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Clinical Research

INITIAL MONITORING OF ADVERSE EVENT FOLLOWING COVID-19 IMMUNISATION IN SUB-URBAN TEACHING HOSPITAL

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ABSTRACT On 14th December 2020, the first vaccine shot of COVID-19 vaccine manufactured by Pfizer-bioNTech was administered in United States of America (USA). Subsequently, the administration of COVID vaccine has increased tremendously throughout the world. Initially in India, two vaccines received approval for emergency use in India- Covishield and Covaxin. This study is an attempt to monitor and report adverse event following COVID immunization in teaching institute. **Methods:** All the subjects receiving the vaccine during the first one month of immunization program in institute are eligible to be included in study. The subjects consenting to participate in the study filled the Case Reporting Form (CRF). The study included either medical staff, paramedical staff or undergraduate and post graduate students from various medical streams such as Bachelor in Dental Surgery (BDS) and Pharmacy. **Results:** The results include data of uptake of vaccine in first 30 working days from initiation of immunization on 22nd January 2021. A total of 599 vaccine doses were administered in first 30 days. Only 277 (46.26%) subjects agreed and submitted completed CRF. Out of these 240 experienced minor Adverse Event Following Immunization (AEFI) such as fever, painful limb, joint pain, headache and myalgia. Only 2 subjects (0.72%) experienced AEFI which required further consultation with medical practitioner. The females and younger age group had significantly higher prevalence of overall AEFIs. **Conclusions:** This study reported minor adverse events following COVID-19 immunization. Overall, there was no serious or severe adverse event reported following COVID-19 vaccination. In India, a well-established safety surveillance system should be implemented for safety monitoring of vaccine to establish public trust and support in vaccine policies.

KEYWORDS : Adverse event, COVID-19, Vaccine, Immunisation

INTRODUCTION

The focal point for origin of virulent disease which later named as COVID-19 was Wuhan city in China.[1] Patients with COVID-19 have presented with different Respiratory Tract Infection symptoms such as fever, cough, pneumonia and even death.[2] The reported mortality ranges from 2 to 5% which appear to be lower than Severe Acute Respiratory Syndrome Corona Virus(SARS-CoV) (10%) and Middle East Respiratory Syndrome Corona Virus (MERS CoV) (35%).[3] However, current reports of risk factors for poor outcomes include age, ischaemic heart disease, hypertension, diabetes mellitus and chronic lung disease.[4] By 13 May, 2021, a total of 160,074,267 cases have been reported around the world and 3,325,260 deaths due to infection have been reported. This has been declared Public Health Emergency of International concern by World Health Organization (WHO) Director General.[5]

At present, there are no approved therapies for the treatment of COVID-19. Various national and international groups are working mutually on a various of preventive and therapeutic interventions. As an outcome of enormous efforts, the first dose of COVID-19 vaccine manufactured by Pfizer-bioNTech was administered in US on 14th December 2020. Subsequently, the administration of COVID vaccine has increased tremendously throughout the world.[6] Uptil 13 May 2021, 1,264,164,553 vaccine doses have been administered. Figure 1 shows the administration of COVID-19 vaccine in various countries.[7] In India, COVID-19 vaccination started on 16th January 2021. Initially in India, for emergency use two vaccines received approval - Covishield (a product Oxford-Astrazeneca vaccine produced by Serum Institute of India) and Covaxin (manufactured by Bharat Biotech). In April 2021, Sputnik V was approved as third vaccine whose administration is expected to begin by end of May.[8-10] India is fastest country to administer over 17crore COVID vaccine doses in 114 days as compared to US (115 days) and China (119 days).[11]

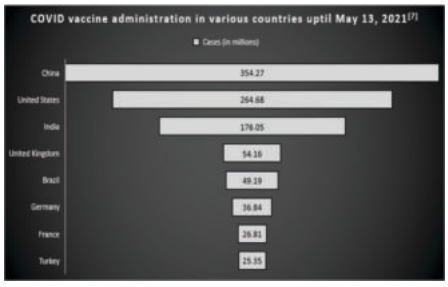

Figure 1: COVID vaccine administration in various countries uptil May 13, 2021[7]

