



12-2021

## Neurological Syndromes After Recent Covid-19 Vaccination; A Possible Association

Ayisha Farooq Khan  
*Aga Khan University Karachi*

Sajid Hameed  
*Aga Khan University Karachi*

Sara Khan  
*Aga Khan University, Karachi*

Mohammad Wasay  
*Aga Khan University Karachi*

Follow this and additional works at: <https://ecommons.aku.edu/pjns>



Part of the [Neurology Commons](#)

### Recommended Citation

Khan, Ayisha Farooq; Hameed, Sajid; Khan, Sara; and Wasay, Mohammad (2021) "Neurological Syndromes After Recent Covid-19 Vaccination; A Possible Association," *Pakistan Journal of Neurological Sciences (PJNS)*: Vol. 16: Iss. 4, Article 9.

Available at: <https://ecommons.aku.edu/pjns/vol16/iss4/9>

# NEUROLOGICAL SYNDROMES AFTER RECENT COVID-19 VACCINATION; A POSSIBLE ASSOCIATION?

Ayisha Farooq Khan<sup>1</sup>, Sajid Hameed<sup>2</sup>, Sara Khan<sup>3</sup>, Mohammad Wasay<sup>4</sup>

<sup>1-4</sup> Department of Medicine, section of Neurology, Aga Khan University, Karachi

**Correspondence Author:** Sajid Hameed Department of Neurology, Aga Khan University, Pakistan **Email:** drsajidhameed92@gmail.com

**Date of submission:** September 09, 2021 **Date of revision:** December 16, 2021 **Date of acceptance:** December 23, 2021

## ABSTRACT

**OBJECTIVE:** Coronavirus disease 2019 (COVID-19) pandemic is one of the deadliest pandemics of our time. Vaccines are our best hope to put an end to this pandemic. An emergency use authorization (EUA) has been given to seven vaccines and more than 4 billion doses have been globally administered. Because of EUA, the large-scale safety trials were not conducted before their use and adverse effects were one of the chief concerns resulting in vaccine hesitancy.

**METHODS:** This is a retrospective observational study. All the inpatients admitted to the Department of Neurology, Aga Khan University during the period from 1st April 2021 to 31st July 2021 with a recent history of COVID-19 vaccination within previous 8 weeks were included in this study. Patients with the pre-existing neurological condition were excluded.

**RESULTS:** Eleven patients were included in the study. Most of our patients were male (82%; n=9) with a median age of 53 ± 14.6 years. 6 of these patients received the Sinopharm vaccine and 2 received AstraZeneca. Six patients had stroke, two had cerebral venous thrombosis, and one patient each had autonomic neuropathy, transverse myelitis, and seizures. The majority of the patients presented within 4 weeks post-vaccination. No mortality was noted. The mean discharge mRS was 1.1. Only one patient had a history of previous COVID-19 infection.

**CONCLUSION:** Almost three-quarters (73%) of inpatients with a recent COVID-19 vaccination had a cerebrovascular disease. This may be a coincidental finding or may indicate a probable association. Our patients also had multiple risk factors in addition to a recent history of COVID-19 vaccination. The potential neurological sequelae of the COVID-19 vaccine will be unraveled as the vaccinated population increases.

**KEY WORDS:** COVID-19; Vaccine; Stroke; CVT; Sinopharm; SinoVac

## INTRODUCTION

Coronavirus disease 2019 (COVID-19) pandemic is one of the deadliest pandemics of our time with approximately 200 million confirmed cases and more than 4 million global deaths, as of August 4, 2021.<sup>1</sup> As the cases continue to rise, vaccines are our best hope to control this pandemic. Thus far, the World Health Organization has given emergency use authorization (EUA) to seven vaccines i.e. Pfizer/BioNTech, Moderna, Oxford-AstraZeneca (AZ), Janssen (Johnson & Johnson), Sinopharm, and Sinovac and more than 4 billion doses have been globally administered.<sup>1,2</sup> COVID-19 vaccine drive in Pakistan initiated in February 2021 and more than 34 million and 7 million doses have been administered in Pakistan and Sindh, respectively.<sup>3,4</sup> Because of EUA, the large-scale safety trials were not conducted before their use and adverse

effects were one of the chief concerns resulting in vaccine hesitancy.

