

Guillain Barre Syndrome as a Complication of COVID-19: A Systematic Review

Mohammad Aladawi, Mohamed Elfil , Baha Abu-Esheh, Deaa Abu Jazar, Ahmad Armouti, Ahmed Bayoumi, Ezequiel Piccione

ABSTRACT: Background: In January 2020, the first case of Guillain Barre syndrome (GBS) due to COVID-19 was documented in China. GBS is known to be postinfectious following several types of infections. Although causality can only be proven through large epidemiological studies, we intended to study this association by a thorough review of the literature. **Methods:** We searched PubMed, EMBASE, and Google scholar and included all papers with English or Spanish full text and original data of patients with GBS and recent COVID infection. Variables of interest were demographics, diagnostic investigations, and the latency between arboviral and neurological symptoms. Further variables were pooled to identify GBS clinical and electrophysiological variants, used treatments, and outcomes. The certainty of GBS diagnosis was verified using Brighton criteria. **Results:** We identified a total of 109 GBS cases. Ninety-nine cases had confirmed COVID-19 infection with an average age of 56.07 years. The average latency period between the arboviral symptoms and neurologic manifestations for confirmed COVID-19 cases was 12.2 d. The predominant GBS clinical and electromyography variants were the classical sensorimotor GBS and acute demyelinating polyneuropathy respectively. Forty cases required intensive care, 33 cases required mechanical ventilation, and 6 cases were complicated by death. **Conclusions:** Studies on COVID-19-related GBS commonly reported sensorimotor demyelinating GBS with frequent facial palsy. The time between the onset of infectious and neurological symptoms suggests a postinfectious mechanism. Early diagnosis of GBS in COVID-19 patients is important as it might be associated with a severe disease course requiring intensive care and mechanical ventilation.

RÉSUMÉ : Apparition du syndrome de Guillain-Barré à la suite d'une infection à la COVID-19 : une étude systématique. **Contexte :** C'est en janvier 2020 qu'on a documenté en Chine le premier cas de syndrome de Guillain-Barré (SGB) attribuable à une infection à la COVID-19. Le SGB est connu pour être post-infectieux et pour apparaître à la suite de plusieurs types d'infections. Bien qu'une réelle causalité puisse seulement être établie par l'entremise de vastes études épidémiologiques, nous nous sommes penchés sur cette association au moyen d'un examen approfondi de la littérature sur le sujet. **Méthodes :** Pour ce faire, nous avons interrogé les bases de données suivantes : PubMed, EMBASE et Google Scholar. À cet égard, nous avons inclus dans notre étude tous les articles complets rédigés en anglais ou en espagnol contenant des données originales à propos de patients atteints du SGB et ayant été infectés récemment à la COVID-19. Les variables qui nous ont le plus intéressés portaient sur leurs caractéristiques démographiques, sur les examens diagnostics qui avaient été effectués et sur la période de latence entre les symptômes dits « arboviraux » et ceux de nature neurologique. Davantage de variables ont été par la suite regroupées pour identifier les variantes cliniques et électro-physiologiques du SGB, les traitements utilisés et l'évolution de l'état de santé de ces patients. On a aussi pu valider la certitude d'un diagnostic de SGB à l'aide des critères de Brighton. **Résultats :** Au total, ce sont 109 cas de SGB que nous avons identifiés. De ce nombre, 99 étaient liés à des cas confirmés d'infection à la COVID-19, l'âge moyen des patients étant de 56,07 ans. La période moyenne de latence entre les premiers symptômes dits « arboviraux » et des manifestations neurologiques pour des cas confirmés d'infection à la COVID-19 a été de 12,2 jours. À noter que les variantes cliniques et électromyographiques prédominantes de la SGB ont relevé respectivement de la forme classique sensorimotrice et de la polyradiculonévrite inflammatoire démyélinisante associées à ce syndrome. Enfin, soulignons que 40 cas ont nécessité le recours aux soins intensifs, que 33 d'entre eux ont entraîné l'utilisation de la ventilation artificielle tandis que 6 autres se sont soldés par un décès. **Conclusion :** Il n'est pas rare que des études portant sur les liens entre le SGB et l'infection à la COVID-19 aient signalé un syndrome de type sensorimoteur démyélinisant avec de fréquentes manifestations de paralysie faciale. La période qui sépare une infection à la COVID-19 de l'apparition de symptômes neurologiques suggère ainsi un mécanisme post-infectieux. Un diagnostic précoce de SGB chez des patients infectés à la COVID-19 est donc important car un tel syndrome peut être associé à une évolution préoccupante de leur état de santé nécessitant des soins intensifs et une ventilation artificielle.

Keywords: Guillain Barre syndrome, GBS, Miller Fisher syndrome, MFS, SARS-CoV2, COVID-19

doi:[10.1017/cjn.2021.102](https://doi.org/10.1017/cjn.2021.102)

Can J Neurol Sci. 2021; 00: 1–11

From the Department of Neurological Sciences, University of Nebraska Medical Center, Omaha, Nebraska, USA (MA, ME, EP); Department of Neurology, Mercy Hospital, Oklahoma City, Oklahoma, USA (BA-E); Department of Neurology, University of Texas Medical Branch – Galveston, Galveston, Texas, USA (DAJ); Department of Neurology, University of South Florida Morsani College of Medicine, Tampa, Florida, USA (AA); and Department of Neurology, Yale University, New Haven, Connecticut, USA (AB)

RECEIVED DECEMBER 7, 2020. FINAL REVISIONS SUBMITTED APRIL 4, 2021. DATE OF ACCEPTANCE APRIL 28, 2021.

Correspondence to: Mohammad Aladawi, MD, 988435 Nebraska Medical Center, Omaha, NE 68198-8435, USA. Email: Mohammad.aladawi@unmc.edu

INTRODUCTION

In December 2019, the COVID-19 epidemic emerged in Wuhan, China, causing global alterations not only in the field of healthcare, but also in all walks of life. The viral agent responsible for this clinical illness is described as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It was documented that SARS-CoV-2 is associated with neurologic manifestations, including headache, dizziness, hypogeusia, and hyposmia.¹ Beside hypogeusia and hyposmia, there has been increased reporting of distinct peripheral nervous system (PNS) diseases in COVID-19 patients.

Guillain Barre syndrome (GBS) is an inflammatory disease of the PNS, characterized by rapidly progressive, symmetrical, and typically ascending weakness of the limbs with reduced or absent deep tendon reflexes, and upper and lower extremities non-length-dependent paresthesia and sensory symptoms at onset. Cranial nerves involvement can also be present in GBS patients, with facial and bulbar muscles often being affected.² GBS can be classified into different distinct clinical variants including classical sensorimotor, paraparetic, pure motor, pure sensory, Miller Fisher syndrome (MFS), pharyngeal-cervical-brachial variant (PCB), bilateral facial palsy with paranesthesia, and Bickerstaff brainstem encephalitis.³ Another classification of GBS based on the electromyography (EMG) findings has also been described, with acute inflammatory demyelinating polyneuropathy (AIDP) being the most common variant. Other EMG variants of GBS according to this classification include acute motor axonal neuropathy (AMAN) and acute motor and sensory axonal neuropathy (AMSAN).⁴

GBS has been linked to a variety of causative pathogens; campylobacter jejuni (*C. jejuni*), cytomegalovirus (CMV), hepatitis E virus, mycoplasma pneumoniae, Epstein-Barr virus (EBV), and Zika virus.⁵⁻⁸ The emergence of Zika virus epidemic in 2016 was noticeably linked to increased incidence of GBS.⁹ GBS has also been linked to Middle East respiratory syndrome coronavirus (MERS-CoV) which is genetically similar to SARS-CoV-2 and was responsible for the outbreak of Middle East Respiratory Syndrome in 2013.¹⁰ In January 2020, the first case of GBS due to SARS-CoV-2 infection was documented in China.¹¹ In this article, we are reviewing all the published cases of GBS that have been linked to SARS-CoV-2, to study their clinical presentations, the average latency period till the onset of GBS symptoms, the global distribution of these cases, and the findings of the ancillary GBS investigations.

