vaccinated[2,3]. However, people had multiple concerns regarding the safety and efficacy of COVID-19 vaccines[4]. In a pooled survey conducted in European countries, only 58 per cent of the 24970 participants were willing to get the COVID-19 vaccine. The authors showed concerns that a significant number of European countries would not be able to reach the estimated herd immunity threshold (67%) with this public attitude towards COVID-19 vaccines[5]. Malik *et al*[6] found noticeable demographic and geographical disparities in vaccine acceptance. Major concerns were regarding adverse events and possible long-term side effects of COVID-19 vaccines. The interim reports of ChAdOx1-S and BBV152 vaccines mention the safety profile of these vaccines along with the efficacy of 63 and 81 per cent, respectively[7-9]. In a press release, the Ministry of Health and Family Welfare, Government of India, informed that 447 adverse events were reported to COVID-19 vaccines among the vaccinated population of 224,301 Indian people[10]. The current study was an attempt to find out common adverse events of the ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombinant) among the Indian healthcare professionals (HCPs) who were vaccinated against COVID-19.

Material & Methods

The present study was a descriptive cross-sectional survey which was conducted at the Postgraduate Institute of Medical Education & Research (PGIMER), Chandigarh, India, during February 13 - March 31, 2021. The target population was the HCPs who received ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombinant) first dose or second dose or both at the PGIMER, Chandigarh. Fifteen hundred HCPs were selected from the record register maintained in the immunization centres. The participants who had their vaccination in the past two weeks were enrolled in the study. An online survey proforma regarding post-vaccination adverse events of the COVID-19 vaccine was developed by using google forms with an informed consent form affixed to it. It comprised information profile sheet and post-vaccination adverse events of COVID-19 vaccination sheet which enlisted all the possible adverse events known in the literature for the available vaccines. The proforma was validated by experts in the field of medicine, public health and nursing. Ethical clearance was obtained from the ethics committee of the institute. Participation was voluntary. Online consent was sought from each participant. The participants were allowed to clarify any aspect of the research. They were free to withdraw from the study at any time. The confidentiality/anonymity of the data was maintained throughout the research process.

Data collection: HCPs were selected with the convenient sampling technique. Their mobile numbers were obtained from the vaccination centres of the institute. They were provided with an online link to fill up the survey proforma on the day of vaccination. It took around 10 min to complete the proforma. The participants were given three days time frames for responding to the survey proforma. Contact details were provided at the end of proforma, in case the participants needed any additional information or any other help.

The self-reported data were coded and analyzed using IBM® SPSS Statistics for Windows, Version 22.0 for Windows (SPSS Inc., Chicago IL, USA, Armonk, NY: IBM Corp. Released 2013). The primary outcome was the incidence of adverse events following immunization (AEFI) and type of AEFIs following COVID-19 vaccination reported by the participants. The secondary outcome was to establish predictors of AEFIs concerning age, gender, co-morbidities and vaccine doses.

Statistical analysis: Descriptive statistics included calculations of means, standard deviations (SDs) and proportions. The significance of differences in the proportion of AEFIs by age, gender, co-morbidities, the dose of vaccination and the type of healthcare workers was tested using the Chi-square test of association. Further, the predictors/risk factors of AEFIs were identified using logistic regression by taking AEFIs as a binary dependent variable, and age (continuous), gender (female=0, male=1), co-morbidities (no=0, yes=1) and the dose of vaccination (first dose, second dose) as binary independent variables. The prevalence of AEFIs was further compared by the type of healthcare workers and specific comorbidities. Adjusted odds ratios estimates were presented with 95 per cent confidence intervals (CIs) and *P* values.

Results

Of the 1500 participants who were given the proforma, 1036 (540 females, 496 males) chose

to participate in the study. Four hundred and sixty four individuals did not respond to the online invite or refused to give consent for participation. The demographic details are mentioned in Table I. The mean and median (interquartile range) age of the participants was 37.7±11.25 and 35 (29-46) yr, respectively. A total of 72.6 per cent of participants belonged to age 18-44 yr. Three hundred and thirty seven (32.5%) participants were postgraduates. Three hundred and four (29.3%) were doctors, 346 (33.4%) were nursing staff, and 98 (9.5%) were paramedical staff. A total of 729 (70%) participants had received the first dose, and 307 (30%) had received both the doses of the COVID-19 vaccine. The co-morbidities such as diabetes mellitus, hypertension, kidney disease, and cardiovascular disease was noted in 111 (10.7%) participants, and 925 (89.3%) did not report any symptoms.

