

Post COVID 19 Vaccination Associated Neurological Complications

Dr. K. Prasanthi

MD General Medicine, DM Neurology Postgraduate, Department of Neurology, Coimbatore Medical College and Hospital.

Abstract: *Background:* During COVID-19 pandemic, many vaccines have been granted emergency use authorizations. Post authorization, a wide spectrum of neurological complications is continuously being reported following COVID 19 vaccination. Emerging reports of neurological complications associated with Covid 19 vaccinations are leading to regulatory, clinical and public health concerns. *Aim:* To study the incidence of neurological complications following COVID-19 vaccination particularly covishield (ChAdOx1nCoV-19) and covaxin (BBV152) in tertiary care hospital in South India. *Methods:* This is an observational study with a sample size of 22 patients, done during June 2021 to February 2022. Patients who presented with neurological complications following covid 19 vaccines, within a time period of one month were assessed based on clinical, radiological, laboratory findings and electrophysiological features. *Results:* 22 patients presented with various neurological manifestations. Among 22 patients, 10 were male patients, 12 were female patients. 15 patients received covishield vaccine and 7 patients received covaxin. Ischemic stroke occurred in 6 patients out of which 5 patients received covishield and 1 patient received covaxin. Hemorrhagic stroke occurred in 1 patient who received covishield. Acute disseminated encephalomyelitis (ADEM) was diagnosed in 5 patients, out of which 3 patients received covaxin, 2 patients received covishield. Guillain Barre syndrome occurred in 6 patients out of which 4 patients received covishield and 2 patients received covaxin. 1 patient presented with optic neuritis who received covishield. 1 patient presented with Bells palsy who received covishield. 1 patient presented with transverse myelitis who received covishield.

1. Introduction

COVID-19 pandemic has seen the development of vaccines at unprecedented speed and scale

Several vaccines including ChAdOx1n COV-19 (covishield) and BBV- 152 covaxin are approved for use and these have been shown to reduce COVID 19 infections, transmission, hospitalizations and death in randomized controlled trials and real- world effectiveness studies.

Since the start of large- scale vaccine programs across the world, neurological complications like Guillain Barre Syndrome, cerebrovascular events, transverse myelitis, cerebral venous thrombosis have been detected.

However, the clinical trials were underpowered to detect these adverse events.

Therefore, detailed assessments of potential neurological adverse events associated with COVID-19 vaccines is needed

2. Material and Methods

This is a prospective observational study done in a tertiary care hospital in South India from June 2021 to February 2022 with a sample size of 22 patients.

Inclusion Criteria

The adult patients who developed neurological complications following covid 19 vaccinations (covishield and covaxin) within a period of 1 month were included in this study.

Exclusion Criteria

- Patients with comorbidities like diabetes mellitus, hypertension, coronary artery disease were excluded.

- Patients with HIV, HbsAg were excluded. These patients were assessed based on clinical presentation, radiological investigations like Computed tomography (CT) / Magnetic Resonance Imaging (MRI) brain and spinal cord, laboratory findings like routine investigations and csf analysis and electrophysiology like nerve conduction studies were done.

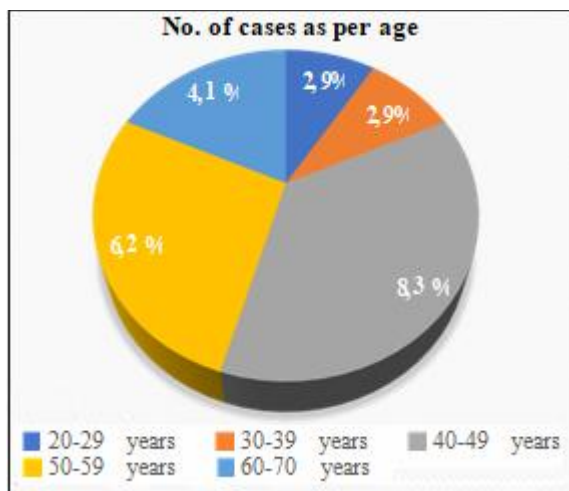
3. Results

- 22 consecutive patients presented with various neurological manifestations.
- 10 were male patients, 12 were female patients.
- Mean age of female patients was 40 years and male patients was 50 years. Demographic data is summarized in Table 1 and Table 2.
- Number of days between receiving the vaccine and presenting with various neurological manifestations ranged between 4 and 30 days with an average of 15 days, while the average days of hospital admission was 10 days. Number of cases based on type of vaccine are summarized in Table 3.
- Of the 22 patients studied, 6 patients had an ischemic cerebrovascular accident, 1 female and 5 males.
- These patients presented with ataxia, dysarthria, motor and sensory deficits.
- 5 patients presented within 3 days of receiving covishield first dose, and 1 patient presented within 4 days of receiving covaxin first dose.
- Magnetic resonance imaging (MRI) of brain of all these patients showed acute infarction. Number of cases based on duration of vaccine are summarized in Table 4.
- 6 patients had Guillain Barre syndrome 3 males, 3 females.
- These patients presented with flaccid symmetrical quadriparesis.