The Indian government is targeting to give 500 million COVID-19 vaccine shots to 250 million people by July 2021. With such mass immunization program, robust surveillance system is necessary to detect and treat adverse events. There have been reports of 46 death and 51 hospitalizations so far but government has not publicly announced conclusions from any investigation. [12] There are no explanations about type of adverse events experienced or categorization by level of health risk or status of investigation. This highlights the need for surveillance of adverse events following COVID-19 vaccinations. This study is an attempt to monitor and report adverse event following COVID immunization in teaching institute.

METHODS:

Subject Recruitment: All the subjects receiving the vaccine during the first one month of immunization program are eligible to be included in study. On the day of vaccination, subjects were given consent forms. The subjects willing to participate and who have submitted the consent form were included in the study. The approval was obtained from ethics committee of the institute (#DIRDS/2021).

Data Collection: The demographic data of subjects vaccinated was obtained from institute records. All the subjects consenting to participate filled Case Report Form (CRF) (Appendix 1). The CRF are standard form which are used for monitoring adverse event following immunization (AEFI) program issued by Ministry of Health and Family Welfare (MoHFW), Government of India. [13] Any type of adverse events occurring after dose of COVID-19 vaccination were included in the study. The forms were collected in the vaccination centre through nodal officer of vaccination centre. Each form was assigned a Case ID and information mentioned was assessed for categorizing of AEFIs. For the purpose of reporting AEFI are categorized as minor, severe and serious explained in Figure 2.

Categorisation of AEFIs		
Minor AFEI	Common self limiting reactions	Examples: Pain, Swelling at injection site, fever, irritability, malaise
Severe AEFI	Can be disabling and rarely life threatening do not lead to long term problems	Examples: severe reaction include non-hospitalised cases of anaphylaxis that has recovered, high fever (>102F)
Serious AEFI	Results in death, requires inpatient hospitalization, results in persistent or significant disability.	Fatal

Figure 2: Categorisation of AEFIs[13]

According to the guidelines of MoHFW, all AEFIs should be entered in AEFI registers. Serious and severe reaction should be reported to the Medical Officer, who will complete Case Investigation Form and will be forwarded to District Immunisation Officer and subsequently forwarded to State and National Immunisation Division.

The study included either medical staff, paramedical staff, students from various medical streams such as BDS and Pharmacy. The CRF were filled with by the subjects themselves. If any clarification regarding CRF was required then nodal officer of vaccination centre, who is a registered medical practitioner, was available for help.

Data Analysis: All the collected data was organised and analyzed by using Microsoft Excel and SPSS version 20.

Results: The results include data of uptake of vaccine in first 30 working days from initiation of immunization on 22nd January 2021. A total of 599 vaccine doses were administered. Generally, in India, covaxin and covishield are currently at the forefront of India's fight against COVID-19 (8). In the study centre only covishield manufactured by Astra Zeneca was administered.

Out of total doses administered, 57.7% were administered to females and remaining 42.3% to males. The average age of subjects receiving vaccine dose was 26.76 (SD 10.58) years. Majority of doses were administered in age bracket of 20-30 yrs (n=451). The table 1 shows demographics distribution of first 599 vaccine doses administered.

Out of 599 doses administered only 277 (46.26%) subjects agreed and submitted completed CRF. After assessment, it was found the 240 (89%) subjects experienced minor AEFI. There was no serious and severe AEFI reported in the study. The commonly experienced AEFI were fever, painful limb, joint pain, headache and myalgia. Table 2 shows the prevalence of AEFIs in the study group.

Only 2 (0.72%) experienced AEFI which required further consultation with medical officer. One of the subjects had urinary retention following immunization and the medical officer examined and reported that this was probably to be anxiety reaction. Another subject reported allergic reaction exhibited as blisters over the lower limbs. The subject reported to medical officer and upon examination this was categorized as allergic reaction for which anti-allergic drugs were prescribed.

