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PATTERN OF ADVERSE EFFECTS REPORTED FOLLOWING COVID-19 VACCINATION AMONG BENEFICIARIES IN GOVT. MEDICAL COLLEGE, RAIGARH, CHHATTISGARH, INDIA

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Abstract

Introduction: *While countries including India, have taken strong measures to contain the spread of Covid-19 through better diagnostics and treatment, vaccines will provide a lasting solution by enhancing immunity and containing the disease spread. Understanding the adverse effects pattern will help make aware citizens, dismiss false rumours and reduce vaccine hesitancy. Hence the present study describes the pattern of adverse effects reported following COVID-19 vaccination among beneficiaries in Government Medical College, Raigarh, Chhattisgarh, India.*
Methods: *A cross-sectional, observational study of pattern of adverse effects reported following COVID-19 vaccination was conducted among 540 beneficiaries in Government Medical College, Raigarh, Chhattisgarh, India from January 2021 to April 2021. Data was collected through online survey which included questions pertaining to immediate & late post vaccination experience.*
Results: *Majority (33%) participants were 18-30 age group and (58%) were male. Overall (73%) respondents reported atleast one post-vaccination symptom. General weakness & tiredness (73.4%), pain at injection site (62%), bodyache (48%), chills (43%) & fever (39%) were the most prevalent symptoms. The frequency of symptoms among 18-30 age group was (85.9%) & more likely to be reported by women (83.2%) compared to men (65.1%). Around (36.9%) beneficiaries who had one or more comorbidities showed post vaccination symptoms. Around (82.1%) of Covishield beneficiaries developed atleast one or more symptoms post vaccination, while (60.3%) of Covaxin beneficiaries developed the same.*
Conclusion: *Nearly two-thirds of study participants reported mild symptoms following vaccination. General weakness & tiredness, pain at injection site, bodyache, chills & fever were the most prevalent symptoms. Symptoms were more common among younger individuals. More Covishield beneficiaries developed atleast one or more symptoms post vaccination compared to Covaxin beneficiaries.*

Key words: *COVID-19 vaccination, adverse effects, Covishield, Covaxin*

Introduction

Corona virus disease 2019 (COVID-19) is an infectious disease caused by a newly discovered coronavirus (SARS-CoV-2), which has spread rapidly throughout the world. In March 2020, World Health Organization (WHO) declared COVID-19 outbreak a pandemic. The pandemic has severely ravaged health systems and economic and social progress globally. While countries, including India, have taken strong measures to contain the spread of COVID-19 through better diagnostics and treatment, vaccines will provide a lasting solution by enhancing immunity and containing the disease spread. In response to the pandemic, the vaccine development process has been fast-tracked. Globally, over 274 candidate vaccines are in different stages of development as on 4 December 2020. Wide spread deployment of COVID-19 vaccine is the best intervention to safeguard against the high mortality and the major adjustments to our way of life [1].

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Drugs Controller General of India (DCGI) has approved the Bharat biotech vaccine against COVID-19, which is a locally manufactured inactivated vaccine named "Covaxin" in collaboration with the Indian council of medical research (ICMR) and National Institute of virology (NIV) on 3rd January 2021 for emergency use along with the "Covishield" Oxford-AstraZeneca vaccine manufactured locally by the Serum Institute of India [1, 2]. At the start of 2021, India has received emergency use authorization for both COVID vaccines. Covishield vaccine is a recombinant technology based non replicating viral vector AZD1222 or ChAdOx1 vaccine which uses an adenovirus from chimpanzees to deliver the gene for the spike protein of SARS-CoV-2 to trigger a robust immune response. The vaccine is given in the dose of 0.5 ml, intramuscular in two doses. Covaxin is an inactivated whole-virion corona virus vaccine. It is expected to be 60% efficacious; the vaccine can be stored at temperatures between 2 °C and 8 °C, economical at a projected cost per dose. The vaccine is given in the dose of 0.5 ml, intramuscular in two doses 4 to 6 weeks apart [2].

