



Guillain–Barre syndrome following COVID-19 vaccination: a study of 70 case reports

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Background and objective: Guillain–Barre syndrome (GBS) has been found to have some interesting association with vaccinations. This paper mainly focuses on exploring different associations between COVID-19 vaccination and GBS.

Methods: Electronic databases such as PubMed, Google Scholar, Cochrane, and Embase were searched using MESH terms for case reports published till 1 August 2023 from which 70 case reports were documented involving 103 individuals from 23 different countries.

Result and discussion: The case reports were from a wide range of individuals aged from 13 to 87 years with an average age of 53 ± 20 interquartile range years along with male predominance. The average time between receiving the vaccine and the onset of symptoms was 13.08 ± 2.14 days. Prominent clinical features included back pain, facial diplegia, weakness, and paraesthesia whereas the main diagnostic studies were cerebrospinal fluid (CSF) analysis and electromagnetic studies. The principal diagnostic clue was albumin-cytological dissociation in CSF while being negative for anti-ganglioside antibodies or SARS-CoV-2. Available treatment options consisted of intravenous immunoglobulin and Plasmapheresis. Patients with comorbidities such as diabetes mellitus, hypertension, dyslipidemia, permanent atrial fibrillation, hypothyroidism, Hashimoto's thyroiditis, Chronic Obstructive Pulmonary Disease, asthma, osteoporosis, migraine, rheumatoid arthritis, osteoarthritis, ulcerative colitis, coeliac disease, seizures, bipolar disorder, endometriosis, multiple sclerosis, bell's palsy, squamous cell carcinoma, prostate cancer were included in our study.

Conclusion: Overall, this review evaluated innovative and clinically relevant associations between COVID-19 vaccination and GBS. Understanding of this uncommon potential side effect of COVID-19 vaccination is crucial for prompt diagnosis and appropriate treatment. Importantly, GBS should not be considered a contraindication to vaccination. This underscores the importance of ongoing research to enhance the safety and efficacy of COVID-19 vaccination efforts.

Keywords: case reports, COVID-19, Guillain–Barre syndrome, vaccine

Introduction

Guillain–Barré syndrome (GBS) is a rare immune-mediated polyradiculoneuropathy characterized clinically by progressive limb weakness. It is the most common cause of acute flaccid

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HIGHLIGHTS

- The study provides new insight into the development of Guillain–Barre syndrome (GBS) following post-vaccination.
- In the present review article, we reviewed the onset of symptoms, clinical features, previous comorbidities, investigations, and outcomes of 103 patients aged between 13 and 87 years with the COVID-19-associated GBS spectrum.
- The treatment included intravenous immunoglobulins, steroids, Plasmapheresis and physiotherapy.
- The clinical consequences of GBS and incomplete recovery of patients in this study emphasize the need for vigilance and in-depth research in this regard.

paralysis with an incidence of about 2 in 100 000 people per year^[1]. Diagnosis of this disease requires a combination of clinical findings supported by nerve conduction studies (NCS) and cerebrospinal fluid (CSF) examination. It is diagnosed by Brighton criteria and the case definitions for Guillain–Barre syndrome^[2] have been attached to Table 1 Despite prompt treatment, there may be no full recovery. Therefore, aetiological factors for the occurrence of GBS should be investigated and controlled.

Table 1
Diagnostic criteria and Brighton case definition for Guillain–Barre syndrome

Diagnostic criteria	Level of diagnostic certainty			
	1	2	3	4
Bilateral and flaccid weakness of limbs	+	+	+	+/-
Decreased or absent deep tendon reflexes in weak limbs	+	+	+	+/-
Monophasic course and time between onset-nadir 12 h–28 days	+	+	+	+/-
CSF cell count < 50/μl	+	+ ^a	-	+/-
CSF protein concentration > normal value	+	+/- ^a	-	+/-
NCS findings consistent with one of the subtypes of GBS	+	+/-	-	+/-
Absence of alternative diagnosis for weakness	+	+	+	

+ Present; - absent ; +/- present or absent
CSF, cerebrospinal fluid; GBS, Guillain–Barre syndrome; NCS, nerve conduction studies.
^aIf CSF is not collected or results not available, nerve electrophysiology results must be consistent with the diagnosis Guillain–Barre syndrome.

Even though the exact pathogenesis is unknown, it is believed that an autoimmune response preceding a viral, or bacterial infection or vaccination plays a role in the development of GBS. The first epidemiological link between vaccines and GBS was highlighted in 1976 when was reported an increased GBS risk among individuals who received the swine flu vaccine^[3]. Speculative studies suggest a post-vaccination immune response attributing to the production of antibodies and T cells that cross-react with ganglioside at nerve membranes due to molecular mimicry^[4]. There are rare reports of GBS after the administration of rabies, influenza, and polio vaccines. SARS-CoV-2 vaccination-related adverse effects range from mild-moderate to severe neurological dysfunction because of the presence of contaminated proteins which may elicit anti-ganglioside antibodies^[5]. The probable cause of GBS occurrence post-vaccination with AstraZeneca is the attachment of adenovirus-vector spike proteins to ganglioside receptors and consequent anti-ganglioside antibody formation^[6]. Other adenoviral vector vaccines such as Sputnik V, Janssen, and Convidecia may have a similar mechanism. In mRNA vaccines such as Pfizer, the mRNA recognizes the spike protein and generates antibodies which may trigger autoantibody formation against myelin and lead to GBS^[7].

mRNA enters the human cell and instructs the cells to identify the spike protein found on the surface of SARS-COV-2, the virus that causes COVID-19. Our bodies then recognize the spike protein as an invader and produce antibodies against it. Later, if these antibodies encounter the actual virus, they are ready to recognize and kill the virus before it can cause illness. In some patients, this immune response can trigger autoimmune processes that lead to the production of antibodies against the myelin and cause GBS.

To date, the FDA approved three double-dose vaccines for the prevention of COVID-19 infection [BNT162b2 (Pfizer); mRNA-1273 (Moderna); Ad26.COVS. S (Johnson & Johnson)]^[8]. The safety profile of the COVID vaccines is still being established and the neurological side effects are of utmost concern. Recent case reports have shown an occurrence of GBS post-COVID vaccination although much regarding the nature of the association and

the characteristics of GBS in this situation remains unclear. GBS is more frequently reported in adenovirus-vector vaccines, but there are also several case reports of GBS with mRNA vaccines^[9]. To bridge the knowledge gap, here we present a comprehensive narrative of 103 studies on GBS involvement.

Methods

We searched PubMed, Google Scholar, Cochrane, and Embase for case reports using search terms “Guillain-Barré Syndrome,” “COVID-19 Vaccines,” “COVID-19,” and “Case report” published till 1st August 2023. The title and abstract were screened and through discussions by three authors, the eligible full-text articles were only included for this review. We included case reports which were free full texts that focused on presenting symptoms, diagnosis, treatment, and pathophysiologic mechanisms linked to our issue. Those articles that were not free and which did not show the linkage between GBS and COVID-19 vaccination were excluded. Editorials, Reviews, and Letters to the Editor were excluded. We used Statistical Package for Social Sciences (SPSS) version 20 and Microsoft Office Excel 2019 for statistical analysis.

Results

We conducted a comprehensive review of published case reports and documented 70 published case reports from peer-reviewed journals. A total of 103 individuals were described on those case reports; among them, the highest number that is 48 people developed GBS following AstraZeneca (Vaxzervia) vaccination followed by 23 after Pfizer, 8 after Johnson& Johnson, Moderna, 6 after Sinopharm, 5 after Sputnik, 2 after Sinovac, Corbevax and one after Vector-based COVID-19 vaccine shown in Figure 1.

Clinical features along with the management of GBS following COVID-19 vaccination are present in the Table 2.

Incidence of case reports of GBS development following the COVID-19 vaccine was reported from 28 countries and among them, the highest,19 were from the USA following the second highest, 9 from Argentina and India and 8 were from the UK and the remaining from other countries are shown in Fig. 2.