Reported neurological symptoms post-vaccination have mostly been mild and occur shortly after vaccination. Fatigue and headache were the most common neurological symptoms reported one-week after a Pfizer or AZ vaccination.<sup>5,6</sup> Parallel studies on Sinovac and Sinopharm vaccine recipients have also shown headache to be the most common neurological symptom (68%), followed by myalgias (60%).<sup>7</sup> This was largely an outpatient-based study.<sup>7</sup> Recent reporting of serious neurological complications such as cerebral venous thrombosis (CVT), transverse myelitis, and Guillain-Barre syndrome (GBS) have raised concerns regarding the safety of these vaccines, with CVT being a major concern, especially after AZ and Janssen vaccination.<sup>8,9</sup> Cases of Bells' palsy, tremor, diplopia,

tinnitus, seizures, and reactivation of herpes zoster have been also reported in post-vaccinated patients.<sup>10,11</sup> The objective of our study is to look for spectrum of neurological disorders in admitted patients with a recent history of COVID-19 vaccination in our population. Secondly, a majority of our population received inactivated COVID-19 vaccine i.e. Sinopharm and Sinovac, in the first phase of vaccination. The published literature regarding the serious adverse effects of inactivated COVID-19 vaccines is limited and our study will provide a useful tool to highlight these probable adverse effects.

## METHODS

This is an observational cross-sectional study. All the patients admitted to the Department of Neurology, Aga Khan University, Pakistan during the period from 1<sup>st</sup> April 2021 to 31<sup>st</sup> July 2021 with a recent history of COVID-19 vaccination during the past eight weeks were included in this study. Patients with pre-existing neurological conditions were excluded. This study was approved by the Ethical Review Committee of the AKUH and informed consent requirement was waived. Statistical analysis was performed using IBM Statistical Package for Social Sciences (SPSS) Statistics for Windows, Version 26.0. (Armonk, NY: IBM Corp). Results were presented as frequency and percentages for qualitative variables and mean and standard deviation for quantitative variables.

## RESULTS

Eleven patients were included in our study. Most of our patients were male (82%; n=9) with a median age of 53 14.6 years (range: 30 – 79 years). Six of these patients received the Sinopharm vaccine, two patients each received AZ and CanSino, while one patient received Sinovac vaccine. Half of the patients had only received the first dose, with CanSino vaccine being administered on a single-dose regimen. The majority of the patients (82%, n=9) presented within 4 weeks post-vaccination (mean 3.5 weeks). No mortality was noted. The mean discharge mRS was 1.1. Only one patient had a history of COVID-19 infection.

Six patients presented after the Sinopharm vaccine; 3 had an ischemic stroke, 1 patient each had a left basal ganglia hemorrhage, CVT, and autonomic neuropathy. The latter was subsequently diagnosed with multiple myeloma. The patients with ischemic stroke had vascular risk factors (DM, HTN, IHD). Patient with CVT also had hyperhomocysteinemia, which is associated with an increased risk for CVT.<sup>12</sup>

Of the two patients presenting after AZ; one had CVT, and the second patient presented with seizures. The

former patient had hyperhomocysteinemia, however, the cause of seizures in the latter patient remained unknown despite extensive workup.

Two patients also presented after CanSino vaccine; one with ischemic stroke and the second with transverse myelitis. The remaining one patient who received Sinovac also presented with an ischemic stroke. Both patients with ischemic stroke had vascular risk factors. Table 1 shows a summary of the patients.

## DISCUSSION

Concerns regarding the safety of COVID-19 vaccines were raised when multiple cases of thromboembolism (n=11), especially CVT (n=9), were initially reported among AZ vaccine recipients (82% females) in early March 2021.<sup>8</sup> This resulted in a temporary suspension of AZ vaccination and an investigation was conducted. By the end of March 2021, around 62 cases of CVT cases post-AZ vaccine were reported by the EU safety database.<sup>13</sup> Most of these patients had serum antibodies against platelet-factor 4 (PF4) and it was suggested that an immune response to PF4 is responsible for the higher incidence of thromboembolism in these patients.<sup>14</sup> In another study, two patients developed transverse myelitis post-AZ vaccine.<sup>15</sup> Besides AZ, cases of thromboembolism are also seen in the Janssen vaccine recipients. Interestingly, most of these cases of thromboembolism and CVT occurred in young women with a median age of 37 years and within two weeks post-vaccination. Both AZ and Janssen have been reinstated for use as the benefits greatly outweigh the risks.<sup>10</sup> An unusual case of new-onset refractory status epilepticus was reported in a 42-year-old female 10 days after the first dose of the AZ vaccine, who had no prior comorbid.<sup>16</sup> The data regarding adverse effects following inactivated COVID-19 vaccines (Sinopharm, SinoVac, and CanSino) is limited. A cross sectional study from UAE on subjects receiving Sinopharm vaccine (n=1000) reported mild adverse effects of fatigue, injection site reaction, and headache.<sup>17</sup> Two other studies reported mild side effects including myalgias, fever and headache within 20 hours post-vaccination in 24% and 16% of subjects receiving Sinopharm, respectively.<sup>18,19</sup> None of the side effects were serious or required hospitalization. At present, there is no published data to support serious adverse events following Sinopharm, Sinovac or CanSino vaccine. However, all patients in our study presented with serious symptoms following a recent COVID-19 vaccination that required hospitalization. No mortality was reported and all patients improved and were discharged home in a stable condition.