COVID-19 vaccines have limited safety data. Therefore, it is important to monitor the safety of these vaccines when administered to a large population. During COVID-19 vaccinations, AEFIs must be rapidly detected and promptly responded to or else it can undermine confidence in the vaccine and immunization programme. All AEFIs should be reported as per the National AEFI Guidelines. Various adverse events to these vaccines have been notified as minor side effects such as vaccine site tenderness and pain, headache, myalgia, nausea, fatigue, etc. [3] There are several vaccines in the pipeline globally and in India [4]. Apart from Sputnik V (with DRL), Cadila Healthcare has developed a Novel Corona Virus-2019-nCov-Vaccine using DNA platform technology and has got approval to conduct phase 3 study in India [5]. Although frequent discussions have been done about the protective efficacy of the vaccine but little is known about the real-world post-vaccination experience outside of clinical trial conditions. Knowledge about what to expect after vaccination will help to educate the public, dispel misinformation and reduce vaccine hesitancy [6]. Understanding the adverse effects pattern will help make citizens aware, dismiss false rumours and reduce vaccine hesitancy. Thus principle aim of this present study is to describe the pattern of adverse effects reported following COVID-19 vaccination among beneficiaries in Government Medical College, Raigarh, Chhattisgarh, India.

Material and Methods

A cross-sectional, observational study regarding pattern of adverse effects reported following COVID-19 vaccinations was conducted among 540 beneficiaries in Government Medical College, Raigarh, Chhattisgarh, India from January 2021 to April 2021. All these beneficiaries were vaccinated in Government Medical College, Raigarh. Line listing of persons including name & contact number was gathered from data generated through COWIN platform. The methodology comprises of primary data collection among 10 percent of all COVID-19 vaccinated beneficiaries in 4 months from January 2021 to April 2021 through systematic random sampling technique. Data was collected through online survey which included questions pertaining to the immediate & late post vaccination experience including socio-demographic characteristics & side effects pattern ranging from their age, gender, education, occupation, socio-economic status, marital status, comorbidities, history of allergy & COVID-19 disease along with post-vaccination experience with immediate & late adverse effects. Socio-economic class categorization was done by using modified BG Prasad classification 2020. Till 1st April 2021 i.e. three month after initiation, 5830 beneficiaries including health care workers, front line workers & general citizens above 45 were vaccinated at this centre. Out of these 5830, we sampled 10 percent of beneficiaries including both Covishield & Covaxin vaccinated individuals through systematic random sampling method which came out to be 583, of which 540 subjects gave consent & responded, hence total 540 subjects were enrolled for the study. Individuals who did not give consent, unable to give response and with whom communication could not be performed were excluded from the study. The study was approved by the Institutional Ethics Committee (IEC) with letter Sr. No./Med./Ethics Commi./2021/99, dated 07/01/2021. Prior informed verbal consent has been taken from the study subjects.

Statistical analysis: Data was entered in Microsoft Excel software, checked for its completeness, correctness & analyzed by using SPSS version 21.0 software. Results on categorical measurements were presented in numbers and percentage. Chi-square tests were used to find the significance of study parameters on categorical scale between two or more groups. P-value of <0.05 has been considered to be statistically significant.

Case definition

An adverse event following immunization (AEFI) is any untoward medical occurrence which follows immunization, and which does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavorable or unintended disease, symptom, sign or abnormal laboratory finding. Reported adverse events can either be true adverse events, i.e. really a result of the vaccine or immunization process, or coincidental events that are not due to the vaccine or immunization process but are temporally associated with immunization [1].

AEFI is categorically reported as minor, severe, or serious. Minor AEFI are minor reactions which are common, self-limiting e.g., pain & swelling at injection site, fever, irritability, malaise, etc. Severe AEFI are non-hospitalized cases with increased severity that do not lead to long-term problems but can be disabling e.g., non-hospitalized cases of anaphylaxis that have recovered, high fever (>102-degree F), hypotonic hypo responsive

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episodes, sepsis, etc. Serious AEFI includes deaths, hospitalizations, clusters, disability, media reports/ community/parental concern following vaccination [7].

Immediate side effects were marked within 30 minutes of observational period post vaccination while late side effects were recorded within 24 hours & 48 hours after vaccination period in both doses. The COVID-19 Vaccine Intelligence Network (Co-WIN) system a cloud-based IT solution to prepare, implement, track, and evaluate COVID-19 vaccination in India, a digital platform will be used to track the enlisted beneficiaries for vaccination and COVID-19 vaccines on a real-time basis [8]. A person with laboratory confirmation by an Oro-nasopharyngeal swab rtPCR/Rapid antigen based testing of COVID-19 infection, irrespective of clinical signs and symptoms have been considered as COVID-19 positive.