METHODS

We searched PubMed, EMBASE, and Google scholar and included all papers with full text available in English or Spanish and reporting original data of patients with GBS and recent COVID infection. This systematic literature review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Figure 1).¹² We used the following keywords on our search: GBS, MFS, COVID-19, SARS-CoV2, and neurological manifestations, and these databases were searched from August 26, 2020 and to February 7, 2021. Titles and abstracts were screened by two researchers (M. Aladawi and M. Elfil). The full texts of the selected papers were read in full by five researchers (M. Aladawi, B. Abu-Esheh, D. Abu Jazar, A. Armouti, and

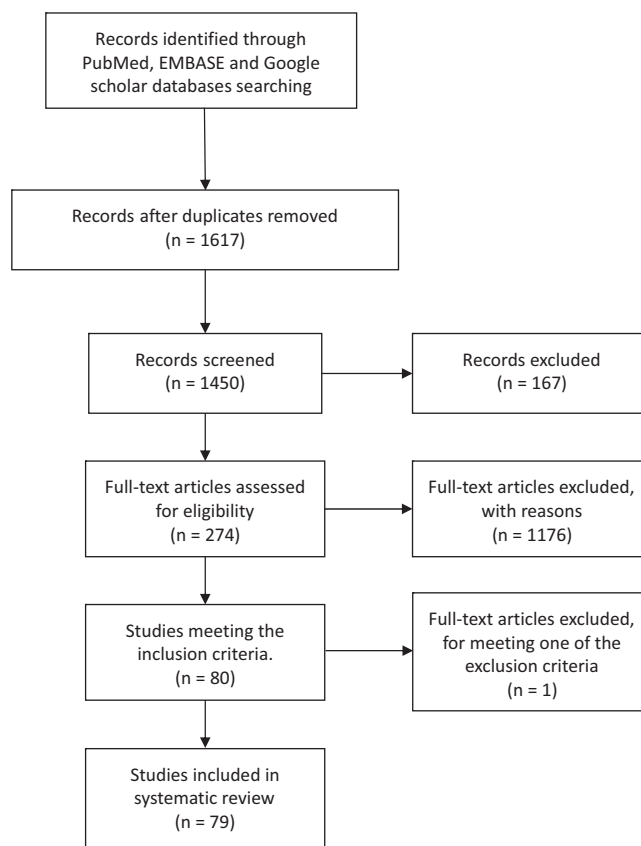


Figure 1: PRISMA figure showing the steps of literature search and paper selection for the systematic review.

A. Bayoumi), and their extracted data were then revised by M. Aladawi.

We included all papers, reports, or bulletins with the full text available in English or Spanish, reporting data of patients with GBS and a probable or confirmed recent COVID-19 diagnosis. Preidentified exclusion criteria were: (1) GBS with proven triggering infection other than SARS-CoV2 (e.g., *C. jejuni*), (2) presence of alternative diagnosis for weakness (e.g., critical illness neuropathy), and (3) latency period between COVID-19 infection and the onset of GBS symptoms of more than 6 weeks. Variables of interest were demographics, COVID-19 diagnostic investigations, latency between constitutional viral symptoms and neurological symptoms, presence of a negative SARS-Cov2 polymerase chain reaction (PCR) at the time of neurological manifestations (Table 1). Studied variables of cases with confirmed COVID-19 infection were pooled into another table to identify clinical characteristics (viral symptoms and neurological symptoms), GBS ancillary diagnostic investigations (cerebrospinal fluid [CSF] findings and testing for antiganglioside antibodies), the predominant clinical and electrophysiological variants of COVID-19-related GBS, received immunomodulatory therapy, disease progression, and clinical outcome (Table 2).

Cases were classified according to the reported diagnostic certainty levels for GBS and COVID-19 infection. To classify the diagnosis of GBS, we employed the Brighton Collaboration Criteria.¹³ The diagnostic certainty of COVID-19 infection was classified as confirmed and suspected. As confirmed cases were

Table 1: Demographics, diagnostic confirmation of COVID-19, latency duration of neurologic symptoms, and PCR testing at the time of neurological manifestations of both suspected and confirmed cases of COVID-19

Author	Country	COVID diagnostics at time of arboviral symptoms			Duration between arboviral and neurological symptoms	Negative repeat PCR at time of neurological symptoms	
		PCR	Serology	Chest radiographic features		Nasopharyngeal swab	Cerebrospinal fluid
Confirmed cases							
Diez-Porras ¹⁴	Spain	Yes	No	No	5 d	No	NA
Granger ¹⁵	Italy	Yes	No	No	22 d	No	NA
Hirayama ¹⁶	Japan	Yes	No	Yes	20 d	Yes	NA
Liberatore ¹⁷	Italy	Yes	No	Yes	23 d	No	NA
Nanda ¹⁸	India	Yes	No	No	10 d	No	NA
Nanda ¹⁸	India	Yes	No	No	6 d	No	NA
Nanda ¹⁸	India	Yes	No	No	7 d	No	NA
Nanda ¹⁸	India	Yes	No	Yes	10 d	No	NA
Atakla ¹⁹	Guinea	Yes	No	Yes	14 d	No	NA
Rajdev ²⁰	USA	Yes	No	Yes	18 d	No	NA
Senel ²¹	Germany	Yes	Yes	No	NA	Yes	Yes
Tard ²²	France	Yes	No	Yes	10 d	No	NA
Chan ²³	USA	Yes	No	No	18 d	No	Yes
Chan ²³	USA	Yes	No	No	23 d	Yes	Yes
Sedaghat ²⁴	Iran	Yes	No	Yes	11 d	No	NA
Ebrahimzadeh ²⁵	Iran	Yes	No	Yes	18 d	No	NA
Ebrahimzadeh ²⁵	Iran	Yes	No	No	10 d	No	NA
Arnaud ²⁶	France	Yes	No	Yes	22 d	No	Yes
Paybast ²⁷	Iran	Yes	No	No	16 d	No	NA
Paybast ²⁷	Iran	Yes	No	No	19 d	No	NA
Coen ²⁸	Switzerland	Yes	Yes	No	6 d	No	Yes
Dinkin ²⁹	USA	Yes	No	No	4 d	No	NA
Dinkin ²⁹	USA	Yes	No	Yes	NA	No	NA
Manganotti ³⁰	Italy	Yes	No	No	18 d	No	Yes
Manganotti ³⁰	Italy	Yes	No	No	30 d	No	Yes
Manganotti ³⁰	Italy	Yes	No	No	14 d	No	Yes
Manganotti ³⁰	Italy	Yes	No	No	33 d	No	NA
Manganotti ³⁰	Italy	Yes	No	No	22 d	No	Yes
Fernández-Domínguez ³¹	Spain	Yes	No	No	15 d	Yes	Yes
Hutchins ³²	USA	Yes	No	Yes	16 d	No	NA
Kilinc ³³	Netherlands	No	Yes	No	28 d	No	Yes
Naddaf ³⁴	USA	No	Yes	Yes	17 d	Yes	Yes
Abrams ³⁵	USA	Yes	No	Yes	10 d	No	Yes
Gigli ³⁶	Italy	No	Yes	Yes	17 d	Yes	NA
Bracaglia ³⁷	Italy	Yes	No	No	0 d	No	NA
Sidig ³⁸	Sudan	Yes	No	Yes	5 d	No	NA
Lascano ³⁹	Switzerland	Yes	Yes	No	15 d	No	Yes
Lascano ³⁹	Switzerland	Yes	No	No	7 d	No	NA
Lascano ³⁹	Switzerland	Yes	No	No	22 d	No	Yes
Camdessanche ⁴⁰	France	Yes	No	Yes	11 d	No	NA
Abolmaali ⁴¹	Iran	Yes	No	Yes	0 d	No	NA

