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COVISHIELD COVID VACCINE IN INDIA – DEMYSTIFYING MYTHS –SAFETY STUDY IN A TERTIARY CARE CENTRE OF SOUTHERN RAJASTHAN

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ABSTRACT **INTRODUCTION**– Nationwide COVID-19 vaccination was carried out in India in a phased manner from 16 Jan 2021 with COVISHIELD. This vaccine was indegeniously prepared by the Serum Institute of India in lines with the Oxford-AstraZeneca, ChAdOx1 (COVISHIELD) developed at Oxford.

OBJECTIVE- This study was done to assess the safety of the indigenously prepared COVISHIELD vaccine in India.

METHODS – This study was carried out in tertiary care centre , RNT Medical college, southern rajasthan, India from jan,2021 to june 2021. People (n=500) who received the first dose of the COVISHIELD vaccine were followed up for seven days to check for any adverse effects or systemic effects post-vaccination. The data was collected by the supervisor with a participant administered questionnaire.Data were analyzed using SPSS v-23 software.

RESULTS – There were no serious adverse or systemic effects noted in 7 days follow up. Systemic symptoms were seen only in 240 (48%) individuals post-vaccination. Fever and bodyache was the most common effect of vaccination in 37.5 %(n=90) individuals followed by Myalgia and fatigue in 21.67 % (n=52) individuals. In most of the individuals the systemic symptoms started at 6-12 hours post-vaccination. There were no reports of fresh onset of systemic symptoms of any kind beyond 48 hours of vaccination. Females and adults tolerated the vaccination better with lesser systemic effects.

CONCLUSION – The absence of serious side effects makes the Serum Institute of India's COVIDSHIELD vaccine safe for use.

KEYWORDS : Covishield, Safety, Adverse Effects, Systemic Effects

INTRODUCTION:

Severe Acute Respiratory Syndrome Corona Virus 2 (SARS CoV2), a coronavirus, causing COVID 19 infection was declared a pandemic on 11 Mar 2020 by the World Health Organization [1]. The pandemic owing to its high infectivity, social distancing and masks are being advocated to curb its spread. The imperative to rein in this disease has encouraged vaccine research worldwide. Vaccine development normally takes years due to its stringent administrative, technological checks and trial protocols. The numerous second and third peaks across nations have made the world realize the need for a quick and effective vaccine. This has accelerated the process of trials and approvals for the early availability of a vaccine. Currently, more than 250 vaccines against SARS-CoV2 are in development worldwide including mRNA, replicating or non-replicating viral-vectored vaccines, DNA vaccines, autologous dendritic cell-based vaccine, aninactivated-virus vaccine [2].

The first COVID vaccine approved was CoronaVac developed by SinoVac Biotech Ltd by China's Central Military Commission for use by Chinese Military and the medical staff in late August 2020. The first nationwide vaccination drive was carried out in Russia in Dec 2020, using vaccine Gam-COVID-Vac, trade named Sputnik V, developed by Gamaleya Research Institute by Russian Ministry of Health [3], which was subsequently followed by other countries like US and UK.

In India, vaccination started in a phase-wise manner on 16 Jan 2021. Initially, Healthcare Workers (HCWs) and frontline workers were vaccinated with either COVISHIELD or COVAXIN vaccine. Second phase was started from 1 march for elderly age group above 60 yrs of age and above 45 years with comorbidities. Third phase was started from 1 april for all above the age of 45 years. Fourth phase of the vaccination drive is started from may 1 for 18 plus age group.

The COVISHIELD used in India, developed by Serum Institute of India in lines with the vaccine developed in the UK by Jenner Institute, University of Oxford. It is a viral vectored vaccine. [2].