A wide variation of age among the patients who developed GBS after receiving the corresponding COVID-19 vaccine was seen. So, the median age was found to be 53±20 interquartile

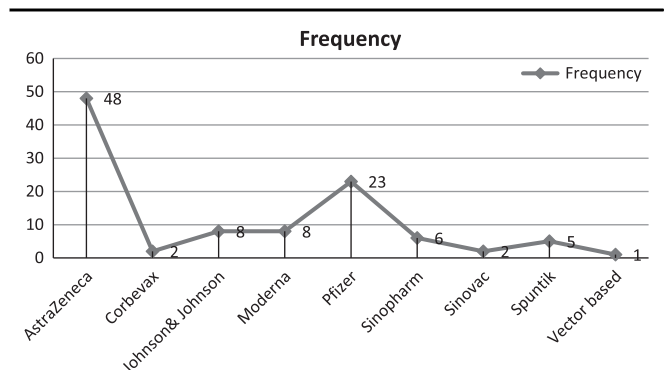


Figure 1. Frequency of Guillain–Barre syndrome following different types of COVID-19 vaccine.

Table 2

Clinical features and management of GBS following COVID vaccine

SN	Authors(s)	Country	Patient(s) age and gender	Vaccine type	Onset of symptoms after vaccine	Comorbid conditions	Clinical signs and symptoms	Investigations	Treatment	Outcome
1	Sadia <i>et al.</i> ^[10]	USA	82-year-old female	First dose of the Pfizer COVID vaccine	14 days	None	Generalized body aches, paraesthesia, and difficulty walking Sustained a fall due to weakness Decreased pinprick in bilateral lower extremities Muscle weakness of 4/5 in hip flexors Areflexia in both upper and lower extremities	CSF study- albumin-cytological dissociation MRI lumbar spine- enhancement of cauda equina nerve roots	IVIg	Full recovery
2	Hasan <i>et al.</i> ^[11]	UK	62-year-old female	First dose of the Oxford/AstraZeneca COVID-19 vaccine	11 days	Bronchiectasis, Asthma, Osteoporosis, Migraine	Initial paraesthesia and numbness in lower limb Gradual ascending weakness of both lower limbs, then upper limbs Neuropathic pain in posterior of legs Muscle power- 3/5 in the right leg and 2/5 in the left leg Ankle reflexes - diminished Difficulty in speech and swallowing Sepsis with aspiration pneumonia	CSF study- albumin-cytological dissociation MRI of spine- collapse of the T8 vertebral body without bony infiltration Nerve conduction study (NCS)- marked, demyelinating, sensorimotor polyneuropathy Ultrasound- C5 root swelling	IVIg Gabapentin and paracetamol for neuropathic pain IV antibiotic for sepsis Intubation followed by tracheostomy and mechanical ventilation	Slow improvement in lower limb weakness but mechanically ventilated in ICU
3	Razok <i>et al.</i> ^[12]	Qatar	73-year-old male	Second dose of Pfizer COVID-19 vaccine	20 days	Hypertension, Rheumatoid arthritis	Progressive bilateral lower limb weakness Lower limb- muscle power 3/5 Reflexes diminished Unable to walk or maintain sitting posture	CBC- mild neutrophilic leukocytosis CSF study- albumin-cytological dissociation MRI of spine- enhanced lumbar and upper part of cauda equina Nerve conduction study (NCS) and electromyogram (EMG)- early polyneuro radiculopathy	IVIg	Full recovery
4	Maramattom <i>et al.</i> ^[9]	India	Case 1 43-year-old female Case 2 67-year-old female Case 3 53-year-old female Case 4 68-year-old female	First dose of ChAdOx1-S vaccine (Covishield TM / Vaxzevria, AstraZeneca)	14 days	None	Case 1- Areflexic quadriplegia with facial diplegia and respiratory failure Case 2- Distal paraesthesia, facial diplegia, dysphagia, limb weakness, right abducens palsy followed by respiratory failure Case 3- Bilateral lower limb weakness, right facial and tongue weakness, back pain, decreased muscle power followed by right trigeminal sensory palsy, LMN facial palsy, areflexic flaccid quadriplegia Case 4- Numbness and weakness in all four limbs followed by LMN facial palsy and areflexic flaccid quadriplegia	CSF study- albuminocytological dissociation Nerve conduction study- demyelinating neuropathy	Case 1-IVIg, mechanical ventilation Case 2- Plasmapheresis, mechanical ventilation Case 3- IVIg, mechanical ventilation Case 4- IVIg	Case 1- full recovery Case 2,3 and 4- bedbound and received rehabilitation
5	Daniel <i>et al.</i> ^[13]	Czech Republic	42-year-old male	First dose of Pfizer	14 days	Bronchial asthma	Paraesthesia of soles of the feet gradually involving hands Unsteady gait with weak knees Right sided muscle weakness and lumbalgia	CSF study- albuminocytological dissociation MRI of lumbosacral spine- Increased signal in the roots of cauda equina Sensitive nerve action potentials-significant reduction in the conduction velocity in upper limbs NCS- motor impairment	IVIg	Partial improvement
6	Allen <i>et al.</i> ^[14]	UK	Case 1- 54-year-old male Case 2- 20-year-old male Case 3- 57-year-old male Case 4- 55-year-old male	Case 1-First dose of AstraZeneca Case 2- first dose of AstraZeneca Case 3- first dose of AstraZeneca Case 4- First dose of AstraZeneca	Case 1- 16 days Case 2- 26 days Case 3- 21 days Case 4- 29 days	Case 1- None Case 2- ulcerative colitis Case 3- asthma, osteoarthritis Case 4- Hypertension	Case 1- Distal dysesthesia in feet and hands followed by facial weakness Case 2- Occipital headache, dysesthesia in lower limbs, facial diplegia Case 3- Dull pelvic pain followed by dysarthria and facial weakness, distal dysesthesia Case 4- bilateral thigh paraesthesia, sacro lumbar region numbness, facial diplegia	Case 1- CSF study- albuminocytological dissociation; NCS- Reduced muscle action potential of muscles supplied by facial nerve Case 2- CSF study- albuminocytological dissociation Case 3- CSF study- albuminocytological dissociation Case 4- CSF study- albuminocytological dissociation; MRI of brain and spine- enhanced facial nerve region	Case 1- Oral prednisolone Case 2- oral prednisolone Case 3- IVIg Case 4- no treatment	Case 1- partial recovery with impairment in facial nerve innervated area Case 2- full recovery Case 3- full recovery Case 4- partial improvement
7	Finsterer <i>et al.</i> ^[15]	Austria	32-year-old male	First dose of vector-based COVID-19 vaccine	8 days	None	Paraesthesia of feet, Bilateral frontal and nuchal headache, Bilateral upper limb weakness, Absent knee jerk, Right facial palsy	Urine toxicology- positive for cannabinoids CSF study- albuminocytological dissociation NCS- slowed velocity, prolonged distal latency, absent F-wave response	IVIg Plasmapheresis	NO improvement

Table 2

(Continued)