Table 1: (Continued)

Author	Country	COVID diagnostics at time of arboviral symptoms			Duration between arboviral and neurological symptoms	Negative repeat PCR at time of neurological symptoms	
		PCR	Serology	Chest radiographic features		Nasopharyngeal swab	Cerebrospinal fluid
Abolmaali ⁴¹	Iran	Yes	No	Yes	10 d	No	NA
Abolmaali ⁴¹	Iran	Yes	No	Yes	9 d	No	NA
L.Chan ⁴²	Canada	Yes	No	Yes	0 d	No	Yes
Sancho-Saldaña ⁴³	Spain	Yes	No	No	15 d	No	Yes
Assini ⁴⁴	Italy	Yes	No	No	20 d	No	Yes
Assini ⁴⁴	Italy	Yes	No	Yes	23 d	No	Yes
Frank ⁴⁵	Brazil	Yes	Yes	No	5 d	No	Yes
Caamaño ⁴⁶	Spain	Yes	No	Yes	10 d	No	Yes
Oguz-Akarsu ⁴⁷	Turkey	Yes	No	Yes	0 d	No	Yes
Toscano ⁴⁸	Italy	Yes	No	Yes	7 d	No	Yes
Toscano ⁴⁸	Italy	Yes	No	No	10 d	No	Yes
Toscano ⁴⁸	Italy	Yes	No	Yes	10 d	No	Yes
Toscano ⁴⁸	Italy	Yes	No	No	5 d	No	Yes
Toscano ⁴⁸	Italy	No	Yes	Yes	7 d	Yes	Yes
Reyes-Bueno ⁴⁹	Spain	No	Yes	No	15 d	Yes	NA
Bigaut ⁵⁰	France	Yes	No	Yes	21 d	No	Yes
Bigaut ⁵⁰	France	Yes	No	Yes	10 d	No	Yes
Padroni ⁵¹	Italy	Yes	No	No	24 d	Yes	NA
Tiet ⁵²	UK	Yes	No	No	14 d	No	Yes
Ameer ⁵³	UK	Yes	No	No	4 d before arboviral symptoms	No	Yes
Wada ⁵⁴	China	Yes	No	Yes	17 d	No	NA
Ray ⁵⁵	UK	Yes	No	No	0 d	No	NA
Guijarro-Castro ⁵⁶	Spain	Yes	No	Yes	21 d	No	NA
Gutiérrez-Ortiz ⁵⁷	Spain	Yes	No	No	5 d	No	Yes
Gutiérrez-Ortiz ⁵⁷	Spain	Yes	No	No	3 d	No	Yes
Agosti ⁵⁸	Italy	Yes	No	Yes	5 d	No	NA
Zhao ¹¹	China	Yes	No	Yes	8 d before arboviral symptoms	No	NA
Khalifa ⁵⁹	KSA	Yes	No	Yes	20 d	No	NA
Farzi ⁶⁰	Iran	Yes	No	Yes	10 d	No	NA
Alberti ⁶¹	Italy	Yes	No	Yes	7 d	No	Yes
Sandeep ⁶²	US	Yes	No	Yes	14 d	Yes	NA
Korem ⁶³	USA	Yes	No	No	14 d	No	NA
Civardi ⁶⁴	Italy	Yes	No	No	10 d	No	Yes
Virani ⁶⁵	USA	Yes	No	No	10 d	No	NA
Khaja ⁶⁶	USA	Yes	No	No	0 d	No	Yes
Lampe ⁶⁷	Germany	Yes	No	No	2 d	No	NA
Ottaviani ⁶⁸	Italy	Yes	No	Yes	10 d	No	Yes
Scheidt ⁶⁹	Germany	Yes	No	No	3 weeks	Yes	NA
El Otmani ⁷⁰	France	Yes	No	Yes	13 d	No	Yes
Lantos ⁷¹	USA	Yes	No	No	4 d	No	NA
Riva ⁷²	Italy	No	Yes	Yes	20 d	Yes	Yes
Helbok ⁷³	Austria	No	Yes	Yes	14 d	Yes	Yes
Webb ⁷⁴	UK	Yes	No	No	7 d	No	Yes

Table 1: (Continued)

Author	Country	COVID diagnostics at time of arboviral symptoms			Duration between arboviral and neurological symptoms	Negative repeat PCR at time of neurological symptoms	
		PCR	Serology	Chest radiographic features		Nasopharyngeal swab	Cerebrospinal fluid
Pfefferkom ⁷⁵	Germany	Yes	No	Yes	14 d	No	Yes
Dufour ⁷⁶	USA	Yes	No	No	21 d	Yes	NA
Jones ⁷⁷	UK	Yes	No	No	22 d	No	NA
Ghosh ⁷⁸	India	Yes	No	No	0 d	No	NA
Mackenzie ⁷⁹	Columbia	Yes	No	No	0 d	No	NA
Mansour ⁸⁰	Morocco	Yes	No	Yes	12 d	No	Yes
Petrelli ⁸¹	Italy	Yes	No	No	15 d	No	NA
Yaqoob ⁸²	NA	Yes	No	Yes	12 d	No	NA
Bueso ⁸³	USA	Yes	No	Yes	22 d	No	NA
Manji ⁸⁴	Tanzania	Yes	No	No	7 d	No	NA
Su ⁸⁵	USA	Yes	No	Yes	6 d	No	Yes
Galán ⁸⁶	Spain	Yes	No	Yes	10 d	No	NA
Barrachina-Esteve ⁸⁷	Spain	Yes	No	Yes	0 d	No	Yes
Marta-Enguita ⁸⁸	Spain	Yes	No	Yes	8 d	No	NA
Gigli ⁸⁹	Italy	No	Yes	Yes	NA	Yes	Yes
Suspected cases							
Gigli ⁸⁹	Italy	No	No	Yes	NA	Yes	NA
Gigli ⁸⁹	Italy	No	No	No	NA	Yes	NA
Gigli ⁸⁹	Italy	No	No	No	NA	Yes	Yes
Gigli ⁸⁹	Italy	No	No	No	NA	Yes	Yes
Gigli ⁸⁹	Italy	No	No	No	NA	Yes	NA
Gigli ⁸⁹	Italy	No	No	No	NA	Yes	Yes
Gigli ⁸⁹	Italy	No	No	Yes	NA	Yes	NA
Manganotti ⁹⁰	Italy	No	No	No	16 d	No	NA
Gale ⁹¹	UK	No	No	Yes	NA	Yes	NA
García-Manzanedo ⁹²	Spain	No	No	Yes	21 d	No	NA

identified by the presence of positive PCR at the time of arboviral symptoms or the presence of positive SARS-CoV2 antibodies whether during arboviral or neurological presentation as in some cases GBS was the presenting manifestation.

RESULTS

We identified 1450 articles in the databases researched, of which 79 papers were included in our systematic review (66 case reports and 13 case series). The selected studies reported on a total of 109 GBS cases with a confirmed or a suspected COVID-19 infection. One case was excluded as it met one of the exclusion criteria; the latency between the onset of COVID-19 infection and the GBS onset of symptoms was 53 d (>6 weeks).⁹³

The applied investigations in confirming COVID-19 infection at the time of arboviral symptoms were COVID-19 PCR testing, detection of SARS-CoV2 antibodies, and suggestive features on chest radiography. Cases with either positive PCR or SARS-CoV2 antibodies were categorized as confirmed cases, whereas

patients diagnosed based on abnormal chest radiographs or clinical suspicion only were categorized as suspected cases. We have identified 99 cases of COVID-19 complicated by GBS that has been confirmed with either PCR testing or serology (Table 1). Table 1 also includes the latency period between arboviral symptoms and neurologic manifestations, the country of reported cases, and repeat COVID-19 PCR at the time of neurological symptoms either from nasopharyngeal, swabs, or in the CSF.