- Nerve conduction study showed Acute motor sensory axonal neuropathy in 4 patients and acute motor axonal neuropathy in 2 patients.
- 4 patients presented within 15 days of receiving covishield first dose 2 patients presented within 10 days of receiving covaxin first dose.
- 5 patients had Acute disseminated encephalomyelitis 3 female and 2 male patients.
- All of them were older than 20 years.
- These patients presented with seizures, encephalopathy, cranial nerve palsy, motor and sensory deficits.
- 3 patients presented within 15 days of receiving first dose 2 presented within 4 days of receiving covishield first dose.
- Magnetic resonance imaging of brain and spinal cord showed features suggestive of ADEM.
- Hemorrhagic stroke occurred in 1 patient within 10 days of receiving first dose of covishield.
- Transverse myelitis occurred in 1 patient within 14 days of receiving first dose of covishield.
- Optic neuritis occurred 1 patient within 10 days of receiving first dose of covishield.
- Bell’s palsy occurred in 1 patient within 7 days of receiving first dose of covishield.
- Number of cases based on neurological complications are summarized in Table 5.

Table 1: Number of cases as per age

Age	No. of Patients	Percentage
20-29 years	2	9%
30-39 years	2	9%
40-49 years	8	37%
50-59 years	6	27%
60-70 years	4	18%
Total	22	100%



Inference - Patients with age more than 40 years are predisposed to neurological complications.

Table 2: Number of cases as per Gender

Gender	Number of Patients
Male	10
Female	12
Total	22

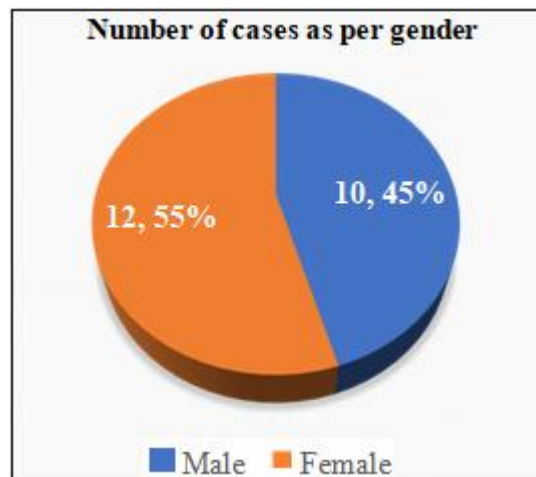
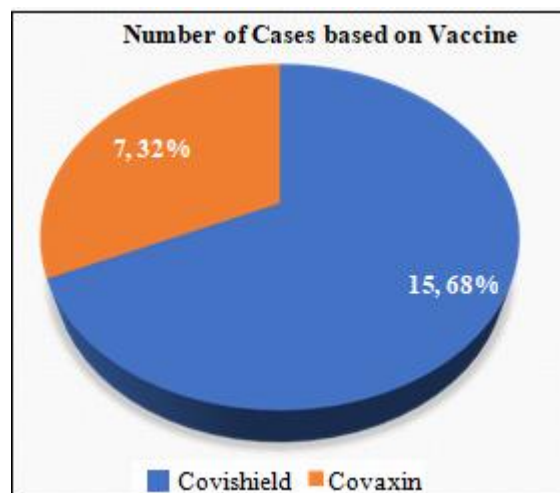


Table 3: Number of cases based on Vaccine

Vaccine	Number of patients	Percentage
Covishield	15	68%
Covaxin	7	32%
Total	22	100%