Reported adverse events following immunization: Of the 1036 participants, 473 (46%) participants experienced one or more minor AEFIs, including local and systemic AEFIs. The AEFIs lasted from one to maximum of seven days. Detailed list of AEFIs is given in Table II. Pain (43.9%) and tenderness (36.5%) at the injection site were among the most common local AEFIs, which were noticed mostly within 24 h of receiving the injection. Systemic AEFIs were noticed in 429 (41.4%) participants. Among systemic AEFIs, fatigue (329 participates, 31.7%) was the most common AEFIs followed by the generalized feeling of unwellness in 296 (28.6%), muscle pain in 240 (23.16%) and fever in 225 (21.7%), headache in 208 (20.07%) and dizziness in 104 (10.03%). A few lesser common side effects included bruising at the injection site abdominal pain, excessive sweating, feeling flushed, itching, skin rashes, lump at the injection site and enlarged lymph nodes, which occurred in 18.53 per cent (n=192) of participants. No serious adverse event was noted during the study. Four hundred thirty eight (42%) participants took over-the-counter oral medications (antipyretics/analgesics like ibuprofen or acetaminophen) for managing the AEFIs. None of the respondents required intravenous analgesia or antipyretics for the adverse event management; although 16 participants sought medical advice from the vaccination team telephonically. One of the participants presented in medical emergency with diarrhoea and pain abdomen. Oral rehydration solution and oral acetaminophen were prescribed, and symptoms resolved in two days. None of the participants needed hospitalization. No mortality was noted post-vaccination. Only 91 (8.8%) participants reported taking a leave from work after vaccination and 102 (9.8%) reported difficulty in performing daily routine activities following vaccination.

Table I. Demographic characteristics of the study population (n=1036)

Characteristics	n (%)
Age distribution (yr), median (IQR)	35 (29-46)
18-44	752 (72.6)
45-59	251 (24.2)
>60	33 (3.2)
Gender	
Female	540 (52.1)
Male	496 (47.9)
Education	
Secondary school pass	38 (3.7)
Higher secondary school pass	83 (8.0)
Diploma	87 (8.4)
Doctorate	87 (8.4)
Graduation	404 (39.0)
Post-graduation	337 (32.5)
Occupation	
Doctors	304 (29.3)
Nursing staff	346 (33.4)
Paramedical staff	98 (9.5)
Administrative staff	58 (5.6)
Others*	230 (22.2)
Comorbidity	
No	925 (89.3)
Yes	111 (10.7)
Prior diagnosed with COVID-19	
No	933 (90.1)
Yes	103 (9.9)
Vaccination dose	
1st dose	729 (70.4)
Both doses	307 (29.6)
Type of appointment	
Invited via SMS from CoWIN portal	347 (33.5)
Spot enrolment	689 (66.5)
Recommend vaccination to others	
No	55 (5.3)
Yes	981 (94.7)

*Others include: Teacher, teaching assistant, retired executive, non-medical students, engineers. COVID-19, coronavirus disease-2019; IQR, interquartile range

Table II. Local and systemic adverse events following immunization reported by the participants (n=1036)

Number of participants who reported 'Yes for AEFI' (n=473)					
Adverse events	Within the first 30 min, n (%)	Within the first 24 h, n (%)	Within 48 h, n (%)	Developed AEFI at any point beyond 48 h, n (%)	Total, n (%)
Tenderness at the injection site	52 (5.0)	163 (15.7)	104 (10.0)	59 (5.7)	378 (36.5)
Pain at the injection site	47 (4.5)	231 (22.3)	118 (11.4)	59 (5.7)	455 (43.9)
Warmth at the injection site	59 (5.7)	83 (8.0)	20 (1.9)	3 (0.3)	165 (15.9)
Swelling at the injection site	31 (3.0)	45 (4.3)	13 (1.3)	13 (1.3)	102 (9.8)
Redness at the injection site	17 (1.6)	27 (2.6)	8 (0.8)	6 (0.6)	58 (5.6)
Generalized feeling of unwell	15 (1.4)	148 (14.3)	93 (9.0)	40 (3.9)	296 (28.57)
Fatigue	21 (2.0)	191 (18.4)	77 (7.4)	40 (3.9)	329 (31.75)
Chills	10 (1.0)	101 (9.7)	42 (4.1)	10 (1.0)	163 (15.73)
Headache	23 (2.2)	118 (11.4)	40 (3.9)	27 (2.6)	208 (20.07)
Joint pain	5 (0.5)	55 (5.3)	33 (3.2)	15 (1.4)	158 (15.25)
Muscle pain	18 (1.7)	124 (12.0)	74 (7.1)	24 (2.3)	240 (23.16)
Fever	11 (1.1)	147 (14.2)	55 (5.3)	12 (1.2)	225 (21.71)
Sore throat	4 (0.4)	25 (2.4)	9 (0.9)	11 (1.1)	49 (4.72)
Running nose	5 (0.5)	15 (1.4)	11 (1.1)	8 (0.8)	39 (3.76)
Cough	8 (0.8)	9 (0.9)	8 (0.8)	10 (1.0)	35 (3.37)
Dizziness	20 (1.9)	49 (4.7)	23 (2.2)	12 (1.2)	104 (10.03)
Decreased appetite	3 (0.3)	23 (2.2)	20 (1.9)	11 (1.1)	57 (5.59)
Others*	52 (5.02)	84 (8.11)	29 (2.79)	27 (2.61)	192 (18.53)