The global distribution of cases was as follows: 32 cases in Italy, 16 cases in the United States, 12 cases in Spain, 9 cases in Iran, 6 cases in France, 6 cases in the United Kingdom, 5 cases in India, 4 cases in Germany, 4 cases in Switzerland, 2 cases in China, 1 case in Guinea, 1 case in Austria, 1 case in Brazil, 1 case in Canada, 1 case in Columbia, 1 case in Japan, 1 case in Morocco, 1 case in Netherlands, 1 case in Sudan, 1 case in Tanzania, 1 case in Turkey, and 1 case in Saudi Arabia.

At the time of the patient's demonstrated neurologic signs and symptoms, repeat SARS-CoV2 PCR swab was negative in 23 cases. Reverse transcription PCR (RT-PCR) for SARS-CoV-2 in

Table 2: Demographics, clinical features, and GBS classification in patients with confirmed cases of COVID-19

Demographics	
Mean age (years)	56.07
Males	71
Females	28
Average latency of neurological symptoms (days)	12.2 (± 7.5)
Arboviral symptoms	
Fever	67/95
Sore throat	12/95
Anosmia/dysgeusia	25/95
Dry cough	60/95
Rash	2/95
Arthralgia/myalgia	18/95
Chest pain	1/95
Shortness of breath	27/95
Headache	10/95
Gastrointestinal symptoms	17/95
Neurological signs and symptoms	
Dysphagia	18/99
Dysarthria	11/99
Sensory symptoms	65/99
Diplopia	11/99
Facial palsy	42/99
Bulbar palsy	12/99
Ocular palsy	11/99
Tetraparesis	64/99
Paraparesis	81/99
Sensory deficits	41/99
Areflexia or hyporeflexia	93/99
Ataxia	18/99
Respiratory dysfunction	30/99
Dysautonomia	20/99
GBS clinical variant	
Classical sensorimotor GBS	64/99
Paraparetic GBS	16/99
Miller Fisher syndrome	9/99
Pharyngeal-cervical-brachial GBS	2/99
Bilateral facial palsy with paranesthesia	3/99
Bickerstaff brainstem encephalitis	0/99
Pure motor GBS	0/99
Pure sensory GBS	1/99
Unclassified	4/99
CSF analysis	
Albuminocytologic dissociation	74/86
Oligoclonal bands	2/86
Normal	10/86

Table 2: (Continued)

Demographics	
Neuroimaging findings	
Cranial nerve enhancement	9/61
Spinal nerve root enhancement	10/61
Unremarkable	44/61
Antiganglioside antibodies	
Anti-GM1	3/50
Anti-GM2	2/50
Anti-GD1a	3/50
Anti-GD1b	3/50
Anti-GD3	1/50
Anti-GQ1b	1/50
Anti-GT1b	1/50
Anti-Gal-C	1/50
Negative antiganglioside Ab	43/50
GBS EMG variant	
AIDP	59/77
AMAN	8/77
AMSAN	10/77
Immunomodulatory treatment	
IVIG	72/98
PLEX	10/98
IVIG and PLEX	7/98
No treatment	8/98
Clinical outcome	
ICU admission	40/99
Mechanical ventilation	33/99
Death	6/99
Brighton criteria	
Level 1–3	84/99
Level 4	9/99
Other variants	6/99

AIDP= acute inflammatory demyelinating polyneuropathy; AMAN=acute motor axonal neuropathy; AMSAN=acute motor and sensory axonal neuropathy; CSF=cerebrospinal fluid; GBS=Guillain Barre syndrome; ICU=intensive care unit; IVIG=intravenous immunoglobulin; PLEX=plasmapheresis.

the CSF was performed in 50 cases in which it was negative. The average latency period between the arboviral symptoms and neurologic manifestations for confirmed COVID-19 cases was 12.2 d (Table 2). There were two cases where neurological manifestations have preceded arboviral symptoms, and nine cases where patients only presented with neurologic deficits with no symptoms of COVID-19, but they had positive COVID-19 testing.

Table 2 shows the pooled data of GBS cases that have been preceded by a confirmed COVID-19 infection. There was a total of 99 cases (71 males and 28 females), the average age was 56.07 years. The most common arboviral symptoms prior to GBS were fever, dry cough, dyspnea, and gastrointestinal symptoms. There

were four cases which did not report patient's arboviral symptoms prior to GBS manifestations. The most commonly reported neurological signs and symptoms were ascending motor weakness (tetraparesis and paraparesis), diminished deep tendon reflexes, sensory disturbances (paresthesia), sensory loss, and facial palsy. GBS was complicated by respiratory failure in 30 cases and dysautonomia in 20 cases.

Clinical GBS variants have been identified in these cases. The most commonly reported GBS variants were classical sensorimotor GBS (64 cases), followed by paraparetic GBS (16 cases), MFS (9 cases), facial diplegia with paresthesia (3 cases), pharyngeal-cervical-brachial GBS (2 cases), and pure sensory GBS (1 case). There were four cases that could not be classified into any of the GBS clinical variants. CSF analysis was performed in 86 cases. Seventy-four cases have shown albuminocytologic dissociation (normal CSF protein <45 mg/dl⁹⁴), 2 cases have shown oligoclonal band, and 10 cases had no abnormalities in the CSF analysis. Antiganglioside antibodies were investigated in 50 cases. The majority of cases had negative antiganglioside antibodies (43 cases). Each of anti-GM1, anti-GD1a, and anti-GD1b were positive in three cases; anti-GM2 was positive in two cases; and each of anti-GD3, anti-GQ1b, anti-GT1b, and anti-Gal-C were positive in one case.

Electromyography (EMG) was performed in 77 cases. The predominant EMG variant of GBS was AIDP (59 cases), followed by AMSAN (10 cases), and AMAN (8 cases). Eighty-nine reports confirmed the use of immunomodulatory treatment for GBS. Seventy-two cases received intravenous immunoglobulin (IVIG) therapy, 10 cases were treated with plasmapheresis (PLEX), and 7 cases were treated with both IVIG and PLEX. In terms of disease progression and the clinical outcomes, 40 cases required admission to the intensive care unit (ICU), 33 cases required mechanical ventilation, and 6 cases were complicated by death.

Brighton criteria were applied to improve the diagnostic certainty for the cases; valid symptomatology included bilateral and flaccid weakness of limbs at the time of presentation, decreased deep tendon reflexes in affected limbs, the presence of a monophasic course of neurologic symptoms, CSF cell count <50/ μ l, elevated CSF protein, EMG findings consistent with one of the subtypes of GBS, and the absence of alternative diagnosis. Accordingly, cases were classified from level 1–4 of diagnostic certainty.¹³ Cases with MFS where the complete triad of ophthalmoplegia, ataxia, and areflexia was not present were classified as level 4.⁹⁵ Cases with other variants such as facial diplegia with paresthesia, PCB variant, and pure sensory GBS has been excluded. Accordingly, 51 cases have fulfilled level 1 of diagnostic certainty, 26 cases have fulfilled level 2, 7 cases have fulfilled level 3, and 9 cases fulfilled level 4. We have concluded that the reported cases have a high-diagnostic certainty of GBS as most of the cases have been classified into level 1–3 of Brighton criteria.

DISCUSSION

Our systematic review shows that the published literature on COVID-19-related GBS commonly report a classic sensorimotor variant of GBS with often facial palsy and a demyelinating electrophysiological subtype. The disease course is frequently severe with high rates of respiratory dysfunction and ICU admission.⁹⁶ The time elapsed between infection and neurologic manifestations, and a negative PCR in spinal fluid might suggest

that there is a postinfectious mechanism implicated in the etiology of COVID-19-related GBS. However, these results should be interpreted with caution as the cases included in this systematic review varied widely in diagnostic ascertainment and reporting of different variables. Moreover, the reported cases were limited to certain geographical areas, which might provide a source of bias.