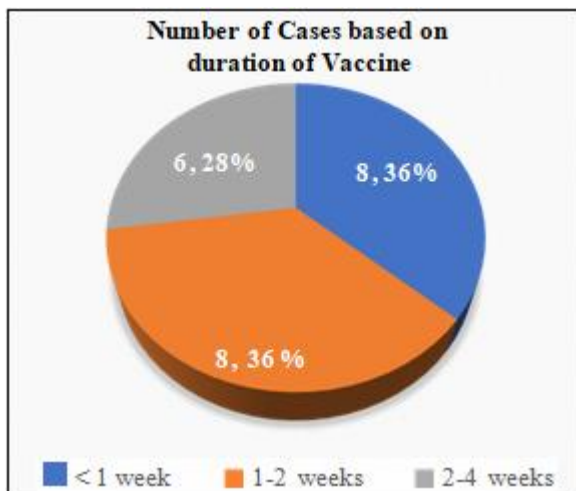
Inference- Patients who received covishield are more prone for neurological complications.

Number of cases based on Duration

Table 5

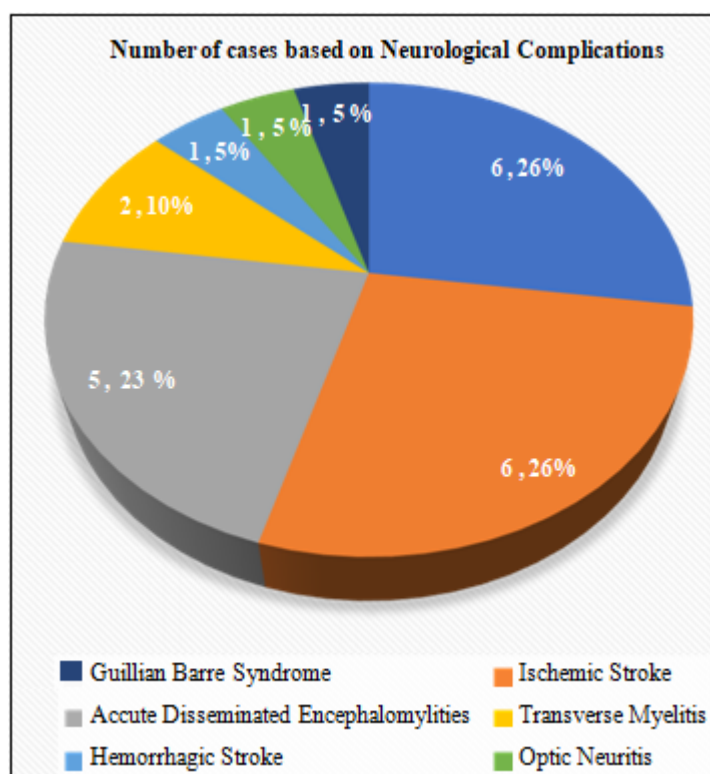
Duration	Number of Patients	Percentage
Less than 1 week	8	36%
1 – 2 weeks	8	36%
2 – 4 weeks	6	28%
Total	22	100%

Inference - Patients who received vaccination within a period of 2-14 days are more prone for neurological complications



Number of cases based on Neurological Complications

Complications	Number of Patients	Percentage
Guillian Barre Syndrome	6	26%
Ischemic Stroke	6	26%
Accute Disseminated Encephalomyelitis	5	23%
Transverse Myelitis	2	10%
Hemorrhagic Stroke	1	5%
Optic Neuritis	1	5%
Bell's Palsy	1	5%
Total	22	100%



Inference - The most common post covid vaccination neurological complications are Guillian barre syndrome and ischemic stroke followed by acute disseminated encephalomyelitis.

4. Discussion

- This study with 22 people investigated the neurological adverse events associated with covishield and covaxin.
- First, there is increased risk of hospital admission for Guillian Barre syndrome within 15 days of receiving covishield and within 10 days of receiving covaxin and incidence is more in patients who received covishield than covaxin first doses.
- After GBS there is an increased risk for ischemic stroke within 3 days of receiving covishield and within 4 days of receiving covaxin first doses.
- Ischemic stroke was found to be high in patients receiving covishield than covaxin.
- After GBS and ischemic stroke there is an increased risk for ADEM within 15 days of receiving covaxin and 4 days of receiving covishield first doses.
- Second, increased risk of hospital admission for hemorrhagic stroke, optic neuritis, Bell's palsy, transverse myelitis within 10-14 days of receiving first dose of covishield was observed.
- As a matter of concern , increasing number of reports about adenoviral vector vaccine induced cerebral vascular adverse events, like cerebral venous thrombosis , arterial stroke and intracerebral hemorrhage is getting published in leading medical journals.¹
- These reports are alarming as post vaccination vascular events culminate either in severe disability or death.
- Vaccine induced cerebral vascular events are generally associated with severe immune mediated thrombotic thrombocytopenia.
- In post vaccination thrombotic thrombocytopenia, a picture like that of heparin induced thrombocytopenia is encountered.