Results

Table 1: Socio-demographic characteristics of COVID-19 Vaccinated Beneficiaries (n=540)

Sr. No.	Socio-demographic Characteristics		Number (No.)	Percentage (%)
1.	Age (in years)	18-30 yrs	178	33.0%
		31-40 yrs	78	14.5%
		41-50 yrs	111	20.5%
		51-60 yrs	132	24.5%
		>60 yrs	41	7.5%
2.	Gender	Male	313	58.0%
		Female	227	42.0%
3.	Education	No formal schooling	14	2.5%
		Primary School	19	3.5%
		Middle school	14	2.5%
		High School	43	8.0%
		Higher Secondary	157	29.0%
		Graduate	243	45.0%
		Post Graduate	50	9.2%
4.	Occupation	Government employee	122	22.5%
		Non-government employee	70	13.0%
		Self-employed	89	16.5%
		Health Worker	65	12.0%
		Homemaker	49	9.0%
		Retired	14	2.5%
		Student	97	18.0%
		Unemployed	34	6.2%
5.	Socio-economic Status	Lower	20	3.7%
		Lower Middle	45	8.3%
		Middle	421	78.0%
		Upper Middle	38	7.0%
		Upper	16	3.0%
6.	Marital Status	Married	367	68.0%
		Un married	172	32.0%

Socio-demographic characteristics of COVID-19 vaccinated beneficiaries were shown in Table 1. A total of 540 persons were included in this study. It was predominated by young population (mean age 27.8 years ± 9.3 years). Majority of them were aged 18-30 years (33%) and (58%) were males. About (45%) of beneficiaries were graduate while around (2.5%) were found to had no formal schooling. The majority (22.5%) of beneficiaries was Government employee & around (12%) were doing health care related jobs. Maximum (78%) of patients came under middle socioeconomic class as per modified BG Prasad classification 2020. Also most (68%) of the beneficiaries were married.

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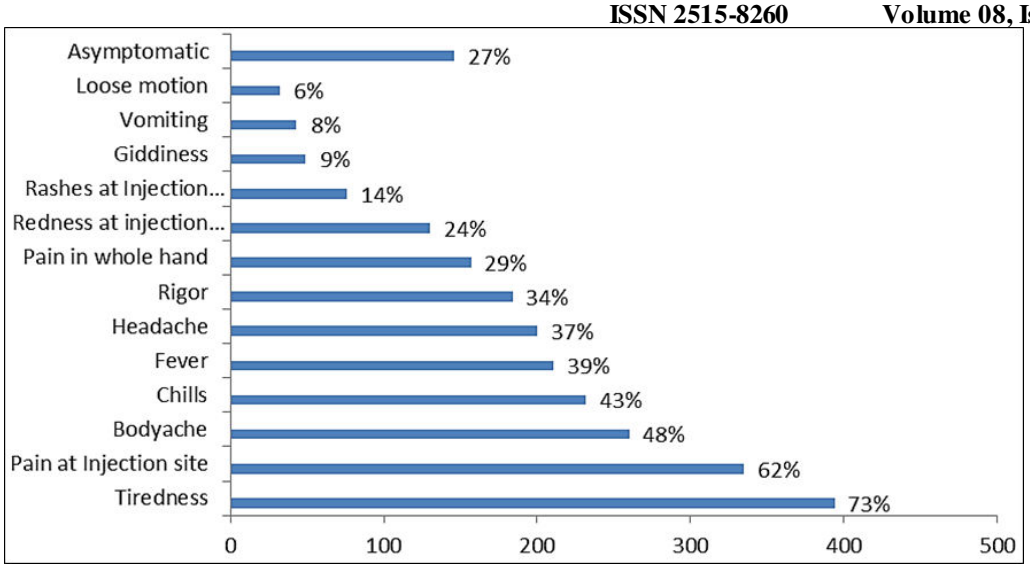

(Multiple responses)

Fig 1: Major Post Vaccination Symptoms of COVID-19 Vaccinated Beneficiaries (n=540)

Major post vaccination symptoms of COVID-19 vaccinated beneficiaries were depicted in Fig. 1. Overall (73%) respondents reported at least one post-vaccination symptom. General weakness & tiredness (73.4%), pain at injection site (62%), bodyache (48%), chills (43%), fever (39%) & headache (28%) were the most prevalent symptoms. Also few of them reported rigor (34%), Pain in entire arm (29%), Redness at injection site (24%) & Rashes at injection site (14%). Limited beneficiaries also reported giddiness (9%), Vomiting (8%) & Loose motion (6%). Interestingly around (27%) did not get any symptoms or discomfort post vaccination. Out of total 540, only 3 of them developed immediate giddiness & chest pain who were referred to casualty after counselling, primary care & discharged after few hours. All other minor symptoms were 1% or less.