The constellation of sensorimotor signs with facial palsy, respiratory insufficiency, and a demyelinating electrophysiological subtype has been described in GBS patients with other viral infections such as CMV and Zika virus, which might indicate that this clinical and electrophysiological variant of GBS is related to viral infections in general.^{8,97} On the other hand, *C. jejuni* is typically associated with pure motor and axonal type of GBS.⁹⁸ Although GBS is generally more common in men as compared with women,⁹⁹ in our systematic review, we have found that the male to female ratio was 2.5:1 which is significantly higher than what is usually reported.¹⁰⁰ This suggests that men might be more prone to COVID-19-related GBS.

In our review, the most common arboviral symptoms were fever and dry cough, which is typical in COVID-19 infection.¹⁰¹ We could not identify a specific arboviral symptom that could be typically preceding the development of GBS. However, we have identified two cases in which GBS manifestations preceded COVID-19 arboviral symptoms, and nine cases that did not present with arboviral symptoms initially. This chronology of GBS preceding the arboviral symptoms has not been previously reported with GBS related to other viral agents. In addition, the asymptomatic infection of COVID-19 might limit the ability to accurately determine the latency period between viral symptoms and the GBS presentation.

The mean duration between the onset of COVID-19 infectious symptoms and GBS presentation was 2 weeks, which is similar to other infections preceding GBS.¹⁰² The latency between COVID-19 infection and GBS was more than a week for most cases, but it should be taken into consideration that COVID-19 can initially be asymptomatic which makes the latency duration arguably longer than reported. This suggests a postinfectious immunopathogenesis rather than direct neuronal damage or a parainfectious mechanism. The fact that COVID-19 PCR of the CSF was not positive in a single report, the negativity of repeat nasopharyngeal PCR at the time of symptoms in almost one-third of the cases, and the absence of elevated white blood cell count in the CSF in majority of cases, further argues against the assumption of COVID-19 infection being directly responsible for the GBS development in this proportion of patients.

Despite the fact that previous epidemiological studies have suggested that COVID-19 might not be associated with GBS,¹⁰³ the chronology of publication of the COVID-19-related GBS cases followed the same pattern of the global spread of COVID-19, as the first cases report was from China followed by Italy, Iran, and USA indicates a positive association.^{11,24,48,65} GBS has been historically related to various pathogens including *C. jejuni*, *M. pneumoniae*, EBV, CMV, Hepatitis E virus, and Zika virus.^{5–9} However, in certain pathogens such as Hepatitis E virus, this association has not been established globally, as it was only reported in Netherlands and Bangladesh.¹⁰⁴ Therefore, immunogenicity of COVID-19 in the development of GBS should consider the variations between different populations,^{105–108} as epidemiologic studies involving certain populations might introduce bias in reporting results.

Interestingly, almost half of the cases were tested for the presence of antiganglioside antibodies in serum. There were only seven cases have tested positive for different antiganglioside antibodies. Historically, different antigangliosides have been linked to different variants of GBS, such as anti-GQ1b in MFS and anti-GD1a in PCB variant.^{109,110} Antiganglioside antibodies are considered to be biomarkers of axonal injury rather demyelination, as they directly target the neuronal membrane gangliosides.¹¹¹ Because most of the COVID-19-related GBS cases reported a demyelinating variant of GBS, it can be anticipated that the presence of antiganglioside antibodies would be low. Thus, the spectrum of immune cascade in COVID-19-related GBS should be expanded by studying other different antibodies affecting the myelin sheath, Schwann cell components, and the neuronal axolemma.^{112,113} One case was reported with positive NF-155 and NF-186 antibodies, which are structural proteins in the node of Ranvier.²²

The possible role of host immunogenetic background in the development of GBS and its variants has been related to human leukocyte antigen (HLA) polymorphism in different populations, this observation might explain the increased reporting of COVID-19 related GBS in the Italy, as one-third of the cases identified in our review were Italian.^{114,115} The role of HLA polymorphism in COVID-19 related GBS has been emphasized in one of the cases reported by Gigli et al.,³⁶ in which SARS-CoV2 antibodies were detected in the CSF. Interestingly, HLA analysis of the reported case showed several HLA alleles that are known to be associated with GBS, such as: HLA-A33,¹¹⁶ DRB1 * 03:01,¹¹⁷ and DQB1 * 05:01.¹¹⁸

With the emergence of COVID-19 pandemic, there have been increasing reports of various neurological complications in infected patients, which was well documented and studied in other coronaviruses.¹ Genomic analysis shows that SARS-CoV-2 is in the same beta-coronavirus (β CoV) clade as MERS-CoV and SARS-CoV, and shares a highly homological sequence with SARS-CoV.¹¹⁹ There has been clinical evidence of neuromuscular sequela in SARS CoV and MERS infection and the most documented neuromuscular syndromes related to these viruses are critical illness polyneuropathy and myopathy, which are hypothesized to occur in the context of severe inflammatory response syndrome (SIRS).¹²⁰ Cases of MERS-related GBS have been reported, yet GBS in these cases has been linked to the treatment received for MERS infection, such as interferon alpha2 and Lopinavir/ritonavir.¹⁰ In contrast to MERS, SARS-CoV2 is likely associated with GBS.

CONCLUSION

Based on this systematic review, most cases of COVID-19-related GBS are of the sensorimotor demyelinating subtype with frequent facial palsy. The latency between infection and onset of neurologic symptoms as well as the absence of viral genome detected by PCR suggest a postinfectious, rather than a direct infectious or para-infectious mechanism. Global reporting of COVID-19-related GBS cases, in addition to testing for different antibodies to different structural proteins and glycolipids in the peripheral nerves, would improve the understanding of the immunological cascade of COVID-19-related GBS. Finally, early diagnosis and identification of GBS in COVID-19 patients

is important as COVID-19-related GBS might be associated with a severe disease course that frequently requires ICU admission and mechanical ventilation.

DISCLOSURES

The authors declare no conflicts of interest.

STATEMENT OF AUTHORSHIP

MA: contributed with the conception and design of the study, acquisition, analysis, and interpretation of data, drafting, revising, and final approval of the article.

ME: contributed with the conception and design of the study, acquisition, analysis and interpretation of data, drafting, revising, and final approval of the article.

BA: contributed with acquisition and extraction of data and drafting the article.

DA: contributed with extraction of data and final approval of the article.

AA: contributed with extraction of data and final approval of the article.

AB: contributed with extraction of data and final approval of the article.

EP: contributed with conception and design of the study, drafting, revising and final approval of the article.