- When heparin binds platelet factor 4 there is generation of antibodies against platelet factor 4.
- Antibodies against platelet factor 4 result in platelet destruction and trigger the intravascular blood clotting.³
- The vector-based vaccines contain genetic material of SARS-COV-2 that can encode the spike glycoprotein.
- Possibly, leaked genetic material binds to platelet factor 4 that subsequently activates formation of autoantibodies.
- These autoantibodies destroy platelets.
- Bayas and co-workers described a case that presented with superior ophthalmic vein thrombosis, ischemic stroke, and immune thrombocytopenia after administration of viral vector-based vaccine.⁶ Al-Mayhani et al. described three cases of vaccine induced thrombotic thrombocytopenia, all presented with arterial strokes.⁷
- In this study no such association between thrombocytopenia and ischemic stroke was found.
- Patients presented with ataxia, dysarthria, homonymous hemianopia, motor and sensory deficits.
- CT brain showed evidence of acute infarction.
- These patients were treated with anti platelets, statins, antiedema measures in necessary patients and physiotherapy.
- All the patients presented with ischemic stroke in our study recovered and got discharged.
- Atheros and Doumas reported a 71 year old female who developed intracerebral hemorrhage after she received the first dose of the Moderna mRNA vaccine.²

Image 1: CT Brain Showed Acute Infarct in left MCA territory

- In another report, Bjornstad-Tuveng et al. described a young woman, who had a fatal cerebral event following vaccination with AstraZeneca's ChAdOx1nCoV-19 vaccine.⁸
- In this study adult male presented with left hemiparesis. CT brain showed evidence of left intracerebral hemorrhage.
- This patient was treated with antiedema measures, statins and physiotherapy, patient recovered and got discharged.
- Guillian barre syndrome is a post infectious disorder of peripheral nerve manifesting with lower motor neuron type of sensory motor quadriplegia.
- Acute motor weakness is frequently preceded by an antecedent microbial infection. Adenovector based vaccines were more frequently associated with Guillian Barre syndrome.^{13,14}
- Post vaccination Guillian Barre syndrome generally affects older adults within 2 weeks of vaccine administration.¹⁵
- Proposed pathogenesis of Guillian barre syndrome is an autoantibody mediated immunological damage of peripheral nerves via mechanisms of molecular mimicry between structural components of peripheral nerves and the microorganism.
- Response to immunotherapy is generally good.
- In our study patients presented within 2 weeks of receiving covishield and covaxin.

- Clinically they presented as ascending flaccid quadriplegia, nerve conduction showed axonal neuropathy. 5 patients were treated with methylprednisolone and 1 patient was given intravenous immunoglobulin. All the patients recovered and were discharged.

Image 2 – CT Brain showed Right Intracerebral Haemorrhage

- Acute disseminated encephalomyelitis (ADEM) is an acute inflammatory demyelinating disorder of the central nervous system that can occur as a result of molecular mimicry and subsequent neuronal damage.
- In the majority, ADEM is a post infectious entity, in many cases it even develops after vaccination.⁹
- In two cases ADEM following Covid 19 vaccination has been reported.¹⁰
- In this study five patients presented with ADEM following Covid 19 vaccination.
- Patients presented with seizures, encephalopathy and magnetic resonance imaging revealed multiple, discrete T2/ FLAIR hyperintense periventricular lesions.
- Patients improved following methylprednisolone treatment.

Image 3 - MRI brain T2/FLAIR showing multiple hyperintense lesions suggestive of ADEM

- Acute transverse myelitis is an inflammatory spinal cord disorder that clinically manifests with paraparesis/quadriplegia, transverse sensory level and bowel/bladder dysfunction.
- Acute transverse myelitis usually is a post infectious disorder.
- MRI demonstrates T2/ FLAIR hyperintensity extending several spinal cord segments.
- Autoimmunity via mechanism of molecular mimicry is usually responsible for spinal cord dysfunction.
- Adenoviral vector based COVID 19 vaccines are more frequently associated with causation of transverse myelitis.
- In this study two patients presented with transverse myelitis, these were treated with methylprednisolone, one patient recovered, and one patient succumbed to death.
- Malhotra and colleagues reported a 36-year-old patient, who had short segment myelitis 21 days after first dose of covishield vaccine.^{11,16}
- Several cases of Bell's palsy have occurred following COVID -19 vaccination.
- The instances of Bell's palsy are most often associated with mRNA vaccines.¹² Vaccine associated Bell's palsy generally responds very well to oral corticosteroids.
- Findings from this study have clinical and public health implications.
- This will need ongoing analysis and monitoring.
- Neurological complications from vaccination in this study are rare.
- However, these complications can cause lifelong disability requiring long term care.
- In this study 21 patients recovered and got discharged, 1 patient succumbed to death.