SN	Authors(s)	Country	Patient(s) age and gender	Vaccine type	Onset of symptoms after vaccine	Comorbid conditions	Clinical signs and symptoms	Investigations	Treatment	Outcome
8	Yash <i>et al.</i> ^[16]	India	52-year-old female	First dose of Oxford-AstraZeneca Covishield vaccine	9 days	None	Lower back pain, extreme fatigue, difficulty in walking and moving Bilateral lower limb weakness with burning sensation Bilateral reduced reflexes and muscle power in lower limb Severe tachypnoea	NCS- mild demyelination of all four limbs COVID-19 IgG antibody- positive CSF study- albuminocytological dissociation	IVIG Mechanical ventilation Tracheostomy	Partial recovery with remaining quadriplegic state
9	Wai M <i>et al.</i> ^[17]	Australia	Case 1- 51-year-old male Case 2- 65-year-old female Case 3- 72-year-old male Case 4- 66-year-old male	Case 1- first dose of AstraZeneca vaccine Case 2- First dose of AstraZeneca vaccine Case 3- First dose of AstraZeneca vaccine Case 4- First dose of AstraZeneca vaccine	Case 1- 14 days Case 2- 7 days Case 3- 21 days Case 4- 21 days	Peripheral neuropathy in case 3	Case 1- low back pain, generalized weakness, diplopia, dysphagia, and impaired balance, flaccid quadriparesis, reduced pinprick sensation in right lower limb, respiratory failure with aspiration pneumonia Case 2- generalized ascending weakness, ocular involvement, respiratory distress, quadriparesis, symmetrical sensory deficit Case 3- ascending weakness and sensory changes, quadriparesis, loss of vibration, proprioception and pinprick sensation in hands and lower limbs Case 4- distal paraesthesia, facial palsy	Case 1- CSF study- albuminocytological dissociation, NCS- demyelination Case 2- CSF study- albuminocytological dissociation; NCS- demyelination Case 3- CSF study- albuminocytological dissociation, NCS- reduced velocity with demyelination Case 4- CSF study- albuminocytological dissociation; NCS- demyelination	Case 1- IVIG, mechanical ventilation Case 2- IVIG, intubation Case 3- IVIG Case 4- IVIG	Case 1- partial recovery Case 2- full recovery Case 3- continuous improvement Case 4- improvement seen
10	Scendoni <i>et al.</i> ^[18]	Italy	82-year-old Female	Second dose of Pfizer COVID-19	14 days	Permanent atrial fibrillation Arterial hypertension	Superficial tactile hypaesthesia of the four limbs distally Areflexia in both upper and lower extremities. Diffuse weakness in limbs with muscle power- 1/5	CSF study- albumin-cytological dissociation Electroneurography showed acute sensory-motor neuropathy Electromyography showed decreased recruitment to the analysis of voluntary muscle activity, with signs of spontaneous activity Anti-ganglioside antibodies, anti-sulfatide IgG (+) and IgM (+ +), anti-GM2 IgM (+) and anti-GM4 IgM (+) antibodies, were positive.	IVIG Physical therapy	Slight improvement, receiving rehabilitation
11	McKean <i>et al.</i> ^[11]	Malta	48-year-old man	First dose of Vaxzevria (AstraZeneca)	10 days	Dyslipidemia	left-sided lower motor neuron facial weakness House Brackman grade V paralysis bilaterally. Severe mid-thoracic back pain	CSF analysis showed a high protein level (1264 mg/l) and 8 x 106/l lymphocytes. Nerve conduction studies showed a severe, multifocal sensorimotor demyelinating polyneuropathy, with reduced compound motor action potentials throughout, reflecting likely hypo excitability	Oral prednisolone and physiotherapy (Initially for 10 days) IVIG and intensive physiotherapy	Full recovery
12	Srivastava <i>et al.</i> ^[19]	USA	Case 1: 67-year-old woman Case 2: 41-year-old male Case 3: 42-year-old male	Case 1: First dose Moderna COVID-19 Vaccine Case 2: First dose of Johnson and Johnson Vaccine Case 3: Second dose of the Pfizer-BioNTech COVID-19	Case 1: 1 day Case 2: 14 days Case 3: 60 days	Case 1: None Case 2: None Case 3: None	Case 1: Lower extremity weakness difficulties ambulating. Case 2: generalized weakness difficulty ambulating Case 3: blurry vision left eye pain worsened with movement	Case 1: MRI of cervical spine revealed intramedullary cord signal changes extending from C1-C3 with patchy enhancement Brain MRI revealed nonspecific deep white matter changes. Case 2: CSF analysis with albumin-cytological dissociation and increased protein. EMG/NCS showed demyelinating polyneuropathy Case 3: Orbital MRI revealed left optic nerve enhancement CSF analysis significant for increased protein.	Case 1: IVIG and plasmapheresis Case 2: IVIG Case 3: IV solumedrol and oral prednisone	Case 1: partial recovery of lower extremity motor strength. Case 2: partial recovery of lower extremity motor strength. Case 3: Significant improvement
13	Suri <i>et al.</i> ^[20]	India	47-year-old man	First dose of AstraZeneca vaccine	17 days	Diabetes mellitus Hypertension	Rapidly progressive pure motor-flaccid quadriparesis Bilateral facial weakness Inability to stand without support	NCV study showed inflammatory demyelinating polyradiculoneuropathy Serum protein electrophoresis revealed polyclonal gammopathy High level of anti-IgG antibody against COVID-19. CSF showed albuminocytological dissociation MRI brain revealed nonspecific ischaemic demyelination, discrete and confluent hyperintensities in white matter. PETMRI showed enhancing thickening of cauda equina	IVIG	Partial recovery

14	Introna et al. ^[21]	Italy	62-year-old man	First dose of AstraZeneca vaccine	10 days	Hypertension	visual discomfort lower back pain progressively worsening sensory ataxia ascending tetra paresis facial weakness Dysphagia Urinary retention Distal paraesthesia	nerve roots extending from L1 vertebral level and mild diffuse leptomeningeal enhancement up to the D11/12 level CSF analysis examination showed albumin-cytologic dissociation with high opening pressure Electrophysiologic study showed severe sensory-motor mixed polyneuropathy Anti-ganglioside antibodies test was positive for IgG GM1	IVIG	Recovery with rehabilitation.
15	Bouattour et al. ^[22]	Tunisia	67-year-old male	First dose of COVID-19 (Pfizer-BioNTech)	7 days	Type II diabetes	weakness of the four limbs progressive ascending weakness	Electroneuromyography showed typical features of AIDP. CSF analysis revealed an albumin-cytological dissociation	IVIG	Full recovery
16	.Min et al. ^[23]	South Korea	Case 1:58-year-old man Case 2:37-year-old woman	Case 1:First dose of the AstraZeneca vaccine Case 2: first dose of AstraZeneca vaccine	Case 1:3 days Case 2: 4 days	Case 1:None Case 2:None	Case 1: Focal aching pain on his right toes then progressed to severe burning and tingling sensations on both feet Mild hypaesthesia in vibration, temperature, and pain on both feet. Case 2: Tingling sensations over both lower extremities	Ca Case 1: Neurological exam revealed mild hypaesthesia in vibration, temperature, and pain on both feet. A nerve conduction study (NCS) revealed decreased sensory nerve action potential amplitudes on both sural nerves, temporal dispersion on the left peroneal nerve, and absent peroneal motor responses on the right skin biopsy revealed an abnormal decrease in intraepidermal nerve fibre density Cerebrospinal fluid (CSF) analysis revealed albumin cytologic dissociation Case 2: Neurological examination revealed cold hypaesthesia in both legs, IENFD demonstrated a small fibre neuropathy EMG revealed motor polyradiculoneuropathy with temporal dispersion of the tibial nerve CSF analysis showed albuminocytological dissociation	Case 1: Gabapentin Case 2:Gabapentin, Duloxetine, and Tramadol	Case 1:Partial recovery Case 2:Partial recovery
17	Nasuelli et al. ^[24]	Italy	59-year-old male	First dose of AstraZeneca	10 days	Hypertension Hyperuricemia	Four limb distal paraesthesia Postural instability Bilateral facial palsy (House-Brackman grade V) gait ataxia, global areflexia, and distal paraesthesia both at the lower and upper limbs	EMG revealed motor polyradiculoneuropathy with temporal dispersion of the tibial nerve CSF analysis showed albuminocytological dissociation	IV immunoglobulin Physiotherapy	Partial recovery
18	Morehouse et al. ^[25]	USA	49-year-old female	First dose of Johnson& Johnson vaccine	5 days	Neurofibromatosis type I Hypothyroidism, Multiple vitamin deficiencies	Reduced tactile sensation and numbness in her right upper extremity, extending from the elbow into her hand and bilateral lower extremities from her knees through her feet. Headache with pain to palpation across her forehead Lightheadedness Aching lumbar pain Hoarseness and dysphagia Urinary Incontinence	An equivocal B12 level of 187 ng/l MRI of the brain revealed small punctate foci and moderate cervical stenosis. CSF analysis elevated albumin and IgG	B12 injection IVIG Plasmapheresis	Partial recovery
19	Andreozzi et al. ^[26]	Italy	Case 1:59-year-old woman Case 2:43-year-old male	Case 1: first dose of COVID-19 vaccine AstraZeneca Case 2: first dose AstraZeneca	Case 1:15 days Case 2:7 days	Case 1:Hashimoto thyroiditis Case 2:None	Case 1: Acute onset of spontaneous burning pain of lower back Lower limb paraesthesia Bilateral facial weakness complete facial diplegia with Bell's phenomenon and lagophthalmos. Case 2: Subacute onset of facial pain Numbness with weakness of eye closure Lower limbs and hands paraesthesia symmetrical weakness in distal muscle groups of both upper and lower limbs. facial diplegia	Case 1: CSF analysis showed albuminocytologic dissociation. Electrophysiological study revealed multifocal demyelinating sensorimotor Case 2: CSF analysis showed albuminocytologic dissociation Electrophysiological study revealed multifocal demyelinating sensorimotor polyradiculoneuropathy	Case 1:IVIG Case 2:IVIG	Case 1:Partial recovery Case 2:Partial recovery
20	Castiglionea et al. ^[27]	Argentina	Case 1:56-year-old woman Case 2:55-year-old	Case 1:First dose of Sputnik V vaccine Case 2:First dose of Sputnik V	Case 1:19 days Case 2:20 days	Case 1:9:None	Case 1: Bilateral facial weakness Distal paraesthesia in all four limbs Case 2: Bilateral facial palsy	Case 1–9: CSF analysis showed albumin-cytological dissociation was present in seven. One group of patients ($n = 4$) presented demyelinating polyneuropathy, and the other ($n = 5$) showed focal	Case 1–9:Eight patients received intravenous immunoglobulin,	Case 1–9:8 patients fully recovered except the patient of case number 3 who died following sudden onset of arrhythmia and