REFERENCES

- Mao L, Wang M, Chen S, et al. Neurological manifestations of hospitalized patients with COVID-19 in Wuhan, China: a retrospective case series study. SSRN Electron J. 2020. doi: [10.2139/ssrn.3544840](https://doi.org/10.2139/ssrn.3544840)
- Leonhard SE, Mandarakas MR, Gondim FAA, et al. Diagnosis and management of Guillain-Barré syndrome in ten steps. *Nat Rev Neurol.* 2019;15:671–83. doi: [10.1038/s41582-019-0250-9](https://doi.org/10.1038/s41582-019-0250-9)
- Hiew FL, Ramlan R, Viswanathan S, Puvanarajah S. Guillain-Barré syndrome, variants & forms fruste: reclassification with new criteria. *Clin Neurol Neurosurg.* 2017;158:114–18. doi: [10.1016/j.clineuro.2017.05.006](https://doi.org/10.1016/j.clineuro.2017.05.006)
- Dimachkie MM, Barohn RJ. Guillain-Barré syndrome and variants. *Neurol Clin.* 2013;31:491–510. doi: [10.1016/j.ncl.2013.01.005](https://doi.org/10.1016/j.ncl.2013.01.005)
- Nachamkin I, Allos BM, Ho T. Campylobacter species and Guillain-Barré syndrome. *Clin Microbiol Rev.* 1998;11:555–67.
- Meyer Sauter PM, Huizinga R, Tio-Gillen AP, et al. Mycoplasma pneumoniae triggering the Guillain-Barré syndrome: a case-control study. *Ann Neurol.* 2016;80:566–80.
- Masajtis-Zagajewska A, Muras K, Mochecka-Thoelke A, Kurnatowska I, Nowicki M. Guillain-Barre syndrome in the course of EBV infection after kidney transplantation—a case report. *Ann Transplant.* 2012;17:133–37.
- Orlikowski D, Porcher R, Sivadon-Tardy V, et al. Guillain-barré syndrome following primary cytomegalovirus infection: a prospective cohort study. *Clin Infect Dis.* 2011;52:837–44. doi: [10.1093/cid/cir074](https://doi.org/10.1093/cid/cir074)
- Counotte MJ, Meili KW, Taghavi K, Calvet G, Sejar J, Low N. Zika virus infection as a cause of congenital brain abnormalities and Guillain-Barré syndrome: a living systematic review [version 1; peer review: 2 approved]. *F1000Research.* 2019;8. doi: [10.12688/f1000research.19918.1](https://doi.org/10.12688/f1000research.19918.1)
- Kim JE, Heo JH, Kim HO, et al. Neurological complications during treatment of middle east respiratory syndrome. *J Clin Neurol.* 2017;13:227–33. doi: [10.3988/jcn.2017.13.3.227](https://doi.org/10.3988/jcn.2017.13.3.227)
- Zhao H, Shen D, Zhou H, Liu J, Chen S. Guillain-Barré syndrome associated with SARS-CoV-2 infection: causality or coincidence? *Lancet Neurol.* 2020;19:383–84. doi: [10.1016/S1474-4422\(20\)30109-5](https://doi.org/10.1016/S1474-4422(20)30109-5)

12. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 2009;6:e1000097. doi: [10.1371/journal.pmed.1000097](https://doi.org/10.1371/journal.pmed.1000097)
13. Fokke C, van den Berg B, Drenthen J, Walgaard C, van Doorn PA, Jacobs BC. Diagnosis of Guillain-Barré syndrome and validation of Brighton criteria. *Brain.* 2014;137:33–43. doi: [10.1093/brain/awt285](https://doi.org/10.1093/brain/awt285)
14. Diez-Porras L, Vergés E, Gil F, Vidal MJ, Massons J, Arboix A. Guillain-Barré-Strohl syndrome and COVID-19: case report and literature review. *Neuromuscul Disord.* 2020;30:859–861. doi: [10.1016/j.nmd.2020.08.354](https://doi.org/10.1016/j.nmd.2020.08.354)
15. Granger A, Omari M, Jakubowska-Sadowska K, Boffa M, Zakin E. SARS-CoV-2–Associated Guillain-Barré syndrome with good response to plasmapheresis. *J Clin Neuromuscul Dis.* 2020;22:58–9.
16. Hirayama T, Hongo Y, Kaida K, Kano O. Guillain-Barré syndrome after COVID-19 in Japan. *BMJ Case Rep.* 2020;13:1–4. doi: [10.1136/bcr-2020-239218](https://doi.org/10.1136/bcr-2020-239218)
17. Liberatore G, De Santis T, Doneddu PE, Gentile F, Albanese A, Nobile-Orazio E. Clinical reasoning: a case of COVID-19-associated pharyngeal-cervical-brachial variant of Guillain-Barré syndrome. *Neurology.* 2020;95:978–83. doi: [10.1212/WNL.00000000000010817](https://doi.org/10.1212/WNL.00000000000010817)
18. Nanda S, Handa R, Prasad A, et al. Covid-19 associated Guillain-Barré syndrome: contrasting tale of four patients from a tertiary care centre in India. *Am J Emerg Med.* 2021;39:125–28. doi: [10.1016/j.ajem.2020.09.029](https://doi.org/10.1016/j.ajem.2020.09.029)
19. Atakla HG, Noudohounsi MMUD, Sacca H, Tassiou NRA, Noudohounsi WC, Houinato DS. Acute Guillain-Barré polyradiculoneuritis indicative of covid-19 infection: a case report. *Pan Afr Med J.* 2020;35:1–6. doi: [10.11604/pamj.suppl.2020.35.150.25745](https://doi.org/10.11604/pamj.suppl.2020.35.150.25745)
20. Rajdev K, Victor N, Buckholtz ES, et al. A case of Guillain-Barré syndrome associated with COVID-19. *J Investig Med High Impact Case Rep.* 2020;8. doi: [10.1177/2324709620961198](https://doi.org/10.1177/2324709620961198)
21. Senel M, Abu-Rumeileh S, Michel D, et al. Miller-Fisher syndrome after COVID-19: neurochemical markers as an early sign of nervous system involvement. *Eur J Neurol.* 2020;27:2378–80. doi: [10.1111/ene.14473](https://doi.org/10.1111/ene.14473)
22. Tard C, Maurage CA, de Paula AM, et al. Anti-pan-neurofascin IgM in COVID-19-related Guillain-Barré syndrome: Evidence for a nodo-paranodopathy. *Neurophysiol Clin.* 2020;50:397–99. doi: [10.1016/j.neucli.2020.09.007](https://doi.org/10.1016/j.neucli.2020.09.007)
23. Chan M, Han SC, Kelly S, Tamimi M, Giglio B, Lewis A. A case series of Guillain-Barré Syndrome following Covid-19 infection in New York. *Neurol Clin Pract.* Published online 2020. doi: [10.1212/cpj.0000000000000880](https://doi.org/10.1212/cpj.0000000000000880)
24. Sedaghat Z, Karimi N. Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information. 2020;(January).
25. Ebrahimzadeh SA, Ghoreishi A, Rahimian N. Guillain-Barré Syndrome associated with the coronavirus disease 2019 (COVID-19). *Neurol Clin Pract.* 2020;2019. doi: [10.1212/cpj.0000000000000879](https://doi.org/10.1212/cpj.0000000000000879)