Table 2: Association of socio-demographic characteristics with incidence of post vaccination symptoms (n=540)

Sr. No.	Parameters		Post vaccination symptoms				p-value
			Yes		No		
			No.	%	No.	%	
1	Age (in years)	18-30	153	85.9%	25	14.1%	$\chi 2 = 46.30$ P < 0.00001
		31-40	66	84.6%	12	15.4%	
		41-50	77	69.3%	34	30.7%	
		51-60	75	56.8%	57	43.2%	
		>60	22	53.6%	19	46.4%	
Total			393	73.0%	147	27.0%	
2	Gender	Male	204	65.1%	109	34.9%	$\chi 2 = 20.81$ P < 0.00001
		Female	189	83.2%	38	16.8%	
Total			393	73%	147	27%	

Association of socio-demographic characteristics with incidence of post vaccination symptoms were shown in Table 2. The chance of having symptoms decreased with advancing age. The frequency of symptoms was 85.9% (18-30 years), 84.6% (31-40 years), 69.3% (41-50), 56.8% (51-60) & 53.6% (>60). Out of total 313 male, (65.1%) developed post-vaccination symptoms while out of total 227 female (83.2%) developed the same. Thus symptoms were more likely to be reported by women compared to men. The association between age, gender distribution and development of post vaccination symptoms were found to be statistically significant p<0.00001.

Table 3: Association of co-morbidity with incidence of post vaccination symptoms (n=540)

Sr. No	Parameters	Post vaccination symptoms				p-value
		Yes		No		
		No.	%	No.	%	

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1	History of COVID-19	Yes	68	67.3%	33	32.7%	$\chi2 = 1.83$ P = 0.17
		No	325	74.0%	114	26.0%	
Total			393	73.0%	147	27.0%	
2	Co-morbidity Present	Yes	34	36.9%	58	63.1%	$\chi2 = 71.82$ P < 0.00001
		No	359	80.1%	89	19.9%	
Total			393	73.0%	147	27.0%	
3	History of any allergy	Yes	26	68.4%	12	31.6%	$\chi2 = 0.39$ P = 0.53
		No	367	73.1%	135	26.9%	
Total			393	73.0%	147	27.0%	

As Table 3 show that the association of co-morbidity with incidence of post vaccination symptoms. Out of total 540 beneficiaries (18.7%) had history of COVID-19 infection, (17%) had comorbidities with diabetes mellitus and hypertension being the predominant ones and (7%) had history of allergy (either from dust, certain food particles or from certain drugs). Around (67.3%) of total beneficiaries who had history of COVID-19 infection showed post vaccination symptoms. Its association was found to be statistically non-significant. Interestingly around (63.1%) of comorbid beneficiaries did not show development of any symptoms post vaccination. Its association was found to be statistically significant with P < 0.00001. Also around (68.4%) beneficiaries who had history of either dust, food or any drug allergy showed post vaccination symptoms although its association was found to be statistically non-significant.

Table 4: Incidence of post vaccination symptoms according to type of COVID-19 vaccines

Sr. No.	**Type of Vaccine**	**Post vaccination symptoms**				**Total**		**p-value**
		Yes		**No**				
		No.	**%**	**No.**	**%**	**No.**	**%**	
1.	Covishield	253	82.1%	55	17.9%	308	57.0%	$\chi2 = 31.73$ P<0.00001
2.	Covaxin	140	60.3%	92	39.7%	232	43.0%	
Total		393	73.0%	147	27.0%	540 (100%)		

Incidence of post vaccination symptoms according to type of vaccines was shown in Table 4.
Among total 540 respondents, 308 (57%) had received Covishield & 232 (43%) received Covaxin. Around (82.1%) of Covishield beneficiaries developed atleast one or more symptoms post vaccination while (60.3%) of Covaxin beneficiaries developed the same. Out of 3 referred beneficiaries 2 of them were had Covishield & 1 had Covaxin. The association between type of vaccine and development of post vaccination symptoms were found to be statistically significant p<0.00001.