COVISHIELD had undergone phase I/II blinded randomized controlled trials in Apr-May 2020 in UK, Brazil, and South Africa with randomization done with the ChAdOx1nCoV 19 vaccine (COVISHIELD), and the MenACWY (standard Meningococcal vaccine) as the test and the control arms respectively. It showed that the spike specific T cell responses peaked on day 14 and IgG response by Day 28, and were boosted following the second dose. Neutralizing antibodies were found in 91% after a single dose and 100% after the second dose of the vaccine. Phase II/ III trials for this vaccine were carried out in the UK from May to Aug 20, with participants being enrolled in an age escalated manner that is between 18-55years, 56-69 years, and 70 years and older cohort. The results showed that the median anti-spike IgG response after 28 days was similar across all age groups. The analysis of data showed an acceptable safety profile among participants of the trial and also showed it to be better tolerated in older individuals [4, 5].

Owing to the urgent need of the hour, the COVISHIELD vaccine was given restricted emergency use approval (EUA) by the Drugs Controller General of India (DCGI) on 03 Jan 21.Government of India subsequently announced its countrywide vaccine rollout.

The rapid approval of the vaccine and the myths being propagated has made the general public doubt the safety of the vaccine [6, 7]. In this study, we have highlighted the adverse and systemic effects on individuals' post-vaccination.

MATERIALS AND METHODS:

This study was conducted in tertiary care centre RNT medical college , in southern rajasthan to document the adverse and systemic reactions following exposure to the COVISHIELD vaccine and to study the factors there of. All the participants(n=500) who consented to the study were included from Jan,2021 to June ,2021. The participants were administered the first dose of the COVISHIELD vaccine. All the vaccines were detained at immunization centres for 30 minutes post administration of the vaccine. They were followed up for adverse and systemic effects over a period of 07 days. The vaccine was administered by a trained vaccinator through an auto disposable syringe into the deltoid muscle and the onset of adverse and systemic effects was monitored by a supervisor through participant administered questionnaire. Individuals complaining of any symptoms post-vaccination were cross-checked by the supervisor for coherence in reporting of symptoms. Data of all the beneficiaries from our centre were compiled and collated in an excel sheet and was analyzed after data cleaning using SPSS v-23. Beneficiaries who did not fill the questionnaire were contacted on the telephone by the supervisor and were asked for their wellness and reactions, thus minimizing loss to follow up.

Statistical Analysis:
Descriptive statistics (Frequency and percentages) were calculated for sample demographic characteristics. Chi-square analysis was done to find out the association of various demographic features with the onset of adverse or systemic reactions among the study participants.

RESULTS:
There were 500 participants in the study whose mean age was 46.7(+-17.50) years. There were no admissions or serious side effects observed over 7 days. Systemic effects post-vaccination were seen in 240 (48%) study participants. The study population comprised of 320(64%) males against 180(36%) females. The study population was divided into 07 subgroups based on their age profile. Comorbid conditions were present in 16% (n=80) of the study population. The demographic features of the study population are given in Table-01.

Table 1: Demographic features of study population

	Total (N=500)
Gender	
Male	320 (64%)
Female	180 (36%)
Age(years)	
19-29	150 (30%)
29-39	70 (14%)
39-49	100 (20%)
49-59	110(22%)
59-69	100(20%)
69-79	60 (12%)
79-89	10 (02%)
Mean Age	46.7(+- 17.50) years
Comorbidity	
Yes	80 (16%)
No	420 (84%)

Table 2: Distribution of symptoms among the study participants

	Total (N=240)
Symptoms present	
Fever and Bodyache	90 (37.5%)
Myalgia and Fatigue	52 (21.67%)
Headache	48(20%)
Flu like symptoms	21(8.75%)
Loose stools	08(3.33%)
Vomitting	05(2.08%)
Rashes/allergic reactions	05(2.08%)
Change in taste	06(2.5%)
Vertigo	05(2.08%)

