



A Study of Neurological and Neuropsychiatric Manifestations Following COVID 19 Vaccination

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Abstract

Background: Corona virus disease 2019 (COVID - 19) caused by Severe Acute Respiratory Syndrome Corona Virus-2(SARSCoV2) has spread worldwide leading to an ongoing pandemic. Vaccination along with practicing social distancing, masks and hand hygiene remain the main strategies for prevention of SARS CoV 2. Globally many vaccines were developed for prevention of the disease. This study aims to find out the neurological and neuropsychiatric events following first dose of Covishield vaccine.

Materials and methods: A longitudinal study was done among health care workers aged more than 18yrs and who were either faculties or students who received first dose of Covishield vaccine from a tertiary care hospital in Thiruvananthapuram during February – March 2021. A structured questionnaire was administered to collect data at the time of vaccination. The participants were followed up at regular intervals of 8 hours, 24 hours, 48 hours, 72 hours and 5 days through phone calls. Data was entered in MS Excel software and analyzed using SPSS 25.

Results: The mean age of the study participants was 28.8 (11.26) years. Among the 322 study participants, 70.2% were females and 29.8% were males. Among the 322 study participants, 78.6% had any of the symptoms following first dose of COVID 19 vaccinations and 21.4% had no symptoms following first dose of COVID 19 vaccinations. Tiredness, fever, headache and myalgia were the predominant symptoms reported in this study.

Conclusion: Anxiety, sadness, depression seizures, double vision, sleep disturbances and giddiness were the reported neuropsychiatric adverse events following COVID 19 vaccination. Covishield vaccine is associated with adverse neuropsychiatric effects even though in a small proportion of participants.

Keywords: COVID 19 vaccination, neurological and neuropsychiatric manifestations

I. Introduction

Corona virus disease 2019 (COVID - 19) caused by Severe Acute Respiratory Syndrome Corona Virus-2(SARSCoV2), was identified in Wuhan, China in Dec 2019. The disease has spread worldwide leading to an ongoing pandemic resulting in millions of death and also disabling millions[1,2,3]. Vaccination along with practicing social distancing, masks and hand hygiene remain the main strategies for prevention of SARS CoV 2.

Globally many vaccines were developed for prevention of the disease which includes Pfizer, Moderna, Sino pharm, Johnson & Johnson, Covishield and Covaxin. Among them introduction of the Oxford AstraZeneca COVID 19 Vaccine, which is a non-replicating viral vector vaccine codenamed AZD1222(chAdOX1) developed By Oxford University using modified chimpanzee adenovirus was historical. Serum Institute of India started producing Covishield, in collaboration with AstraZeneca which has got an efficacy of 80% [4]. The vaccination was rolled out among health care workers followed by frontline workers and general public later. The recommended dosage was two doses intramuscularly (0.5 ml) with an interval of 8-12 weeks. Vaccine administration invariably is associated with some adverse events, which could act as a hindrance for the acceptability among public. Reporting the adverse events related to COVID 19 vaccination helps to strengthen the pharmacovigilance system of the country [5]. Apart from the common local and systemic side effects that can be produced by a vaccine, thrombotic events and GuillenBarre syndrome has also been reported from Covishield vaccine administration [6]. A temporal association and investigation of cases for causality may be needed to establish an epidemiological link [7,8]. This study mainly focuses on the various adverse events, especially neurological and neuropsychiatric effects following administration of 1st dose of Covishield vaccine.

II. Objectives

Primary objective: To estimate the incidence of neurological and neuropsychiatric events following administration of first dose of Covishield vaccine.

Secondary objective: To find out the determinants of adverse events following administration of first dose of Covishield vaccine.

III. Methodology

A longitudinal study was done among health care workers aged more than 18 yrs and who were either faculties or students who received first dose of Covishield vaccine from a tertiary care hospital in Thiruvananthapuram during February – March 2021. The sample size was calculated based on a previous study done in where the proportion of individuals who developed adverse events following immunization was 57% following first dose of Covishield vaccine [9]. An absolute precision of 6% and non-response rate of 20% was taken for estimating sample size. A total of 332 participants were selected for the study. Those who didn't give consent were excluded from the study. After getting informed consent, a structured questionnaire was administered to collect data at the time of vaccination. The participants were followed up at regular intervals of 8 hours, 24 hours, 48 hours, 72 hours and 5 days through phone calls. Socio-demographic variables, details of vaccination and reported adverse events following vaccination were collected. Data was entered in MS Excel software and analyzed using SPSS Version 25. Quantitative variables were expressed as mean and standard deviation and categorical variables were expressed as proportion.

IV. Results

The mean age of the study participants was 28.8 (11.26) years. Among the 322 study participants, 70.2% were females and 29.8% were males. The study population included doctors, staff nurses, students and other non-medical staff of a teaching institution. Table 1 shows baseline characteristics of 322 study participants.