*Others include: Bruising at the injection site, abdominal pain, enlarged lymph nodes, excessive sweating, feeling flushed, itching and skin rashes, lump at the site of injection. AEFI, adverse events following immunization

The reported AEFIs differed by gender, age and the dose of vaccination (Table III). The proportion of females experiencing AEFIs was significantly higher as compared to males [282 *vs.* 191, $P<0.001$, adjusted odds ratio 1.743 (95% CI, 1.351-2.249)], younger participants (18-44 yr age group) experienced significantly more AEFIs compared to older participants *i.e.*, 45-59 yr [adjusted odds ratio 0.602, 95% CI, 0.441-0.823, $P<0.001$], and >60 yr [adjusted odds ratio 0.275, 95% CI, 0.113-0.670, $P<0.004$], and a significantly higher proportion of participants reported AEFIs after the first dose as compared to the second dose [381 vs. 92, $P<0.001$, adjusted odds ratio 2.499 (95% CI, 1.872-3.336), $P<0.001$].

Discussion

Centers for disease control and prevention (CDC) USA, have already outlined the possible adverse events following various COVID-19 vaccines. These include tiredness, fever, chills, nausea, vomiting, joint pain, pain and swelling at the injection site[11]. However, these get subsided within a day or two. In the present study, more than half of the participants did not experience any of the AEFIs. It was observed that tenderness, pain at the local site and fatigue were among the most common side effects of the COVID-19 vaccine, with most experiencing these AEFIs within 24 h.

According to the WHO, the reported adverse events to COVID-19 vaccines were fever, fatigue, headache, muscle pain, chills, diarrhoea and pain at the injection site and most of these were mild to moderate and short-lasting[12]. The majority of these events were experienced within 24 h of vaccination. A study by CDC researchers showed that 78.7 per cent of tested sources of adverse event reports submitted during the first month of US vaccination involved women[13]. In the present study also, the proportion of females experiencing AEFIs was significantly higher as compared to males. Further, reported AEFIs differed by age and the dose of vaccination in the current study. The younger participants experienced significantly more AEFIs as compared to older participants, and a higher proportion of participants reported AEFIs after the first dose as compared to the second dose. It has been reported by the CDC that the adverse events after

Table III. Adverse events following immunizations by age, gender, co-morbidity status and dose of the vaccination

Subgroups	AEFI experienced							*P* value for AOR estimates
	No (n=563; 54.3%), n (%)	Yes (n=473; 45.7%), n (%)	*P* value	Unadjusted		Adjusted		
				OR	95% CI	OR	95% CI	
Age group (yr)								
18-44	381 (67.7)	371 (78.4)	<0.001	1		1		
45-59	156 (27.7)	95 (20.1)		0.625	0.467-0.838	0.602	0.441-0.823	0.001
>60¥	26 (4.6)	7 (1.5)		0.276	0.119-0.645	0.275	0.113-0.670	0.004
Gender								
Females	258 (24.9)	282 (27.2)	<0.001	1.754	1.363-2.235	1.743	1.351-2.249	<0.001
Males¥	305 (29.4)	191 (18.4)		1		1		
Comorbidity								
Yes	60 (5.8)	51 (4.9)	0.95	1.013	0.682-1.504	1.397	0.888-2.140	0.152
No¥	503 (48.6)	422 (40.7)		1		1		
Vaccination dose								
1st	348 (33.6)	381 (36.8)	<0.001	2.559	1.926-3.339	2.499	1.872-3.336	0.001
2nd	215 (20.8)	92 (8.9)		1		1		

¥Reference group for binary logistic regression (AOR is the OR when each variable has been adjusted for the other variables listed in this Table, Hosmer-Lemeshow test for adjusted model *P*=0.492). AEFI, adverse events following immunization; OR, odds ratio; AOR, adjusted OR; CI, confidence interval

the second dose may be more intense as compared to the first shot[11]. This difference might be the result of the use of different vaccine manufacturing techniques leading to different timings of the immune response. Further studies are needed to look upon the physiological changes happening after each dose of vaccine that can lead to a set of immunological responses in the body.

The major limitation of this study was that the effectiveness of the vaccine was not assessed. Furthermore, this study was conducted among HCPs who self-reported their symptoms/adverse events, and convenient sampling was done. Thus, selection and recall bias may be there, and the results may not be accurately applied to the general public.

In conclusion, our findings suggested that majority of the adverse events post-vaccination were mild, without any major health consequences. This may help change the attitude of the people to pro-vaccination.

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***Conflicts of Interest*:** None.

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