26. Amaud S, Budowski C, Ng Wing Tin S, Degos B. Post SARS-CoV-2 Guillain-Barré syndrome. *Clin Neurophysiol.* 2020;131:1652–54. doi: [10.1016/j.clinph.2020.05.003](https://doi.org/10.1016/j.clinph.2020.05.003)
27. Paybast S, Gorji R, Mavandadi S. Guillain-Barré syndrome as a neurological complication of novel COVID-19 infection: a case report and review of the literature. *Neurologist.* 2020;25:101–103. doi: [10.1097/NRL.0000000000000291](https://doi.org/10.1097/NRL.0000000000000291)
28. Coen M, Jeanson G, Culebras Almeida LA, et al. Guillain-Barré syndrome as a complication of SARS-CoV-2 infection. *Brain Behav Immun.* 2020;87:111–12. doi: [10.1016/j.bbi.2020.04.074](https://doi.org/10.1016/j.bbi.2020.04.074)
29. Dinkin M, Gao V, Kahan J, et al. COVID-19 presenting with ophthalmoparesis from cranial nerve palsy. *Neurology.* 2020;95:221–23. doi: [10.1212/WNL.00000000000009700](https://doi.org/10.1212/WNL.00000000000009700)
30. Manganotti P, Bellavita G, D'Acunto L, et al. Clinical neurophysiology and cerebrospinal liquor analysis to detect Guillain-Barré syndrome and polyneuritis cranialis in COVID-19 patients: a case series. *J Med Virol.* 2020;1–9. doi: [10.1002/jmv.26289](https://doi.org/10.1002/jmv.26289)
31. Fernández-Domínguez J, Ameijide-Sanluis E, García-Cabo C, García-Rodríguez R, Mateos V. Miller-Fisher-like syndrome related to SARS-CoV-2 infection (COVID 19). *J Neurol.* 2020;267:2495–96. doi: [10.1007/s00415-020-09912-2](https://doi.org/10.1007/s00415-020-09912-2)
32. Hutchins KL, Jansen JH, Comer AD, et al. COVID-19-associated bifacial weakness with paresthesia subtype of Guillain-Barré syndrome. *Am J Neuroradiol.* 2020;41:1707–11. doi: [10.3174/ajnr.A6654](https://doi.org/10.3174/ajnr.A6654)
33. Kilinc D, van de Pasch S, Doets AY, Jacobs BC, van Vliet J, Garssen MPJ. Guillain-Barré syndrome after SARS-CoV-2 infection. *Eur J Neurol.* 2020;27:1757–58. doi: [10.1111/ene.14398](https://doi.org/10.1111/ene.14398)
34. Naddaf E, Laughlin RS, Klein CJ, et al. Guillain-Barré syndrome in a patient with evidence of recent SARS-CoV-2 infection. *Mayo Clin Proc.* 2020;95:1799–801. doi: [10.1016/j.mayocp.2020.05.029](https://doi.org/10.1016/j.mayocp.2020.05.029)
35. Abrams RMC, Kim BD, Markantone DM, et al. Severe rapidly progressive Guillain-Barré syndrome in the setting of acute COVID-19 disease. *J Neurovirol.* 2020;26:797–99. doi: [10.1007/s13365-020-00884-7](https://doi.org/10.1007/s13365-020-00884-7)
36. Gigli GL, Vogrig A, Nilo A, et al. HLA and immunological features of SARS-CoV-2-induced Guillain-Barré syndrome. *Neurol Sci.* 2020;41:3391–94. doi: [10.1007/s10072-020-04787-7](https://doi.org/10.1007/s10072-020-04787-7)
37. Bracaglia M, Naldi I, Govoni A, Brillanti Ventura D, De Massis P. Acute inflammatory demyelinating polyneuritis in association with an asymptomatic infection by SARS-CoV-2. *J Neurol.* 2020;267:3166–168. doi: [10.1007/s00415-020-10014-2](https://doi.org/10.1007/s00415-020-10014-2)
38. Sidig A, Abbasher K, Digna MF, et al. COVID-19 and Guillain-Barré Syndrome – a case report. *Res Sq Prepr.* Published online 2020:1–8.
39. Lascano AM, Epiney JB, Coen M, et al. SARS-CoV-2 and Guillain-Barré syndrome: AIDP variant with a favourable outcome. *Eur J Neurol.* 2020;27:1751–53. doi: [10.1111/ene.14368](https://doi.org/10.1111/ene.14368)
40. Camdessanche JP, Morel J, Pozzetto B, Paul S, Tholance Y, Botelho-Nevers E. COVID-19 may induce Guillain-Barré syndrome. *Rev Neurol (Paris).* 2020;176:516–18. doi: [10.1016/j.neurol.2020.04.003](https://doi.org/10.1016/j.neurol.2020.04.003)
41. Abolmaali M, Heidari M, Zeinali M, et al. Guillain-Barré syndrome as a parainfectious manifestation of SARS-CoV-2 infection: a case series. *J Clin Neurosci.* 2021;83:119–22. doi: [10.1016/j.jocn.2020.11.013](https://doi.org/10.1016/j.jocn.2020.11.013)
42. Chan JL, Ebadi H, Sarna JR. Guillain-Barré syndrome with facial Diplegia related to SARS-CoV-2 infection. *Can J Neurol Sci/J Can des Sci Neurol.* Published online 2020:1–3. doi: [10.1017/cjn.2020.106](https://doi.org/10.1017/cjn.2020.106)
43. Sancho-Saldaña A, Lambea-Gil Á, Capablo Liesa JL, et al. Guillain-Barré syndrome associated with leptomeningeal enhancement following SARS-CoV-2 infection. *Clin Med J R Coll Physicians London.* 2020;20:E93–94. doi: [10.7861/CLINMED.2020-0213](https://doi.org/10.7861/CLINMED.2020-0213)
44. Assini A, Benedetti L, Di Maio S, Schirinzi E, Del Sette M. Correction to: New clinical manifestation of COVID-19 related Guillain-Barré syndrome highly responsive to intravenous immunoglobulins: two Italian cases (*Neurological Sciences*, (2020), 41, 7, (1657–1658), [10.1007/s10072-020-04484-5](https://doi.org/10.1007/s10072-020-04484-5)). *Neurol Sci.* 2020;41:2307. doi: [10.1007/s10072-020-04517-z](https://doi.org/10.1007/s10072-020-04517-z)
45. Frank CHM, Almeida TVR, Marques EA, et al. Guillain-Barré syndrome associated with SARS-CoV-2 infection in a pediatric patient. *J Trop Pediatr.* Published online 2020:1–6. doi: [10.1093/tropej/fmaa044](https://doi.org/10.1093/tropej/fmaa044)
46. Juliao Caamaño DS, Alonso Beato R. Facial diplegia, a possible atypical variant of Guillain-Barré syndrome as a rare neurological complication of SARS-CoV-2. *J Clin Neurosci.* 2020;77:230–32. doi: [10.1016/j.jocn.2020.05.016](https://doi.org/10.1016/j.jocn.2020.05.016)
47. Oguz-Akarsu E, Ozpar R, Mirzayev H, et al. Guillain-Barré syndrome in a patient with minimal symptoms of COVID-19 infection. *Muscle and Nerve.* 2020;2:54–57. doi: [10.1002/mus.26992](https://doi.org/10.1002/mus.26992)
48. Toscano G, Palmerini F, Ravaglia S, et al. Guillain-Barré syndrome associated with SARS-CoV-2. *N Engl J Med.* 2020;382:2574–76. doi: [10.1056/NEJMc2009191](https://doi.org/10.1056/NEJMc2009191)