Table 2

(Continued)

SN	Authors(s)	Country	Patient(s) age and gender	Vaccine type	Onset of symptoms after vaccine	Comorbid conditions	Clinical signs and symptoms	Investigations	Treatment	Outcome
			male Case 3:87-year-old male Case 4:50-year-old male Case 5:39-year-old man Case 6:42-year-old man Case 7:52-year-old female Case 8:43-year-old male Case 9:65-year-old man	vaccine Case 3: first dose of Sputnik V vaccine Case 4: first dose of Covishield/AstraZeneca Case 5: First dose of Sputnik V vaccine Case 6: first dose of Covishield/AstraZeneca vaccine Case 7: first dose of AstraZeneca vaccine Case 8: second dose of Sputnik V vaccine Case 9: First dose of AstraZeneca vaccine.	3:17 days Case 4:20 days Case 5:10 days Case 6:28 days Case 7:13 days Case 8: 13 days Case 9:7 days		Paraesthesia in both hands and feet. Case 3: Bilateral facial weakness Distal paraesthesia in all four limbs Case 4: Bilateral facial palsy Generalized areflexia Paraesthesia Case 5: Severe bilateral facial weakness Altered taste Paraesthesia in both feet. Case 6: Bilateral facial weakness Radicular pain and paraesthesia. Case 7: Bilateral facial palsy Paraesthesia was present in all four limbs. Case 8: Bilateral facial weakness radicular pain and paraesthesia. Case 9: Severe cramping pain in his legs Numbness in his feet and hands Progressive bilateral facial weakness Bilateral lower extremity paraesthesia and weakness. Absent lower extremity deep tendon reflexes reduced upper and lower extremity sensory response to light touch	amplitude involvement and distal latencies along both facial nerves. Ganglioside antibody panel was positive in four patients (two anti-GM1, two anti-GD1a and one anti-sulfatide antibody, respectively).	and in one Plasmapheresis	cardiac arrest before treatment.
21	Thant <i>et al.</i> ^[26]	USA	66-year-old, male	Single dose of the Johnson & Johnson	14 days	Diabetes mellitus Hypertension Prostate cancer	Bilateral lower extremity paraesthesia and weakness. Absent lower extremity deep tendon reflexes reduced upper and lower extremity sensory response to light touch	CSF analysis showed elevated protein 75.0 mg/dl and albumin-cytological dissociation.	IVI Rehabilitation.	Improved initially but then his symptoms started to worsen.
22	Tabatabaee <i>et al.</i> ^[29]	Iran	Case 1: 46-year-old man Case 2: 36-year-old man Case 3: 32-year-old man	Case 1: second dose of AstraZeneca vaccine Case 2: first dose of the Sinopharm vaccine Case 3: First dose of Sinopharm COVID-19 vaccination,	Case 1:3 days Case 2:5 days Case 3:14 days	Case 1:None Case 2:None Case 3:None	Case 1: Lower limb weakness with power 4/5 and pain Upper limb weakness with muscle power 4/5 deep tendon reflexes were absent Case 2: Progressive generalized weakness Difficulty walking clumsiness of his hands. Muscle strength in bilateral lower extremities showed 3/5 in all muscle groups. Deep tendon reflexes were diminished in all four limbs. Case 3: Acute ascending weakness. Loss of dexterity in hands and muscle strength 4/5 in both proximal and distal limbs Deep tendon reflexes were diminished in all four limbs	Case 1: Cerebrospinal fluid (CSF) examination revealed a high protein reading with no cells electromyography nerve conduction studies showed features consistent with an acute motor axonal neuropathy. Case 2: The examination of CSF examination had slight elevation of protein (54 mg/dl) with white cell count of zero. EMG-NCS showed features consistent with an AMAN form of GBS Case 3: CSF examination had a normal protein level of 30 mg/dL with no white cells. EMG-NC showed features consistent with an AMAN variant of GBS	Case 1:IVI Case 2:IVI Case 3:IVI and rehabilitation	Case 1:Partial improvement Case 2:Partial improvement Case 3:Partial improvement
23	Hughes <i>et al.</i> ^[30]	USA	65-year-old, male	First dose of Pfizer	2 days	None	Lower extremity weakness and paraesthesia ascending to bilateral hands	Brain and spine MRI was normal. Cerebrospinal fluid showed elevated protein without pleocytosis. Electromyography demonstrated prolongation of lower extremity F waves.	IVI	Full recovery
24	Silva <i>et al.</i> ^[31]	Brazil	62-years-old Female	First dose of AstraZeneca	21 days	Hypertension Congestive Heart Failure	Ascending and progressive paraesthesia in the upper and lower limbs Loss of strength of the upper and lower limbs Dysphagia	Cranial computed tomography showed no abnormalities. CSF analysis showed protein levels of 110 mg/dl, an appropriate level of glucose (71 mg/ dl) compared with concomitant serum glucose and the CSF white blood	IVI	Partial recovery and rehabilitation