- Mortality rate is low in patients with vaccination induced neurological complications.

5. Conclusion

This observational study identifies neurological adverse events that are specific covishield and covaxin

Gullian Barre Syndrome and ischemic stroke were the most common complications observed in patients receiving covishield than covaxin and presented within 4- 7 days of receiving first dose vaccines followed by acute disseminated encephalomyelitis which is more with covaxin than covishield presented within 5-15 days of receiving fist dose vaccines

Hemorrhagic stroke, optic neuritis, transverse myelitis, Bell's palsy were observed in patients within 10-14 days of receiving covishield

21 patiesnts recovered and got discharged while 1 patient succumbed to death

Mortality rate is very low in patients with neurological events following vaccination.

But however large scale studies are needed to prove causality

References

- [1] Goss AL, Samudralwar RD, Das RR, Nath A. ANA investigates neurological complications of COVID -19 vaccines . Am Neurol Assoc. 2021; 89 (5) ; 856-857
- [2] Athyros VG, Doumas M. 2021 A possible case of hypertensive crisis with intracranial haemorrhage after mRNA Anti covid-19 vaccine . Angiology. ;33197211018323.10.1177/00033197211018323
- [3] Iba T, Levy JH Warkentin TE.2021 Recognizing vaccine induced immune thrombotic thrombocytopenia. Crit care Med.10.1097/ CCM.
- [4] Ledford H. COVID vaccines and blood clots.Nature .2021; 592 (7855) : 495-496. doi:10.1038/d41586-021-00998-w.
- [5] McGonagle D, De Marco G, Bridgewood C. Mechanisms of Immunothrombosis in vaccine induced thrombotic thrombocytopenia (VITT) compared to natural SARS-CoV-2 infection.J Autoimmun.2021, doi:10.1016/J.jaut.2021
- [6] Bayas A, Menacher M, Christ M, Behrens L, Rank A, Naumann M. Ischemic stroke after ChAdOx1nCoV-19 vaccination.
- [7] Al -Mayhani T, Saber S, Stubbs MJ, et al. Ischemic stroke as a presenting feature of ChAdOx1nCoV-19 vaccine induced immune thrombotic thrombocytopenia. J Neurol Neurosurg Psychiatry. 2021;92(11) :1247-1248 doi: 10.1136/jnnp -2021-326984.
- [8] De Melo Silva ML Jr, Lopes DP . 2021 Large hemorrhagic stroke after ChAdOx1nCoV-19 vaccination : a case report. Acta Neurol Scand.10.1111/ane.13505
- [9] Ozgen Kenangil G, Ari BC, Guler C, Demir MK. Acute disseminated encephalomyelitis after coronavirus 2 vaccination : a case report.
- [10] Vogrig A, Janes F, Gigli GL. Acute disseminated encephalomyelitis after SARS CoV-2 vaccination .
- [11] Tahir N, Koorapati G, Prasad S, et al. SARS -CoV-2 vaccination induced transverse myelitis. Cureus.2021;13(7):e 16624.
- [12] Collela G, Orlandi M, Cirillo N. 2021 Bell's palsy following COVID-19 vaccination. J Neurol.1-3.doi: 10.1007/s00415-021-10462-4.
- [13] Maramattom BV, Krishnan P, Paul R, et al. Guillian barre syndrome following ChAdOx1nCoV-19 vaccine. Ann Neurol . 2021; 90(2):312-314. doi: 10.1002/ana.26143.
- [14] Finsterer J. Exacerbating Guillian Barre syndrome eight days after vector based COVID -19 vaccination. Case report infectious disease .2021; 2021: 3619131.
- [15] McKean N, Chircop C. Guillian barre syndrome after COVID -19 vaccination. BMJ Case report.2021; 14(7):e 244125.
- [16] Singh Malhotra , H. et al. COVID 19 vaccination associated myelitis. QJM. doi.org/10.1093/qjmed/hcab069(2021)