Table 3: Distribution of the Symptoms as per their onset and duration

Time taken for onset of symptoms								
		<2hrs	2-6 hrs	6-12hrs	12-24 hrs	24-48 hrs	48 hrs	P value
Fever & Bodyache	Yes	0	17	24	42	7	0	<0.001
	No	14	34	52	0	0	0	
Headache	Yes	4	24	20	0	0	0	<0.001
	No	10	27	56	42	7	0	
Myalgia & Fatigue	Yes	10	10	32	0	0	0	<0.001
	No	4	41	44	42	7	0	
Duration that symptom lasted								
Fever & Bodyache	Yes	0	5	20	60	10	0	<0.001
	No	9	42	39	10	0	0	
Headache	Yes	5	34	7	3	0	0	<0.001
	No	4	13	49	66	10	0	
Myalgia & Fatigue	Yes	4	8	32	8	0	0	<0.001
	No	5	39	24	60	10	0	

DISCUSSION:
COVISHIELD vaccine has been studied for safety in various published Phase I/II/III trials. Serum Institute of India had developed this vaccine with 5x1010 viral particles per dose. There were nil reports of serious side effects requiring hospitalization or causing them to miss their hospital routine activities over a period of seven days of follow up post-vaccination. In a study carried out by Feng Cai Zhu et al at Wuhan, China, using recombinant adenovirus type 5 vectored COVID vaccine with a similar dosage of viral particles, there was 1% reported serious effects in a study population of n=129 [8].This study population did not have participants from India. Our study population size was larger than that of the above study; hence the absence of serious side effects is significant in this population.

In our study, study population is 500 in which 48% (n=240) individuals had systemic and local reactions post-vaccination. Fever and bodyache was the most common effect of vaccination in 37.5% (n=90), followed by Myalgia and fatigue in 21.67% (n=52), headache in 20 % (n=48), flu-like symptoms in 8.75% (n=21), diarrhoea in 3.33%(n=8), vomiting in 2.08%(n=05), rashes in 2.08%, change in taste in 2.5%(n=6), vertigo in 2.08%(n=05).

In most of the individuals the systemic symptoms started at 6-12 hours post-vaccination. There were no reports of fresh onset of systemic symptoms of any kind beyond 48 hours of vaccination. The duration of the above symptoms in the majority was for 2-6 hours for headache (n=24) and 6-12 hours for myalgia(n=32) and 12-24 hrs for fever(n=42), all results are significant (P value<0.001). None of the systemic symptoms lasted for more than 48 hours in any individual. There was pain at the injection site observed in 22.4 % (n=112) of the study population, which in majority lasted for 24-48 hours without affecting routine daily activities.

In Phase II/III trial data published on the same vaccine with lesser viral particles (2.2x1010 particles per ml) by Maheshi et al, the observed systemic effects were much higher, ranging from 65% to 86% across various age groups [5]. The population size studied in this study was 560 and they were studied over a period of 28 days post-vaccination. This result may be translated into better tolerance of the vaccine in our study population.

In comparison to the study published by Feng Cai Zhu et al, the number of systemic effects in our study were higher in case of fever (22.01% vs 16%) and lower as in cases of fatigue and myalgia (25.74% vs 52%), headache (17.16% vs 28%), diarrhea (3.5% vs 8%), vomiting (0.8% vs 1%). There were no individuals with symptoms like hypersensitivity, dyspnoea, or pruritus as observed in the study by Feng Cai Zhu et al [8]. Males were likely to have a higher probability of having systemic effects than females post-vaccination (OR=2.08, p=0.01). Since this study is the first of its kind in India to the best of our knowledge, the significance of this finding will get clearer as and when data from the various geographical location of the country gets published. Presently there is no reason which we could attribute to explain this difference across genders.

CONCLUSION:
Our study has tried to address the concerns of the safety of the COVISHIELD vaccine in light of the doubts in the general public after emergency approval of the vaccine. The absence of serious side effects and none of the systemic effects affecting daily activities is the highlight of the study. The comparatively lower serious side effects and systemic effects in our population might indicate better tolerability in this geographical area. In this context, our study becomes more relevant in disseminating short term safety data post-vaccination. This will undoubtedly help individuals in their decision in self vaccination.

Limitation:
This study was done as a short term safety study after the first dose of vaccination. The authors plan to look at the long term safety effects and the effects post second dose of vaccination.

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Conflict of interest - Nil

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