25	Rohilla <i>et al.</i> ^[32]	India	13-years-old, Female	First dose of Corbevax	3 days	None	Bilateral upper limb, lower limb, and truncal weakness	cell count was one cell/ul. No organisms were identified on Gram stain. NCS showed pure motor axonal polyneuropathy with absent compound muscle action potential (CMAP) in all sampled nerves of upper and lower limbs.	Plasmapheresis	Full recovery
26	Introna <i>et al.</i> ^[33]	Italy	62-year-old, Male	First dose of AstraZeneca	10 days	Hypertension	Visual discomfort Absent deep tendon reflexes Bilateral optic disc oedema	MRI normal CSF showed albumin-cytologic dissociation glucose at day-6 from symptoms onset. CSF microscopy and culture were negative.	IVIg	Partial recovery with rehabilitation
27	Biswaset <i>al.</i> ^[34]	India	49-year-old, male	First dose of AstraZeneca	7 days	None	Weakness of bilateral upper limb	MRI showed diffuse disc bulge at C5–C6 level with effacing anterior thecal sac and encroaching into the bilateral neural foramina and no presence of myelopathy. NCS showed demyelinating involvement of upper and lower limbs with preganglionic axonal involvement.	IVIg and Steroids	Full recovery
28	Dalwadi <i>et al.</i> ^[35]	USA	86-year-old Female	Second dose of Moderna SARS-CoV-2 vaccine	2 days	Atrial fibrillation Diabetes mellitus Aortic stenosis Ischaemic stroke	Lower extremity weakness and pain.	CSF analysis demonstrated albumin-cytological dissociation CSF immunological studies was negative including protein electrophoresis, gram stain, glucose, viral PCR panel, paraneoplastic antibody evaluation anti-ganglioside antibodies. NCS demonstrated low amplitude right peroneal, tibial, and ulnar motor evoked responses with normal distal latencies, segmental conduction velocities, and sensory responses, consistent with acute axonal motor neuropathy.	Plasmapheresis	Partial recovery
29	Rossetti <i>et al.</i> ^[36]	USA	38-year-old, Male	First dose of Johnson & Johnson	32 days	None	Bilateral hand and foot paraesthesia Dysarthria Bilateral facial weakness, Absence of classic ascending limb weakness.	CSF showed albuminocytoplasmic dissociation	IVIg	Partial recovery
30	Lanman <i>et al.</i> ^[37]	USA	58-year-old, female	First dose of Pfizer	3 days	History of childhood absence seizures	Worsening back pain Paraesthesia in distal extremities. Gait unsteadiness presyncope episodes and constipation. Bilateral distal predominant lower extremity weakness, decreased sensation in a length-dependent pattern, Areflexia.	EMG/NCS showed a diffuse sensorimotor polyneuropathy with mixed demyelinating and axonal features consistent with GBS.	IVIg and steroids	Full recovery
31	Dang <i>et al.</i> ^[38]	Australia	63-year-old male	first dose of Oxford-AstraZeneca vaccine	14 days	None	Bilateral oculomotor nerve palsy Ataxia Facial diplegia Lower limb weakness	CSF study- albumin-cytological dissociation MRI of brain- enhanced facial and oculomotor nerve bilaterally NCS and needle EMG- chronic axonal neuropathy with reduced motor and sensory amplitudes without any acute abnormality	IVIg	Partial recovery with persistent lower limb weakness
32	Yunsung <i>et al.</i> ^[39]	USA	16-year-old female	Second dose of Pfizer	2 days	None	Bilaterally ascending upper and lower extremity numbness and paraesthesia Signs of LMN lesion Reduced pinprick and vibration sensation Mild ataxia	MRI- enhanced cauda equina CSF study- albumin-cytological dissociation NCS- prolonged latency and slowed conduction velocity	None	Almost full recovery with minimally diminished vibration and reflexes
33	Ogata <i>et al.</i> ^[40]	Japan	70-year-old man	second dose of the Pfizer-BioNTech COVID-19 vaccine	1 day	None	Bilateral distal leg paraesthesia, gait disturbance, constipation Tongue paraesthesia and dysgeusia Hyperalgesia, severely impaired position, and vibration sense Dysautonomia, that is constipation and nocturia	CSF study- albumin-cytological dissociation Antibody against SARS-CoV-2 spike protein- positive NCS- demyelinating neuropathy.	IVIg, methylprednisolone pulse therapy	Partial recovery
34	Nagalli <i>et al.</i> ^[41]	USA	49-year-old female	First dose of mRNA-1273 (Moderna vaccine)	10 days	Hypertension, Hyperlipidemia, hypothyroidism, and bipolar disorder	Ascending weakness involving limbs followed by ataxia and falls Numbness in lower limbs and voice change Decreased power and reflexes in extremities and reduced light touch in upper limbs	CSF study- albumin-cytological dissociation NCS- low amplitude, absent sural Response and decreased peroneal motor response Electromyography- borderline reduced recruitment with borderline high amplitude, long duration motor unit potentials in the triceps, deltoid, vastus medialis, and tensor fascia Lata muscles.	Endotracheal intubation, plasmapheresis, midodrine for hypotension	Partial improvement
35	Aldeeb <i>et al.</i> ^[42]	Qatar	81-year-old female	First dose of Pfizer vaccine	7 days			NCS and electromyography- demyelinating polyneuropathy with secondary axonal degeneration	IVIg	Full recovery

Table 2

(Continued)

SN	Authors(s)	Country	Patient(s) age and gender	Vaccine type	Onset of symptoms after vaccine	Comorbid conditions	Clinical signs and symptoms	Investigations	Treatment	Outcome
36	Jun Woo <i>et al.</i> ^[43]	South Korea	Case 1- 42-year-old male Case 2- 48-year-old female	Case 1-first dose of AstraZeneca COVID-19 vaccine Case 2- first dose of Pfizer COVID-19 vaccine	Case 1- 14 days Case 2- 14 days	Hypertension, Type II diabetes mellitus Dyslipidemia, Case 1-previous history of tuberculosis Case 2- hypertension and diabetes	Generalized weakness Paraesthesia in the lower limbs Tingling sensation in the hands and feet Case 1- facial palsy and tetraplegia, swallowing difficulty with respiratory distress with aspiration pneumonia Case 2- calf numbness and limb weakness, severe myalgia, left facial palsy with slight dysarthria	Case 1- CSF study- albumin-cytological dissociation; Electromyogram- early axonal-type polyneuropathy without F waves Case 2- CSF study- albumin-cytological dissociation; EMG- motor-dominant mixed polyneuropathy	Case 1- IVIG, plasmapheresis, intubation Case 2- IVIG antihypertensive	Case 1- partial recovery with remaining facial weakness Case 2- full recovery
37	Zubair <i>et al.</i> ^[44]	USA	30-year-old female	First dose of Johnson & Johnson	14 days	Heterozygous factor V Leiden deficiency	Bifrontal headache, hyperacusis and dysgeusia on the left Weakness of the upper and lower face Facial diplegia with dysarthria, dysphagia, and hand paraesthesia Decreased pinprick sensation in the hands and feet	MRI - Chiari 1 malformation	Prednisone Valacyclovir Acetaminophen, Diphenhydramine, IVIG	Full recovery
38	Silfat <i>et al.</i> ^[45]	UK	67-year-old male	First dose of the AstraZeneca COVID-19 vaccine	14 days	None	Left-sided bell's palsy Worsening gait, bilateral leg weakness, bilateral facial weakness, and difficulty in chewing food Upper limb weakness Fluctuating level of consciousness	CSF study- albumin-cytological dissociation MRI of head- enhancement of the facial nerve bilaterally MRI of cervical spine- moderate spondylotic changes at the C5-C6 level	Prednisolone IVIG Physiotherapy	full
39	Chang <i>et al.</i> ^[46]	Taiwan	48-year-old female	First dose Oxford-AstraZeneca COVID-19 vaccine	14 days	Asthma Endometriosis	Lower extremity numbness and paraesthesia Progressive whole-body muscle soreness Facial numbness and temporomandibular joint pain on mastication	Cerebrospinal fluid analysis revealed albumin-cytological dissociation. Her pinprick sensation was impaired on physical exam.	IVIG Gabapentin Prednisolone Rehabilitation Xanax (for the pain) and acupuncture. ILIB was also administered.	Full recovery
40	Prasad <i>et al.</i> ^[47]	USA	41-year-old man	First dose of Johnson & Johnson vaccine	12 days	Morbidly obese	Acute onset of urinary retention Subjective weakness and paraesthesia in all extremities Bilateral facial weakness.	CSF analysis showed albumin-cytological dissociation EMG showed a prolonged distal latency with conduction block and slow conduction velocity in bilateral tibial, peroneal nerve, and absent F waves	Initially prednisone and valacyclovir Intravenous immunoglobulin.	Full recovery.
41	Kanabar <i>et al.</i> ^[48]	UK	Case 1: 61-year-old woman Case 2: 56-year-old man	Case 1: First dose of the AstraZeneca COVID-19 vaccine Case 2: First dose of the AstraZeneca COVID-19 vaccine	Case 1: 10 days Case 2: 7 days	Case 1: Multiple sclerosis Case 2: None	Case 1: Bifacial weakness with prominent lower facial involvement. Lower limb weakness Tingling in her feet and hands Case 2: Sudden-onset severe back pain Lower limb radicular pain Waist down numbness sensation and heaviness in his legs. Tingling and numbness in his fingertips	Case 1: CSF analysis was acellular with a protein level of 1.64 g/L. Motor nerve conduction studies showed demyelinating polyneuropathy Case 2: CSF analysis showed a protein level of 1.6 g/l and two lymphocytes only.	Case 1: Intravenous immunoglobulins Case 2: Intravenous immunoglobulins	Case 1: Full recovery Case 2: Full recovery
42	Fakari <i>et al.</i> ^[49]	Iran	60-year-old man	Three dose of Sinopharm	20 days after last dose	Hypothyroidism Hypertension	Mild paraesthesia of his fingertips Weakness of both upper and lower distal extremities Absent Deep tendon reflexes	Neurophysiology: low amplitude sensory response and reduced amplitude of motor response in lower limb without any decrease in velocity. MRI :Normal CT Chest scan: atelectasis in lung bases	Intravenous immunoglobulin	Full recovery
43	Hernandez <i>et al.</i> ^[50]	Spain	23 years male	Pfizer second dose	1 day	Renal disease secondary to glomerulopathy Hypothyroidism Hypertension	Proximal weakness of the right and left upper limb Descending and distal progression affecting all 4 limbs Areflexia	Electromyoneurography: symmetric motor demyelinating polyradiculoneuropathy,	IVIG	Partial recovery
44	Belluci <i>et al.</i> ^[51]	Italy	57 year man	Pfizer first dose	5 days	Bell's palsy		Csf analysis: Albuminocytological dissociation	IVIG	Full recovery