Further, the difference in AEFI among various groups was studied and it was noted that females had significantly higher prevalence of overall AEFIs. Also, it was found that AEFIs like fever, headache, bodyache/myalgia, joint pain, anxiety, painful single limb, altered taste, allergic reaction, chills, abscess at injection site and rash were significantly more in females than males. There was no difference in prevalence of AEFIs like chest pain, breathlessness, vomiting, nightsweat.

Further the difference in prevalence of AEFIs according to age was studied. It was found that there was no AEFI reported in subjects who were 50 years or above. Table 4 shows the difference in prevalence of the AEFI within various age groups (age groupings mentioned in table 1). It has been noted that there is difference in few AEFIs according to age such as fever ($p<0.001$), bodyache ($p=0.017$), joint pain ($p=0.036$), painful single limb ($p=0.003$), which are also most prevalent ADRs.

Multiple comparison of different parameters among various age showed a statistically significant difference (p value <0.05) like fever, bodyache, joint pain, painful single limb. There was observed no statistical significant difference ($p>0.05$) among various age groups regarding headache, anxiety, altered taste, allergic reaction, chest pain, night sweat, chills, breathlessness, rashes, injection site abcess, vomiting, seizure.

DISCUSSIONS:

Despite of study being conducted in teaching institute and all the included participants are associated with health care system, participation in the study is less than 50%. This indicated lack of awareness about importance of adverse event reporting even in health care professionals. The major obstacle in adverse event reporting are inadequate knowledge and awareness among health professionals (14). Paudyal et al stated that up to 94% of adverse drug reactions are not reported. Underreporting delays safety signals compromising patient safety. It has been recommended that educational interventions combined with financial incentives tend to increase ADR reporting by healthcare professionals (15).

Indian health system does not have a portal for the reporting of adverse events by the public. For instances, AEFI can be reported through the CO-WIN App (app for recording and maintaining the COVID vaccine data). Currently, the CO-WIN app is open to administrators not subjects for reporting the AEFI (16). Various countries have launched various applications during COVID-19 pandemic which can be installed in smart phones for contact tracing and registration of vaccines. Indian government has also launched Aarogya Setu app. But this has fueled a lot of problems of compliance with patient privacy and human right issues (17). It has been suggested that there should be provision where the subjects can directly contact and report any AEFI such as call centres as everyone might not be able to use and access smart phones or internet, which are prone to data protection issues (12,16).

By January 2021, 173 vaccines are in preclinical development phase and 64 in various phases of clinical trials. By end of January 2021, emergency approval was granted to nine vaccines in various parts of world by respective regulatory authorities (18). The emergency approval for 11 vaccines was granted on basis of interim reports or clinical trials reports. In situation of pandemic, timely dissemination of information and positive outcomes of clinical trials and their translation into the clinical practice is very important (19).

In this study only AEFI of Covishield has been reported. The minor AEFI reported in this study are similar to those reported in literature (20). Tenderness, pain, warmth, redness, itching, swelling or bruising at the injection site, all of which generally resolve within a day or two. There were 54,571 adverse reaction reports of covishield being documented and out of which thrombotic adverse reactions were only 28. Three mortalities were related to pulmonary embolism; one fatality to thrombosis. It has been reported that 17 million people have been administered AstraZeneca vaccine and these are very rare events. The Emergency Medicine Association's (EMA) Pharmacovigilance Risk Assessment Committee (18 March 2021) decided that the vaccine was safe, effective and the benefits overshadowed the risks. Inorder to assess the causality with higher specificity, it is recommended that detailed thrombotic adverse event reports, including patients' characteristics and comorbidities should be evaluated (20).

A Korean study reported that females and younger age groups experienced vaccine-associated adverse reactions more frequently which is consistent with findings of this study. (21) Also, another Czech study conducted in healthcare reported higher side effects among younger age group. (22) In present study there were 38 subject above the age of 50 years and none of them had any AEFI. The vaccines are supposed to trigger the immune system and younger subjects have stronger immune system and hence, the effect of vaccine is there (23). However, in present study, subjects in this age brackets were few and further studies including large number of subjects in this age group and should be conducted to make any conclusive statement.