Discussion

Nearly two-thirds of survey respondents reported mild symptoms following vaccination while rest one-third did not report any event. General weakness & tiredness (73.4%), pain at injection site (62%), bodyache (48%), chills (43%) & fever (39%) were the most prevalent symptoms which was anticipated post vaccination. None of the symptoms were of serious nature or requiring hospitalization. Only 3 of them developed immediate giddiness & chest pain that were referred to casualty after counseling, provision of primary care & discharged after few hours. Similarly a study done by Jayadevan R *et al*., [6] found that tiredness (45%), myalgia (44%), fever (34%), headache (28%), local pain at injection site (27%) & joint pain (12%) were found to be the most prevalent symptoms. Another study of Shrivastava RK *et al*., [9] found that the pain at the injection site (5%), headache (3%), fatigue (3%) & fever (2%) to be the most common adverse events following immunization. Another similar study done by Joshi U *et al*., [10] reported that mild AEFI within 30 minutes like transient headaches, light-headedness and dizziness, tingling in eyes, and increase in blood pressure. After few hours of vaccination, some complained of myalgia, nausea, tenderness at the injection site and feverish feeling.
Almost all beneficiaries (94%) had symptoms after having their first dose, while only few (28%) developed either similar or mild symptoms after having their second dose. Maximum (71%) of the total adverse events were reported on day 1 after vaccination, while rest (29%) were reported on day 2 after vaccination which were treated with tablet Paracetamol for fever, pain and reassurance & counselling. In a study by Jayadevan R *et al*., [6] among those who reported symptoms, 79% noticed them within the first 12 hours. Another study by Shrivastava RK *et al*., [7] found 12 of the 15 AEFI were reported on day 1 after vaccination, while 3 were reported on day 2 after vaccination.
The frequency of symptoms was 85.9% in 18-30 years, 84.6% in 31-40 years, 69.3% in 41-50, 56.8% in 51-60 & 53.6% in >60 years thus probability of developing symptoms decreased with advancing age. There was a clear linear correlation between age and post-vaccination symptoms, suggesting that vaccine reactogenicity declined with age. Symptoms were more likely to be reported by women (83.2%) compared to men (65.1%). These findings were consistent with result of Jayadevan R *et al*., [6] in which chance of having symptoms also decreased with advancing age. Also post-vaccination symptoms were reported (74.7%) in women compared to men (58.6%).

In this study, (67.3%) beneficiaries who had history of COVID-19 infections showed post vaccination symptoms. Interestingly (63.1%) of comorbid beneficiaries did not show development of any symptoms post vaccination. Also (68.4%) beneficiaries who had history of either dust, food or any drug allergy showed post vaccination symptoms although its association was found to be statistically non-significant. In a study of Jayadevan R *et al*., [6] symptom profile was not different to those who did not have a past history.

In our study, the frequency of experiencing symptoms following Covishield and Covaxin vaccine were (82.1%) and (60.3%) respectively, whereas study by Jayadevan R *et al*., [6] found that it to be 66.6% for Covishield and 55% for Covaxin. The findings of the survey correlated with results from published trials of vaccines. In the phase 2/3 trial of Astra-Oxford ChAdOx1 nCoV-19, at least one systemic symptom was reported following vaccination with the standard dose by 86% participants in the 18-55 years group [11]. While discussing post vaccination experience, it is noteworthy that placebo injections produce comparable symptoms. Symptoms are known to correlate with neutralizing antibody levels during COVID-19 [12], the presence of symptoms following vaccination does not reliably predict antibody response [13]. Since reported post-vaccination symptoms were mild, short-lived and anticipated this should help reduce vaccine hesitancy.

Limitations

The study was conducted among 10 percent of persons who were vaccinated in only single center in 3 months. Greater awareness and anticipation of potential adverse effects among few group, could also get reflected in the reporting rate. Hence, the reported incidence of post-vaccination symptoms could be an overestimation. The online survey was done on memory basis & based on trust of respondents thus it was not possible to verify the information provided by each.

Conclusion

Nearly two-thirds of study participants reported mild symptoms following vaccination. General weakness & tiredness, pain at injection site, bodyache, chills & fever were the most prevalent symptoms. These events were anticipated with an immunologic response often correlated with vaccines and consistent with the findings from previously published studies & phase trials. In majority of cases, the symptoms were milder and no serious events were reported. Symptoms were more common among younger individuals. There was no significant association between these symptoms and among those who had a past history of COVID-19 or any allergy. More Covishield beneficiaries developed atleast one or more symptoms post vaccination compared to Covaxin beneficiaries.

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