45	Hiits <i>et al.</i> ^[52]	USA	58 year male	Moderna first dose	3 days	Hypertension	Disequilibrium,difficulty climbing stairs,foot hypaesthesia, Areflexia Lower limb weakness,ataxic gait Ascending Symmetric weakness and paraesthesia in lower extremities Diarrhoea Abent DTR	Electrophysiology study: Demyelinating sensory-motor polyneuropathy CSF analysis: Albuminocytological dissociation CT and MRI brain: normal MRI spine: degenerative changes with some stenosis at C5/6	IVG plasmapheresis	Partial improvent Discharge after 309 days of hospitalization
46	Hai <i>et al.</i> ^[53]	Vietnam	Case 1: 38 year male Case 2: 29 year male	Case 1: Oxford Astrazeneca first dose Case 2: Oxford Astrazeneca second dose	Case 1: 4 days Case 2: 21 days	Case 1: None Case 2: none	Case 1: bilateral eyebrow sagging, inability to close the eyes, and impaired balance bilateral eyebrow sagging, inability to close the eyes, and impaired balance paraesthesia of both limbs in a "stocking-glove" distribution Case 2: limb weakness with motor strength of 4/5 in both upper and lower limb limb weakness with motor strength of 4/5 in both upper and lower limb	Case 1: CSF analysis: Albuminocytological dissociation with protein 1.9 g/l Nerve conduction: demyelinating pathology Case 2: CSF analysis: Albuminocytological dissociation with protein 4.0 g/l electromyography introduced motor-dominant mixed polyneuropathy	Case 1: Plasma pheresis Case 2: Plasma pheresis	Case 1: Full recovery Case 2: Full recovery
47	Siddiqi <i>et al.</i> ^[54]	Pakistan	53 year male	Sinovac- coronavac First dose	8 days	Hypertension Ischaemic heart disease	Progressive ascending paralysis of lower limbs, diplopia , ataxia	CSF analysis: cytoalbumino dissociation Nerve conduction study: prolonged latencies with reduced conduction velocities and prolonged F waves delineating acute inflammatory demyelinating polyneuropathy CT head: Normal	Physiotherapy only due to patient wish	Full recovery
48	Shalash <i>et al.</i> ^[55]	Egypt	Case 1: 39 years male Case 2: 29 years male Case 3: 35 years male Case 4: 43 years male Case 5: 55 years male Case 6: 59 years male Case 7: 29 years female	Case 1:Pfizer second dose Case 2: Janssen 2nd dose Case 3: Astrazeneca 2nd dose Case 4: Astrazeneca 2nd dose Case 5: Pfizee 2nd dose Case 6: Sinopharm 3rd dose Case 7: Astrazeneca 2nd dose	Case 1: 1:5 days Case 2: 20 days Case 3: 3:30 days Case 4: 4:14 days Case 5: 5:30 days Case 6: 7:60 days	Case 1:None Case 2:None Case 3:None Case 4:Ischaemic Heart disease Case 5:None Case 6:Diabetes Mellitus, Hypertension, ischaemic heart disease Case 7: portal and splenic vein thrombosis two months ago	Case 1: Bilateral upper eyelid partial ptosis, bilateral ULs and LLS tingling and numbness, bilateral LLs and ULs flaccid weakness (proximal more than distal), truncal weakness, areflexia, bilateral glove and stocking hypesthesia Case 2: Bilateral ULs and LLs tingling and numbness, bilateral LLs and ULs flaccid weakness (proximal more than distal), areflexia, stretch signs, left facial nerve weakness Case 3: Bilateral ULs and LLs tingling and numbness, bilateral LLs flaccid weakness (proximal more than distal), areflexia, stretch signs Case 4: Bilateral ULs and LLs tingling and numbness, bilateral ULs weakness (distal more than proximal), areflexia, stretch signs Case 5: Low back pain, bilateral LLs tingling and numbness, bilateral LLs flaccid weakness (proximal more than distal), areflexia Case 6: Tingling in both LLs then ULs and bilateral LLs and ULs flaccid weakness (proximal more than distal) then bilateral facial nerve weakness, areflexia Case 7: Bilateral LLs tingling and numbness followed by bilateral ULs tingling and numbness then developed bilateral ULs and LLs flaccid weakness more on left, areflexia and bilateral facial nerve weakness	Case 1:NCV:Sensory and motor axonal neuropathy CSF analysis: cytoalbumino dissociation protein:38mg/dl Case 2:NCV:Axonal polyneuropathy of both lower limbs, with proximal neurogenic affection, Case 3:NCV:bilateral axonal polyradiculoneuropathy of both lower limbs Case 4:NCV: bilateral axonal polyradiculoneuropathy of LLs Case 5:CSF: cytoalbumino dissociation protein: 40.4mg/dl,no cells NCV: bilateral axonal polyradiculoneuropathy of LLs Case 6:CSF: cytoalbumino dissociation protein:112mg/dl,no cells Case 7:Mixed axonal and demyelinating polyradiculoneuropathy	Case 1: Plasmapheresis Case 2: Plasmapheresis Case 3: plasmapheresis Case 4: Plasmapheresis Case 5: Plasmapheresis Case 6: Plasmapheresis Case 7: Plasmapheresis	Case 1:Complete recovery Case 2:Partial recovery Case 3:Full recovery except residual numbness Case 4:Partial improvement Case 5:Complete improvement Case 6:Compelete improvement as regard weakness but still has tinging sensation in both upper and lower limbs. Case 7:Partial improvement with regard to upper limb weakness
49	Carranza <i>et al.</i> ^[56]	USA	53 year female	Johnson and Johnson First dose	14 days	Hypothyroidism Bells palsy	progressive proximal weakness, paresthesias, and difficulty standing up from a chair and walking areflexia absent DTR	CSF:Cytoalbumino dissocaiation Protein 47mg/dl MRI Lumbar Spine:enhancement of the cauda equine nerve roots without over thickening ,suggestive of	IVG	Full recovery

Table 2

(Continued)