Table 1: Sociodemographic characteristics (N=322)

Variable	Frequency	Percentage	
Age category(Years)	<20	60	18.6
	21-30	151	46.9
	31-40	68	21.1
	41-50	27	8.4
	51-60	4	1.2

	61-70	12	3.7
Gender	Male	96	29.8
	Female	226	70.2
Profession	Doctor	58	18
	Nurse	36	11.2
	Other staff	34	10.6
	Student	194	60.2
Allergic history	Drugs	8	2.5
	Foods	9	2.8
	No allergy	304	94.4
	Vaccine	1	.3
Comorbidity	Present	21	6.5
	Absent	301	93.5
History of SARS CoV 2 infection	Yes	19	5.9
	No	303	94.1

Table 2: Comorbidity profile of participants (N=21)

Comorbidity	Frequency
Diabetes Mellitus	9
Hypertension	10
Heart disease	2

Table 3: Incidence of symptoms following first dose of Covishield vaccine (N=322)

Symptoms		Frequency	Percentage
Symptoms	Present	253	78.6
	Absent	69	21.4
Symptoms within	2 hours	16	5.0
	4 hours	17	5.3
	6 hours	58	18
	8 hours	60	18.6
	More than 8 hours	102	31.7
Symptoms last	12 hours	60	18.6
	12-48 hours	131	40.7
	48-72 hours	47	14.6
	More than 72 hours	15	4.7

Table 4: Proportion of adverse events following first dose of Covishield vaccine.

Symptoms		Frequency	Percentage
Tiredness	Present	202	62.7
	Absent	120	37.3
Loss of taste	Present	17	5.3
	Absent	305	94.7
Smell difficulty	Present	2	0.6
	Absent	320	99.4
Swallowing difficulty	Present	8	2.5
	Absent	314	97.5
Depression	Present	4	1.2
	Absent	318	98.8
Sadness	Present	8	2.5
	Absent	314	97.5
Anxiety	Present	8	2.5
	Absent	314	97.5
Paresis of legs	Present	82	25.5
	Absent	240	74.5
Paresis of hands	Present	93	28.9
	Absent	229	71.1
Facial Weakness	Present	1	0.3
	Absent	321	99.1
Seizures	Present	1	0.3
	Absent	321	99.1
Double vision	Present	1	0.3
	Absent	321	99.1

Giddiness	Present	17	5.3
	Absent	305	94.7
Sleep disturbances	Present	52	16.1
	Absent	270	83.9
Body pain	Present	20	6.2
	Absent	302	93.8
Headache	Present	20	6.8
	Absent	300	93.2
Temperature(° F)	>100	30	9.3
	99-100	126	39.1
Regained routine activities	24 hours	4	1.2
	48 hours	176	54.7
	72 hours	53	16.5
	96 hours	9	2.8
	more than 5 days	11	3.4

Table 4: Association of symptoms following vaccine with baseline characteristics.

Variable		Symptoms following vaccine		X ² Value	P Value
		Yes	No		
Gender	Male	69(71.9%)	27(28.1%)	2.321	0.128
	Female	180(79.6%)	46(20.4%)		
Profession	Doctor	37(63.8%)	21(36.2%)	20.592	<0.001
	Nurse	34(94.4%)	2(5.6%)		
	Student	20(58.8%)	14(41.2%)		
	Other staff	158(81.4%)	36(18.6%)		
Allergic history	Drugs	7(87.5%)	1(12.5%)	6.386	0.094
	Foods				

		5(55.6%)	4(44.4%)		
	No allergy				
		237(78%)	67(22%)		
	vaccine	0(0%)	1(100%)		
Comorbidity	Yes	231(76.7%)	70(23.3%)	0.901	0.343
	No	18(85.7)	3(14.3%)		
COVID infection Past	Yes	13(68.4%)	6(31.6%)	.339	.395
	No	236(77.9%)	67(22.1%)		

V. Discussion

In this study, among the 322 study participants, 78.6% had any of the symptoms following first dose of COVID 19 vaccination and 21.4% had no symptoms following first dose of COVID 19 vaccination. In this study, majority of the individuals were healthy adults, who were either staff or students of a tertiary care hospital. Among the study participants, 6.5% had any of the reported co-morbidities (Diabetes, hypertension and cardiovascular disease) and 5.3% had reported history of allergy to food or drugs.