Our study has certain limitations. Our study is a single-center study, consisting only of admitted

patients. We had a small number of patients with a cross-sectional observational study design. Most of the patients also had multiple risk factors for their neurological syndromes. Hence, a cause-and-effect relationship cannot be established.

## CONCLUSION

Almost three-quarters (73%) of our inpatients with a recent COVID-19 vaccination had a cerebrovascular disease. This may be a coincidental finding or may indicate a probable association. This should be further investigated and looked for in other centers as well. However, only time will unravel the potential neurological sequelae of COVID-19 vaccines, particularly as the vaccinated population increases.

## REFERENCES

1. Johns Hopkins University Coronavirus Resource Center. [Online]. Available from: <https://coronavirus.jhu.edu/map.html> [Accessed 4 August 2021]
2. Coronavirus disease (COVID-19): Vaccines. [Online]. Available from: [https://www.who.int/news-room/q-a-detail/coronavirus-disease-\(covid-19\)-vaccines](https://www.who.int/news-room/q-a-detail/coronavirus-disease-(covid-19)-vaccines) [Accessed 4 August 2021]
3. NCOC Government of Pakistan. Vaccine statistics. [Online]. Available from: <https://ncoc.gov.pk/covid-vaccination-enphp> [Accessed 5 August 2021]
4. Health Department Government of Sindh. Daily Situation Report. [Online]. Available from: [https://www.sindhhealth.gov.pk/upload/daily\\_status\\_report/Daily\\_Situation\\_Report\\_For\\_5th\\_August\\_2021.pdf](https://www.sindhhealth.gov.pk/upload/daily_status_report/Daily_Situation_Report_For_5th_August_2021.pdf) [Accessed 9 August 2021]
5. 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; 10(7): 1428. doi: 10.3390/jcm10071428
6. Menni C, Klaser K, May A, Polidori L, Capdevila J, Louca P, et al. Vaccine side-effects and SARS-CoV-2 infection after vaccination in users of the COVID Symptom Study app in the UK: a prospective observational study. *Lancet Infect Dis*. 2021; 21(7): 939–949. doi: 10.1016/S1473-3099(21)00224-3
7. Bhopal SS, Olabi B, Bhopal R. Vaccines for COVID-19: learning from ten phase II trials to inform clinical and public health vaccination programmes. *Public Health*. 2021; 193: 57–60. doi: 10.1016/j.puhe.2021.01.011
8. Greinacher A, Thiele T, Warkentin TE, Weisser K, Kyrle PA, Eichinger S. Thrombotic Thrombocytopenia after ChAdOx1 nCov-19 Vaccination. *N Engl J Med*. 2021;384(22):2092-2101. doi: 10.1056/NEJMoa2104840.
9. US Food and Drug Administration. FDA and CDC Lift Recommended Pause on Johnson & Johnson (Janssen) COVID-19 Vaccine Use Following Thorough Safety Review. [Online]. Available from: <https://www.fda.gov/news-events/press-announcements/fda-and-cdc-lift-recommended-pause-johnson-johnson-janssen-covid-19-vaccine-use-following-thorough> [Accessed 5 August 2021]
10. Cirillo N. Reported orofacial adverse effects of COVID 19 vaccines: the knowns and the unknowns. *J Oral Pathol Med*. 2021;50(4):424-427. doi: 10.1111/jop.13165
11. Goss AL, Samudralwar RD, Das RR, Nath A. ANA investigates: neurological complications of COVID 19 vaccines. *Ann Neurol*. 2021;89(5):856-857. doi: 10.1002/ana.26065
12. Cantu C, Alonso E, Jara A, Martínez L, Ríos C, Fernandez MD, et al. Hyperhomocysteinemia, low folate and vitamin B12 concentrations, and methylene tetrahydrofolate reductase mutation in cerebral venous thrombosis. *Stroke*. 2004;35(8):1790-4. doi: 10.1161/01.STR.0000132570.24618.78
13. European Medicines Agency. Vaxzevria (previously COVID-19 Vaccine AstraZeneca)-Safety updates 2021. [Online]. Available from: <https://www.ema.europa.eu/en/medicines/human/EPAR/vaxzevria-previously-covid-19-vaccine-astrazeneca#safety-updates-section>. [Accessed 9 August 2021].
14. Schultz NH, Sørvoll IH, Michelsen AE, Munthe LA, Lund-Johansen F, Ahlen MT, et al. Thrombosis and thrombocytopenia after ChAdOx1 nCoV-19 vaccination. *N Engl J Med*. 2021;384(22):2124-2130. doi: 10.1056/NEJMoa2104882
15. Voysey M, Clemens SA, Madhi SA, Weckx LY, Folegatti PM, Aley PK, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *Lancet*. 2021;397(10269):99-111. doi: 10.1016/S0140-6736(20)32661-1
16. Aladdin Y, Shirah B. New-onset refractory status epilepticus following the ChAdOx1 nCoV-19 vaccine. *J Neuroimmunol*. 2021;357:577629. doi: 10.1016/j.jneuroim.2021.577629
17. Saeed BQ, Al-Shahrabi R, Alhaj SS, Alkorkhardi ZM, Adrees AO. Side effects and perceptions following Sinopharm COVID-19 vaccination. *Int J Infect Dis*.