SN	Authors(s)	Country	Patient(s) age and gender	Vaccine type	Onset of symptoms after vaccine	Comorbid conditions	Clinical signs and symptoms	Investigations	Treatment	Outcome
50	Bazrafshan <i>et al.</i> ^[57]	Iran	68-year-old woman	Oxford/Astrazeneca 2nd dose	4 days	None	Paraesthesia and numbness of both hands progressing to feet Gait instability Absent DTRs	acute inflammatory demyelinating polyradiculoneuropathy NCS: cute inflammatory demyelinating polyradiculoneuropathy	IVIg	Full recovery
51	Prado <i>et al.</i> ^[58]	Philippines	35 years male	Inactivated SARS-CoV-2 vaccine (Sinopharm) 2nd dose	10 days	None	throbbing headaches associated with photophobia and lumbar pains bilateral facial nerve paralysis. hyperacusis, dysgeusia and decreased lacrimation left tongue numbness followed by dysarthria and left facial weakness all occurring within a day. Weakness of the right facial muscles characterized by inability to close the eye, dysarthria and dysgeusia in the right tongue, along with hyperacusis and pain in bilateral mastoids	NCS: revealed preserved compound muscle action potential (CMAP), sensory nerve action potential (SNAP), motor and sensory nerve conduction velocities and F-wave latencies in the median, ulnar, radial, peroneal, tibial and sural nerves. decreased bilateral facial CMAP amplitudes, further supported by blink reflex findings of prolonged bilateral R1's, R2's and contralateral R2's. CSF analysis: cytoalbumino dissociation protein 331.7 mg/dl, wbc 0	Acyclovir prednisolone	Full recovery
52	Donaldson <i>et al.</i> ^[59]	Canada	45-year-old man	Astrazeneca 1st dose	14 days	Crohns disease	Bells palsy left facial weakness , bilateral severe muscle weakness bilateral ascending paresthesias to the knee as well as the left upper limb, diplopia and right sixth nerve palsy.	EMG :emyelinating polyradiculopathy. CSF analysis: cytoalbumino dissociation	IVIg	Patial recovery
53	Del solar <i>et al.</i> ^[60]	Chile	50 year woman	CoronaVac 1st dose	2 days	Coeliac disease	Lumbar pain and progressive flaccid tetraparesis	CSF: normal NCV: axonal motor polyneuropathy	IVIg	Full recovery
54	Lazaro <i>et al.</i> ^[61]	Spain	60 year male	Moderna first dose	9 days	HIV Supraglottic squamous cell carcinoma Acute bronchitis	Lower limb weakness, upper limb paraesthesia Petechiae over lower limbs severe tetraparesis in the following 24 h, tetraplegia, global areflexia, and severe impairment of deep sensation, predominantly in the lower extremities	Thrombocytopenia: 14 000 cell/m ³ Electromyographic study : sensorimotor polyradiculoneuropathy with demyelinating characteristics, absence of sensory potentials in the median nerve and the ulnar nerve, with preservation of the sural nerves,	IVIg	Full recovery
55	Abicic <i>et al.</i> ^[62]	Croatia	24 year female	Pfizer 1st dose	18 days	None	Binocular horizontal diplopia Neurological examination :impaired abduction and elevation of both eyes, more prominent in the left eye	CSF: Albuminocytological dissoaction albumin MRI/CT brain: Normal	IVIg	Full Recovery
56	Bijoy <i>et al.</i> ^[63]	USA	60 years old man	Moderna 1st dose	28 days	ruptured left middle cerebral artery aneurysm status post clipping 2005 with residual right eye blindness and right leg weakness with gait instability	loss of balance, weakness of his legs and fatigue hyporeflexia	CSF: cytoalbumino dissociation protein 90mg/dl, wbc 0 Electromyogram: demyelination pattern CT head and CT angiogram of head and neck: normal	IVIg	Full recovery
57	Katada <i>et al.</i> ^[64]	Japan	44 year woman	Pfizer 2nd dose	2 days	Dysmeborrhea, insomnia, palmoplantar pustulosis, poerated umbilical hernian	Gradually progressive ascending weakness of arms and legs Sensory ataxia Paraesthesia in lower limbs Absent DTR	CSF : Alubumino cytological dissoaction MRI spine : Normal	IVIg	Partial recovery
58	Hwang <i>et al.</i> ^[65]	South korea	47 year male	Moderna 1st dose	28 days	None	Quadriplegiawith areflexia Dyspnoea itchy rash all over body and an eschar on chest Absent DTRs	NCS:axonal type sensimotor polyneuropathy CSF : cytoalbumino dissociation protein 71.2 mg/dl, leucocyte 16/mm ³ MRI Brain and Spine: Normal Anti R tsutsugumashi antibody titre 1:2560	IVIg Mechanical ventilation	Partial improvement
59	Oshibe <i>et al.</i> ^[66]	Japan	71 year woman	Pfizer 1st dose	7 days	None	Paraesthesia, progressive weakness,difficulty walking, diarrhoea,bladder dysfunction	CSF: Albumino cytological dissociation NCS: functional axonal disturbance	IVIg	Full Recovery
60	Kim <i>et al.</i> ^[67]	South Korea	21 year male	Pfizer 1st dose	21 days	None	facial diplegia and mild ataxia ,mild motor weakness areflexia,gait instability paraesthesia in all extremities urinary and erectile dysfunction	CSF: Albumino cytological dissociation NCS: a sural sparing pattern with mild prolongation of the F waves and decreased compound motor action potentials in the motor nerves without significant demyelinating features. The facial nerve conduction	IVIg	Moderate Recovery

61	Kentaro <i>et al.</i> ^[68]	Japan	70-year-old man	Moderna 2nd dose	7 days	Surgery for Aortic regurgitation Hyperlipidemia Hypertension Hyperuricemia	Diplopia mild ataxia Absent DTRs	study revealed bilateral prolongation of R1 and R2, which were compatible with bilateral facial palsy. MRI Lumbar Spine: prominent enhancement in the nerve roots of the cauda equina	Serum anti-GQ1b: positive MRI Head MRI angiography : Normal	IVIG	Full Recovery
62	Pirola <i>et al.</i> ^[69]	Brazil	47-year-old woman	Astrazeneca 1st dose	7 days	None	Weakness in b/l upper and lower limbs Ataxia Axial cerebellar ataxia,dysphonia	CSF: albuminocytological dissociation proten:148.9, leucocytes 1 Electroneuromyography: moderate primarily motor and sensory demyelinating polyneuropathy with proximal motor block		IVIG	Full Recovery
63	Chen <i>et al.</i> ^[70]	USA	70 year female	Pfizer 2nd dose	14 days	Hypertension Breast cancer in remission	progressive gait imbalance, diplopia and headache partial global ophthalmoparesis, bilateral ptosis, slowed saccades in restricted range, minimally responsive pupils with a degree of light near dissociation	CSF: albuminocytological dissociation NCS:acute left facial neuropathy, reduced fibular and tibial motor amplitudes, and a mildly prolonged ulnar F-wave relative to the F estimate		IVIG	Partial recovery
64	Hussein <i>et al.</i> ^[71]	Saudi Arabia	46-year-old woman	first dose of the Pfizer vaccine	5 days	diabetes, hypertension, hypothyroidism, and migraine	Numbness and tingling in both feet and ankles Ascending weakness of the lower extremities	Serum GQ1b IgG antibodies titres : 1:12 800 Cerebrospinal fluid analysis showed one white blood cell with a high protein concentration of 1.39 g/l indicating albuminocytological dissociation	Intravenous immunoglobulin and plasma exchange		Gradual improvement after plasma exchange.
65	Rachna <i>et al.</i> ^[72]	India	13-year-old female	first dose of recombinant protein subunit COVID-19 vaccine (<i>Corbevax</i>)	3 days	none	bilateral upper limb, lower limb and truncal weakness	Nerve conduction study of the four extremities reported acute demyelinating sensory and motor polyneuropathy with prolonged F-wave latencies.	plasmapheresis therapy		patient improved clinically
66	Bimarsh <i>et al.</i> ^[73]	Nepal	78-year-old male	second dose of the AstraZeneca vaccine	4 days	none	bilateral weakness of the lower limbs	Nerve conduction studies revealed acute inflammatory demyelinating polyneuropathy	intravenous immunoglobulins along with physiotherapy		patient improved clinically
67	Kenny <i>et al.</i> ^[74]	USA	59-year-old male	2nd dose of Pfizer	60 days	none	lower back pain numbness and tingling of the bilateral lower extremities urinary retention constipation	MRI of his cervical spine demonstrated signs of osteoarthritis with the spinal cord intact. Nerve conduction and electromyography studies revealed demyelination and dysfunctions in the engagement of distal muscles below the knee	intravenous immunoglobulin (IVIG)		Partial recovery.
68	Hyunj Lee <i>et al.</i> ^[75]	Taiwan	Case 1:43- year-old woman Case 2:54- year-old man	Case 1:first dose of Vaxzevria Case 2:first dose of Vaxzevria	Case 1:9 days Case 2:12 days	none	Case 1: progressive numbness in entire body dyspnoea and diplopia Case 2: progressive numbness in entire body	Case 1: nerve conduction velocity (NCV) test suggested lumbosacral polyradiculopathy. Case 2: NCV test findings were compatible with demyelinating polyradiculoneuropathy and superimposed bilateral trigeminal neuropathy.	Case 1:fresh frozen plasma exchange Case 2:Human immunoglobulin treatment		Case 1:Partial recovery; she could later walk with a cane Case 2:Gradual improvement
69	Laura Donaldson <i>et al.</i> ^[76]	Canada	45-year-old man	first dose AstraZeneca SARS-CoV-2	12 days	Crohn's disease	bilateral facial weakness bilateral ascending paraesthesia to the knee as well as the left upper limb diplopia	Lumbar puncture showed highly elevated protein (2.0 g/l) with white blood cell count of 14. EMG findings were consistent with demyelinating polyradiculopathy.	Intravenous Immunoglobulin (IVIG)		he had regained most of the strength in his limbs. Facial paralysis and ocular motility showed only minimal improvement.
70	Lanka Wijekoon <i>et al.</i> ^[77]	Sri Lanka	41-year-old male	first dose of BBIBP-CorV	18 days	type 2 diabetes	numb legs and arms pain in his upper back bilateral facial weakness	Cerebral-spinal fluid (CSF) analysis revealed a cell protein dissociation, with elevated CSF protein (62.2 g/dl) nerve conduction study (NCS) revealed reduced motor nerve conduction velocities in bilateral peroneal nerves and prolonged distal motor latencies in the bilateral peroneal and right tibial nerve. Serum sodium was low at 123 mmol/l	Intravenous immunoglobulin (IVIG)		Complete recovery