In this study, 5.0% developed symptoms within 2 hours, 5.3% developed symptoms within 4 hours, 18% developed symptoms within 6 hours and 31.7% developed symptoms after eight hours. Tiredness was the predominant symptom reported in this study, followed by weakness of limbs, fever, sleep disturbances, headache and body pain. Even though proportions of other reported symptoms were less, difficulty in swallowing, anosmia, double vision, giddiness and seizures were also reported. Psychiatric symptoms like depression, sadness and anxiety were reported in 6% of participants. Acute flaccid paralysis was developed in one study subject who was investigated and found out to have Guillain-Barre syndrome. In a study conducted in Korea, fatigue (93%) was the most common AEFI reported followed by malaise (84%) pain and tenderness at the site of injection [10]. There were no serious events requiring hospitalization, and majority of the study participants returned back to their normal life within 72 hours, similar to the study done in Korea. In a study conducted in Nepal, pain at injection site, fever, fatigue, headache, chills, dizziness, and nausea were the side effects complaint after second dose of Covishield vaccination [11]. Similar adverse events are being reported from Canada also [12].

VI. Conclusion

Tiredness, fever, headache and myalgia were the predominant symptoms reported in this study. Anxiety, sadness, depression seizures, double vision, sleep disturbances and giddiness were also reported in a small proportion of individuals. Covishield vaccine is associated with adverse neuropsychiatric effects even though in a small proportion of participants.

References

- [1.] Ma O, P M, E K, Ş K, I E, K G, et al. Clinical manifestation, diagnosis, prevention and control of SARS-CoV-2 (COVID-19) during the outbreak period. *Infez Med* [Internet]. 2020 Jun 1 [cited 2021 Sep 29];28(2). Available from: <https://pubmed.ncbi.nlm.nih.gov/32275257/>
- [2.] Eijk LE van, Binkhorst M, Bourgonje AR, Offringa AK, Mulder DJ, Bos EM, et al. COVID-19: immunopathology, pathophysiological mechanisms, and treatment options. *J Pathol* [Internet]. [cited 2021 Sep 25]; Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8013908/>
- [3.] Andrade BS, Siqueira S, Soares WR de A, Rangel F de S, Santos NO, Freitas A dos S, et al. Long-COVID and Post-COVID Health Complications: An Up-to-Date Review on Clinical Conditions and Their Possible Molecular Mechanisms. *Viruses* [Internet]. 2021 Apr [cited 2021 Sep 29];13(4). Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8072585/>
- [4.] Covishield, Covaxin: findings of a large efficacy study [Internet]. *The Indian Express*. 2021 [cited 2021 Nov 22]. Available from: <https://indianexpress.com/article/explained/covishield-covaxin-findings-large-efficacy-study-7634573/>
- [5.] Shrestha S, Khatri J, Shakya S, Danekhu K, Khatiwada AP, Sah R, et al. Adverse events related to COVID-19 vaccines: the need to strengthen pharmacovigilance monitoring systems. *Drugs Ther Perspect*. :1.
- [6.] Wm O, P G, A de S. AstraZeneca COVID-19 vaccine and Guillain- Barré Syndrome in Tasmania: A causal link? *J Neuroimmunol* [Internet]. 2021 Nov 15 [cited 2021 Nov 18];360. Available from: <https://pubmed.ncbi.nlm.nih.gov/34560365/>
- [7.] M F, Gm L, M P. COVID-19 vaccine-associated immune thrombosis and thrombocytopenia (VITT): Diagnostic and therapeutic recommendations for a new syndrome. *Eur J Haematol* [Internet]. 2021 Aug [cited 2021 Nov 18];107(2). Available from: <https://pubmed.ncbi.nlm.nih.gov/33987882/>
- [8.] Wm O, P G, A de S. AstraZeneca COVID-19 vaccine and Guillain- Barré Syndrome in Tasmania: A causal link? *J Neuroimmunol* [Internet]. 2021 Nov 15 [cited 2021 Nov 18];360. Available from: <https://pubmed.ncbi.nlm.nih.gov/34560365/>
- [9.] Kamal D, Thakur V, Nath N, Malhotra T, Gupta A, Batlish R. Adverse events following ChAdOx1 nCoV-19 Vaccine (COVISHIELD) amongst health care workers: A prospective observational study. *Med J Armed Forces India*. 2021 Jul;77(Suppl 2):S283.
- [10.] Jeon M, Kim J, Oh CE, Lee J-Y. Adverse Events Following Immunization Associated with Coronavirus Disease 2019 Vaccination Reported in the Mobile Vaccine Adverse Events Reporting System. *J Korean Med Sci* [Internet]. 2021 May 3 [cited 2021 Nov 1];36(17). Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8093606/>
- [11.] Pokharel K, Dawadi BR, Karki A. Side Effects after Second Dose of Covishield Vaccine among Healthcare Workers: A Descriptive Cross-sectional Study. *JNMA J Nepal Med Assoc*. 2021 Jun;59(238):577.
- [12.] Government of Ontario M of H and L-TC. MERS-CoV (Novel Coronavirus) - Ministry Programs - Health Care Professionals - MOHLTC [Internet]. Government of Ontario, Ministry of Health and Long-Term Care;[cited2021Nov18].Availablefrom: https://www.health.gov.on.ca/en/pro/programs/publichealth/coronavirus/2019_guidance.aspx