CONCLUSION:

This study reported minor adverse events following COVID-19 immunization such as fever, painful limb, joint pain, headache and myalgia. Overall, there was none serious or severe adverse event reported following COVID-19 vaccination. It was also found that minor adverse events such as fever, headache, myalgia, joint pain, anxiety were more in females than males. Further, it was found that younger age group subjects reported significantly higher AEFI.

In future, development of COVID-19 vaccine will be presenting new challenges in terms of safety and efficacy. To maintain public trust and support in vaccine policies, robust and ongoing assessment of the risk vs benefit is needed. In India, a well-established safety surveillance system should be implemented. Coordination of post approval vaccine safety monitoring efforts through harmonized protocols and outcomes will enable timely identification and evaluation of safety signals. Further, causality assessment should be done to evaluate possible links between vaccine and AEFIs. A transparent system for safety monitoring of vaccine is important for the achieving a successful immunization program.

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Table 1: Demographic distribution of vaccine doses administered

	All participants		Participants included in study	
N	599		277	
Age	26.76 yrs (SD=10.58)		23.78 yrs (SD = 8.08)	
Age group distribution (years)				
Above 18 and below 20	28		27	
20-29	451		227	
30-39	54		8	
40-49	29		8	
50-59	15		1	
60-69	20		6	
70-79	3		0	
Gender Distribution	Females	346 (57.7%)	Females	194 (70.03%)
Gender Distribution	Males	253 (42.3%)	Males	83 (29.97%)
Gender Distribution	Administrative Staff	15	Administrative Staff	0
Gender Distribution	Paramedics	346 (57.7%)	Paramedics	0
Gender Distribution	Medical Practitioner	346 (57.7%)	Medical Practitioner	22
Gender Distribution	Nursing Staff	346 (57.7%)	Nursing Staff	0
Gender Distribution	Post Graduate	346 (57.7%)	Post Graduate students	8
Gender Distribution	Under Graduate Students	346 (57.7%)	Under Graduate Students	247
Gender Distribution	Support Staff	346 (57.7%)	Support Staff	0

Table 2: Commonly experienced AEFI's

AEFI	N	Percentage
Fever	199	71.8
Headache	47	16.9
Bodyache/Myalgia/Weakness	34	12.2
Joint Pain/Swelling	68	24.5
Anxiety	14	5.0
Painful single limb	70	25.2
Altered taste	11	3.9
Allergic reaction	14	5.0
Chest Pain	5	1.8
Chills	36	12.9
Breathlessness	9	3.2
Abscess at site of injection	32	11.5
Vomiting	4	1.4
Palpitations/night sweats	2	0.7
Rashes	10	3.6

Table 3: T-Test of different AEFIs based on gender.

Variable	Gender	Mean	Std. Deviation	Std. Error Mean	p value
ADR	F	.91	.292	.021	.009
	M	.77	.423	.046	
Fever	F	.82	.386	.028	.000
	M	.48	.503	.055	
Headache	F	.21	.406	.029	.004
	M	.08	.280	.031	
Bodyache	F	.16	.363	.026	.000
	M	.04	.188	.021	
Joint pain	F	.28	.450	.032	.036
	M	.17	.377	.041	
Anxiety	F	.07	.251	.018	.011
	M	.01	.110	.012	
Painful single limb	F	.19	.395	.028	.002
	M	.39	.490	.054	
Altered taste	F	.05	.222	.016	.048
	M	.01	.110	.012	
Allergic reaction	F	.07	.260	.019	.000
	M	0.00	0.000	0.000	
Chest pain	F	.02	.143	.010	.622
	M	.01	.110	.012	
Chills	F	.16	.368	.026	.008
	M	.06	.239	.026	
Breathless	F	.04	.187	.013	.603
	M	.02	.154	.017	
Injection site abscess	F	.16	.363	.026	.000
	M	.02	.154	.017	
Vomitting	F	.02	.124	.009	.824
	M	.01	.110	.012	
Night Sweat	F	.01	.102	.007	.354
	M	0.00	0.000	0.000	
Rash	F	.05	.223	.016	.034
	M	0.00	0.000	0.000	

*F: Females; M: Males

Table 4: Analysis of Variance (ANOVA) of different AEFIs among various age groups.