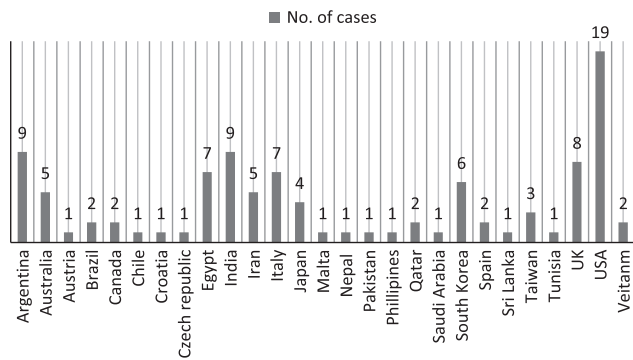


Figure 2. Reports of Guillain-Barré syndrome from countries following COVID-19 vaccination.

range (IQR) years. Elderly people seem to be affected more may be due to gradual loss of nerve myelination with increased age. 47 people had pre-existing chronic illnesses and the remaining 57 did not have any illness before the development of GBS. Although chronic illness reduces the immunity of a person and is prone to another disease; here it didn't show such importance.

Also, there is a male predominance of 62% (64/103) compared to a female of 36% (39/103). The median time between receiving the COVID-19 vaccine and the onset of symptoms was noted to be 13.08 ± 11 IQR days.

Discussion

The epidemiological relationship between COVID-19 vaccination and GBS is becoming clearer. The most common symptom of GBS, an autoimmune disorder of the peripheral nerve system, is rapidly progressing ascending paralysis^[46]. This study will be crucial for promoting early detection and treatment because GBS complications can result in serious morbidity and death^[78].

We reviewed the onset of symptoms, clinical features, previous comorbidities, investigations, and outcomes of 103 patients aged between 13 and 87 with the COVID-19-associated GBS spectrum. Our study demonstrated a correlation between the COVID-19 vaccine and GBS; patients reported ascending progressive paraesthesia of distal lower and upper limbs following the administration of various COVID-19 vaccines.

Most instances of the condition occurred following the administration of vector-based vaccines, with the AstraZeneca vaccine being the most frequently cited. The most frequent symptom among those who received the AstraZeneca vaccine was a motor deficit. The time frame between vaccination and the appearance of neurological symptoms varied greatly, ranging from 1 to 60 days with a median of 13 ± 11 IQR days. The majority of symptoms appeared after the first dose and only 23 cases were from the second dose and 2 cases after the third dose of vaccination. The complications varied in severity, from mild symptoms to severe and potentially life-threatening conditions. In eight cases, the patients presented with sudden onset back pain before weakness in the lower limbs. In another issue, the clinical manifestations of GBS were facial diplegia which may be associated with other systemic diseases like Lyme disease, sarcoidosis, and diabetes^[79].

The Pfizer vaccine was found to be second in ranking for its association with GBS related to COVID-19 vaccines, even though no neurological side effects were reported in the phase III clinical

trial^[6]. A noteworthy observation was that the majority of GBS cases happened after receiving the second dose of the Pfizer vaccine, which was different from other vaccines.

It has been previously reported, albeit rarely, that the COVID-19 vaccine may be associated with autoimmune diseases affecting the central nervous system^[80]. There are various theories about how this association may occur, such as similarities between vaccine components and myelin or axon components that trigger immune responses, exposure to vaccine viruses or vaccine-related products leading to the degradation of the axon or myelin membranes, and genetic predisposition^[81]. Although the presence of a temporal link between vaccination and GBS suggests a possible causal relationship, it is not strong enough evidence on its own. Furthermore, the wide range of time intervals between vaccination and the onset of GBS symptoms, ranging from 1 to 60 days, suggests that the relationship between the two is complex and involves multiple factors. Only 3 patients had previous autoimmune conditions like rheumatic arthritis for which the person was taking medication before the development of GBS.

Our findings align with previous reports that indicate a possible association between COVID-19 vaccines and GBS with unique clinical characteristics, such as severe quadriplegia, frequent bilateral facial palsy, or atypical incomplete forms. Ongoing monitoring and additional research using rigorous methodologies are necessary to fully understand the significance of this association. Moreover, in patients with other autoimmune diseases, we were unable to determine if GBS was due to an autoimmune disease or the vaccination itself. The analysis is limited in comparing the clinical features of GBS after adenoviral vector vaccines with other vaccines. Third, the study included cases of patients after the administration of primary vaccine and the outcomes may not apply to booster shots.

Future perspectives and recommendations

In the future, we can collect the blood samples of the patient and monitor their immune response to the particular vaccine by using laboratory techniques like enzyme-linked immunosorbent assay (ELISA), hemagglutination test, polymerase chain reaction (PCR), etc. before going through vaccination. Patients with prior infections like CMV, EBV, Zika virus, or other infections should avoid administering the vaccine before recovery. Furthermore, researchers may explore the potential differences in GBS incidence and characteristics between primary vaccine administration and booster shots. Moving forward, the comparison of the clinical features of GBS across various vaccine types may be studied.

Conclusion

The medical sciences have been put to the test by the COVID-19 epidemic. Our attempts to prevent and treat this disease have been closely correlated with our understanding of the disease and its aetiology. The creation and use of these vaccinations in just two years is evidence of how quickly evidence-based medicine is developing and integrating with the healthcare system. Medical practitioners should be aware of any neurological side effects after receiving the SARS-CoV-2 vaccine, even if they are rare. A high level of awareness and quick action are required in these situations. To demonstrate a clear causal relationship between

GBS with the presently advised immunizations, more rigorous research is necessary. Until then, the advantages of COVID-19 protection for both persons and society outweigh the apprehensive danger of these unfavourable outcomes by a wide margin.

Ethical approval

Ethical approval was not required for this review.

Consent

Informed consent was not required for this review.

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No funding was received for this study.

Conflicts of interest disclosure

There are no conflicts of interest.

Research registration unique identifying number (UIN)

Not applicable.

Guarantor

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Data availability

Datasets generated during and/or analyzed during the current study are publicly available, available upon reasonable request.

Provenance and peer review

Non commissioned, externally peer-reviewed.

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