2021;111:219-226. doi:  
10.1016/j.jjid.2021.08.013.

18. Jayadevan R, Shenoy RS, Anithadevi TS. Survey of symptoms following COVID-19 vaccination in India. medRxiv. 2021 Jan 1. doi:  
10.1101/2021.02.08.21251366

19. Hatmal MM, Al-Hatamleh MA, Olaimat AN, Hatmal

M, Alhaj-Qasem DM, Olaimat TM, et al. Side Effects and Perceptions Following COVID-19 Vaccination in Jordan: A Randomized, Cross-Sectional Study Implementing Machine Learning for Predicting Severity of Side Effects. Vaccines. 2021. 9(6); 556.  
<https://doi.org/10.3390/vaccines9060556>

**TABLE 1: PATIENTS WITH NEUROLOGICAL DISORDERS FOLLOWING COVID-19 VACCINATION**

NO.	A/G	Comorbids	Symptoms	Diagnosis	COVID-19 vaccine	Vaccine Dose	Time (weeks)*	PH of COVID-19 infection	Outcome (mRS)
1	57M	DM, HTN	Vertigo, vomiting headache, dysarthria	Ischemic Stroke – Left PICA	Sinopharm	2 <sup>nd</sup>	7	No	2
2	32 M	None	Headache	Hemorrhagic Stroke – Left BG	Sinopharm	1 <sup>ST</sup>	4	No	1
3	79 F	HTN, IHD	Right arm weakness and slurring of speech	Ischemic Stroke – Left MCA	Sinopharm	2 <sup>nd</sup>	3½	No	3
4	60 M	HTN	Burning sensation in the lower extremities	Autonomic neuropathy	Sinopharm	2 <sup>nd</sup>	1½	No	1
5	44 F	None	Headache	CVT	Sinopharm	2 <sup>nd</sup>	4	No	1
6	68 M	DM, IHD	Numbness in right upper and lower extremity	Ischemic Stroke – Left MCA	Sinopharm	2 <sup>nd</sup>	5	No	0
7	30 M	None	Fever, headache and seizure	Seizure.	AZ	1 <sup>ST</sup>	1½	Yes, 5 days back	0
8	53 M	HTN, IHD	Seizure	CVT	AZ	1 <sup>ST</sup>	4	No	0
9	63 M	DM, HTN IHD	Vertigo, right facial weakness and dysphagia	Ischemic Stroke – Right posterior circulation	CanSino	1 <sup>ST</sup>	4	No	1
10	39 M	HTN	Burning sensation abdomen, urinary retention and constipation	Transverse myelitis	CanSino	1 <sup>ST</sup>	1	No	1
11	58 M	DM, HTN	Right-sided body numbness and weakness	Ischemic Stroke- Left MCA	Sinovac	1 <sup>ST</sup>	3	No	2; LAMA

**ABBREVIATIONS:**

A/G = Age/Gender; AZ = Astrazeneca; COVID-19 = Coronavirus disease 2019; CVT = Cerebral venous thrombosis; DM = Diabetes mellitus; F = Female; HTN = Hypertension; IHD = Ischemic heart disease; LAMA= Left against medical advice; M = male; MCA = Middle cerebral artery; mRS= Modified Rankin Score; PH = Past history; PICA = Posterior inferior cerebellar artery \*Time between last vaccine dose and symptoms

Conflict of interest: Author declares no conflict of interest.

Funding disclosure: Nil

Author's contribution:

**Ayisha Farooq Khan:** data collection, data analysis, manuscript writing, manuscript review

**Sajid Hameed:** data collection, data analysis, manuscript writing, manuscript review

**Sara Khan:** concept, data analysis, manuscript writing, manuscript review

**Mohammad Wasay:** concept, data analysis, manuscript writing, manuscript review



This is an Open Access article distributed under the terms of the Creative Commons Attribution-Non Commercial 2.0 Generic License