AEFI		Sum of squares	df	Mean squares	F	p value
ADR	Between Groups	8.025	5	1.605	18.044	.000
	Within Groups	24.015	270	.089		
	Total	32.040	275			
Fever	Between Groups	6.236	5	1.247	6.773	.000
	Within Groups	49.721	270	.184		
	Total	55.957	275			
Headache	Between Groups	.490	5	.098	.687	.634
	Within Groups	38.506	270	.143		
	Total	38.996	275			
Bodyache	Between Groups	1.437	5	.287	2.809	.017
	Within Groups	27.617	270	.102		
	Total	29.054	275			
Joint Pain	Between Groups	2.203	5	.441	2.425	.036
	Within Groups	49.044	270	.182		
	Total	51.246	275			
Anxiety	Between Groups	.274	5	.055	1.135	.342
	Within Groups	13.016	270	.048		
	Total	13.290	275			
Painful single limb	Between Groups	3.304	5	.661	3.682	.003
	Within Groups	48.446	270	.179		
	Total	51.750	275			
Altered Taste	Between Groups	.077	5	.015	.397	.851
	Within Groups	10.484	270	.039		
	Total	10.562	275			
Allergic reaction	Between Groups	.068	5	.014	.277	.925
	Within Groups	13.222	270	.049		
	Total	13.290	275			
Chest Pain	Between Groups	.045	5	.009	.499	.777
	Within Groups	4.865	270	.018		
	Total	4.909	275			
Chills	Between Groups	.360	5	.072	.629	.678
	Within Groups	30.944	270	.115		
	Total	31.304	275			
Breathlessness	Between Groups	.087	5	.017	.544	.743

	Within Groups	8.620	270	.032		
	Total	8.707	275			
Injection site abcess	Between Groups	.494	5	.099	.960	.443
	Within Groups	27.796	270	.103		
	Total	28.290	275			
Vomit	Between Groups	.089	5	.018	1.242	.290
	Within Groups	3.853	270	.014		
	Total	3.942	275			
Seizure	Between Groups	.002	5	.000	.115	.989
	Within Groups	.994	270	.004		
	Total	.996	275			
Night sweat	Between Groups	.008	5	.002	.232	.948
	Within Groups	1.977	270	.007		
	Total	1.986	275			
Rash	Between Groups	.046	5	.009	.257	.936
	Within Groups	9.591	269	.036		
	Total	9.636	274			

REFERENCES:

1. Ahmed SS. The Corona Virus Disease 2019 (COVID 19): A Review. Journal of Advances in Medicine and Medical Research 2020;32(4). Available from: https://www.journaljammr.com/index.php/JAMMR/article/view/30393
2. World Health Organization. Available from:_www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports. [Last accessed on Jan 12, 2021].
3. Pascarella G, Strumia A, Piliego C, et al. COVID-19 diagnosis and management: a comprehensive review. J Intern Med. 2020;288(2):192-206
4. Zhou F, Yu T, Du R, Fan G, Liu Y, Xiang J et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The Lancet 2020; 395 (10229):1054-62.
5. Conti P, Gallenga CE, Tete G, Caraffa A, Ronconi G, Younges A, et al. How to reduce likelihood of coronavirus-19 (CoV-19 or SARS-CoV-2) infection and lung inflammation medicated by IL-1. J. Biol. Regul. Homeost. Agents 2020;34(2):333-338.
6. Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Pfizer-BioNTech COVID-19 Vaccine- United States, Decemeber 14-23, 2020. MMWR Morb Mortal Wkly Rep 2021; 70:46-51.
7. World Health Organisation. COVID-19 vaccines. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/covid-19-vaccines. [Last accessed on September 15, 2021].
8. Kumar, V.M., Pandi-Perumal, S.R., Trakht, I. et al. Strategy for COVID-19 vaccination in India: the country with the second highest population and number of cases. npj Vaccines 2021; 6:60 . https://doi.org/10.1038/s41541-021-00327-2.
9. Ministry of Health and Family Welfare: Vaccination Update. Available from: https://www.mohfw.gov.in/ [Last accessed on May 21,2021].
10. World Health Organisation. Interim recommendations for use of the ChAdOx1-S [recombinant] vaccine against COVID-19 (AstraZeneca COVID-19 vaccine AZD1222 Vaxzevria™, SII COVISHIELD™. (Document No. WHO/2019-nCoV/vaccines/SAGE_recommendation/AZD1222/2021.3)
11. Bright, B., Babalola, C.P., Sam-Agudu, N.A. et al. COVID-19 preparedness: capacity to manufacture vaccines, therapeutics and diagnostics in sub-Saharan Africa. Global Health 2020 17: 24. https://doi.org/10.1186/s12992-021-00668-6.
12. MoHFW. Update on COVID-19 Vaccination- Day 42. Available from https://pib.gov.in/Pressreleaseshare.aspx?PRID=1701203 [Last accessed on September 15,2021].
13. MoHFW. Adverse Event Following Immunisation. Available from https://nhm. gov. in/New_ Updates_ 2018/NHM_Components/Immunization/ Guildelines_for_ immunization/AEFI_Surveillance_and_Response_Operational_Guidelines_2015.pdf. [Last accessed on May 26, 2021].
14. Mulchandani R, Kakkar AK. Reporting of Adverse Drug Reactions in India: A Review of the Current Scenario, Obstacles and Possible Solutions'. Int J Risk Saf Med 2019; 30(1): 33-44.
15. Paudyal V, Al-Hamid A, Bowen M, Hadi MA, Hasan SS, Jalal Z, Stewart D. Interventions to improve spontaneous adverse drug reaction reporting by healthcare professionals and patients: systematic review and meta-analysis, Expert Opinion on Drug Safety. 2020. 19:9, 1173-1191.
16. MoHFW. COVID-19 Vaccines Operational Guidelines. Available from https:// www.mohfw.gov.in/pdf/COVID19VaccineOG111Chapter16.pdf. [Last accessed on May 26,2021].
17. Kaur S; Gill S; Bhardwaj N; Kaur R. Mitigating the Impact of COVID-19 Through Technological Interventions Is India Legally Equipped: Aarogya App Case Study. MLU 2021; 21: 1146-1150.
18. Kaur R, Dutta S, Bhardwaj P, Charan J, Dhingra S, Mitra P et al. Adverse Events Reported from COVID-19 Vaccine Trails: A systematic review. Ind J Clin Biochem 2021;27, 1-13.
19. Kaur S, Singh H, Kaur K. Compilation of registered clinical trials for the treatment of COVID-19 infection. Int J Basic Clin Pharmacol. 2021; 10:457-63.
20. Tobaiqy, M., Elkout, H., & MacLure, K. Analysis of Thrombotic Adverse Reactions of COVID-19 AstraZeneca Vaccine Reported to Eudra Vigilance Database. Vaccines 2021;9(4), 393.
21. Bae S, Lee YW, Lim SY, Lee JH, Lim JS, Lee S, Park S, Kim SK, Lim YJ, Kim EO, Jung J, Kwon HS, Kim TB, Kim SH. Adverse Reactions Following the First Dose of ChAdOx1 nCoV-19 Vaccine and BNT162b2 Vaccine for Healthcare Workers in South Korea. J Korean Med Sci. 2021;36(17):e115.
22. Riad A, Pokorná A, Attia S, Klugarová J, Koščík M, Klugar M. Prevalence of COVID-19 Vaccine Side Effects among Healthcare Workers in the Czech Republic. J Clin Med. 2021 Apr 1;10(7):1428.
23. Willeyard C . How anti-ageing drugs could boost COVID vaccines in older people. Nature 2020; 586, 352-354. doi: https://doi.org/10.1038/d41586-020-02856-7