49. Reyes-Bueno JA, García-Trujillo L, Urbaneja P, et al. Miller-Fisher syndrome after SARS-CoV-2 infection. *Eur J Neurol.* 2020;27:1759–61. doi: [10.1111/ene.14383](https://doi.org/10.1111/ene.14383)
50. Bigaut K, Mallaret M, Baloglu S, et al. Guillain-Barré syndrome related to SARS-CoV-2 infection. *Neurol Neuroimmunol Neuroinflammation.* 2020;7:4–6. doi: [10.1212/NXI.00000000000000785](https://doi.org/10.1212/NXI.00000000000000785)
51. Padroni M, Mastrangelo V, Asioli GM, et al. Guillain-Barré syndrome following COVID-19: new infection, old complication? *J Neurol.* 2020;267:1877–79. doi: [10.1007/s00415-020-09849-6](https://doi.org/10.1007/s00415-020-09849-6)
52. Tiet MY, Alshaikh N. Guillain-Barré syndrome associated with COVID-19 infection: a case from the UK. *BMJ Case Rep.* 2020;13:1–4. doi: [10.1136/bcr-2020-236536](https://doi.org/10.1136/bcr-2020-236536)
53. Ameer N, Shekhda KM, Cheesman A. Guillain-Barré syndrome presenting with COVID-19 infection. *BMJ Case Rep.* 2020;13:3–5. doi: [10.1136/bcr-2020-236978](https://doi.org/10.1136/bcr-2020-236978)
54. Wada S, Nagasaki Y, Arimizu Y, et al. Neurological disorders Identified during treatment of a SARS-CoV-2 infection. *Intern Med.* 2020;59:2187–89. doi: [10.2169/internalmedicine.5447-20](https://doi.org/10.2169/internalmedicine.5447-20)
55. Ray A. Miller Fisher syndrome and COVID-19: Is there a link. *BMJ Case Rep.* 2020;13:19–22. doi: [10.1136/bcr-2020-236419](https://doi.org/10.1136/bcr-2020-236419)
56. Guijarro-Castro C, Rosón-González M, Abreu A, García-Arratibel A, Ochoa-Mulas M. Guillain-Barré syndrome associated with SARS-CoV-2 infection. Comments after 16 published cases. *Neurologia.* 2020;35:412–15. doi: [10.1016/j.nrl.2020.06.002](https://doi.org/10.1016/j.nrl.2020.06.002)
57. Gutiérrez-Ortiz C, Méndez-Guerrero A, Rodrigo-Rey S, et al. Miller Fisher syndrome and polyneuritis cranialis in COVID-19. *Neurology.* 2020;95:e601–605. doi: [10.1212/WNL.00000000000009619](https://doi.org/10.1212/WNL.00000000000009619)
58. Agosti E, Giorgianni A, D'Amore F, Vinacci G, Balbi S, Locatelli D. Is Guillain-Barré syndrome triggered by SARS-CoV-2? Case report and literature review. *Neurol Sci.* Published online 2020. doi: [10.1007/s10072-020-04553-9](https://doi.org/10.1007/s10072-020-04553-9)
59. Khalifa M, Zakaria F, Ragab Y, et al. Guillain-Barré syndrome associated with severe acute respiratory syndrome coronavirus 2 detection and coronavirus disease 2019 in a child. *J Pediatric Infect Dis Soc.* 2020;9:510–13. doi: [10.1093/jpids/piaa086](https://doi.org/10.1093/jpids/piaa086)
60. Farzi MA, Ayromlou H, Jahanbaksh N, Bavil PH, Janzadeh A, Shayan FK. Guillain-Barré syndrome in a patient infected with SARS-CoV-2, a case report. *J Neuroimmunol.* 2020;346:577294. doi: [10.1016/j.jneuroim.2020.577294](https://doi.org/10.1016/j.jneuroim.2020.577294)
61. Alberti P, Beretta S, Piatti M, et al. Guillain-Barré syndrome related to COVID-19 infection. *Neurol Neuroimmunol Neuroinflammation.* 2020;7:1–3. doi: [10.1212/NXI.00000000000000741](https://doi.org/10.1212/NXI.00000000000000741)
62. Rana S, Lima AA, Chandra R, et al. Novel coronavirus (Covid-19)-associated Guillain-Barré syndrome: Case report. *J Clin Neuromuscul Dis.* 2020;21:240–42. doi: [10.1097/cnd.00000000000000309](https://doi.org/10.1097/cnd.00000000000000309)
63. Korem S, Gandhi H, Dayag DB. Guillain-Barré syndrome associated with COVID-19 disease. *BMJ Case Rep.* 2020;13. doi: [10.1136/bcr-2020-237215](https://doi.org/10.1136/bcr-2020-237215)
64. Civardi C, Collini A, Geda DJ, Geda C. Antiganglioside antibodies in Guillain-Barré syndrome associated with SARS-CoV-2 infection. *J Neurol Neurosurg Psychiatry.* 2020;91:1361–62. doi: [10.1136/jnnp-2020-324279](https://doi.org/10.1136/jnnp-2020-324279)
65. Virani A, Rabold E, Hanson T, et al. Guillain-Barré Syndrome associated with SARS-CoV-2 infection. *IDCases.* 2020;20:e00771. doi: [10.1016/j.idcr.2020.e00771](https://doi.org/10.1016/j.idcr.2020.e00771)
66. Khaja M, Roa Gomez GP, Santana Y, et al. A 44-year-old hispanic man with loss of taste and bilateral facial weakness diagnosed with Guillain-Barré syndrome and Bell's Palsy associated with SARS-CoV-2 infection treated with intravenous immunoglobulin. *Am J Case Rep.* 2020;21:1–6. doi: [10.12659/AJCR.927956](https://doi.org/10.12659/AJCR.927956)
67. Lampe A, Winschel A, Lang C, Steiner T. Guillain-Barré syndrome and SARS-CoV-2. *Neurol Res Pract* 2020;2:19.
68. Ottaviani D, Boso F, Tranquillini E, et al. Early Guillain-Barré syndrome in coronavirus disease 2019 (COVID-19): a case report from an Italian COVID-hospital. *Neurol Sci.* 2020;41:1351–54. doi: [10.1007/s10072-020-04449-8](https://doi.org/10.1007/s10072-020-04449-8)
69. Scheidl E, Canseco DD, Hadji-Naumov A, Bereznaï B. Guillain-Barré syndrome during SARS-CoV-2 pandemic: a case report and review of recent literature. *J Peripher Nerv Syst.* 2020;25(2):204–207. doi: [10.1111/jns.12382](https://doi.org/10.1111/jns.12382)
70. El Otmani H, El Moutawakil B, Rafai MA, et al. Covid-19 and Guillain-Barré syndrome: more than a coincidence! *Rev Neurol (Paris).* 2020;176:518–19. doi: [10.1016/j.neurol.2020.04.007](https://doi.org/10.1016/j.neurol.2020.04.007)
71. Lantot JE, Strauss SB, Lin E. COVID-19-associated Miller Fisher syndrome: MRI findings. *Am J Neuroradiol.* 2020;41:1184–86. doi: [10.3174/ajnr.A6609](https://doi.org/10.3174/ajnr.A6609)
72. Riva N, Russo T, Falzone YM, et al. Post-infectious Guillain-Barré syndrome related to SARS-CoV-2 infection: a case report. *J Neurol.* 2020;267:2492–94. doi: [10.1007/s00415-020-09907-z](https://doi.org/10.1007/s00415-020-09907-z)
73. Helbok R, Beer R, Löscher W, et al. Guillain-Barré syndrome in a patient with antibodies against SARS-CoV-2. *Eur J Neurol.* 2020;27:1754–56. doi: [10.1111/ene.14388](https://doi.org/10.1111/ene.14388)
74. Webb S, Wallace VCJ, Martin-Lopez D, Yogarajah M. Guillain-Barré syndrome following COVID-19: a newly emerging post-infectious complication. *BMJ Case Rep.* 2020;13:1–4. doi: [10.1136/bcr-2020-236182](https://doi.org/10.1136/bcr-2020-236182)
75. Pfefferkorn T, Dabitz R, von Wernitz-Keibel T, Aufenanger J, Nowak-Machen M, Janssen H. Acute polyradiculoneuritis with locked-in syndrome in a patient with Covid-19. *J Neurol.* 2020;267:1883–84. doi: [10.1007/s00415-020-09897-y](https://doi.org/10.1007/s00415-020-09897-y)
76. Dufour C, Co T-K, Liu A. GM1 ganglioside antibody and COVID-19 related Guillain Barre Syndrome – a case report, systemic review and implication for vaccine development. *Brain, Behav Immun – Health.* 2021;12:100203. doi: [10.1016/j.bbih.2021.100203](https://doi.org/10.1016/j.bbih.2021.100203)
77. Jones R, Kolbe H, Barton A. Post Covid-19 Guillain-Barre syndrome: case report. *Morecambe Bay Med J.* 2020;8:229–31.
78. Ghosh R, Roy D, Sengupta S, Benito-León J. Autonomic dysfunction heralding acute motor axonal neuropathy in COVID-19. *J Neurovirol.* 2020;26:964–66. doi: [10.1007/s13365-020-00908-2](https://doi.org/10.1007/s13365-020-00908-2)
79. Mackenzie N, Lopez-Coronel E, Alberto Dau C, et al. A concomitant Guillain-Barre syndrome with COVID-19: a first case-report in Colombia. 1–9. <https://doi.org/10.21203/rs.3.rs-61279/v1>
80. Charra B. Guillain Barre syndrome & Covid-19: a case report. *Ann Clin Med Case Rep.* Published online 2021;V5.
81. Petrelli C, Scendonì R, Paglioriti M, Logullo FO. Acute motor axonal neuropathy related to COVID-19 infection: a new diagnostic overview. *J Clin Neuromuscul Dis.* 2020;22:120–21. doi: [10.1097/cnd.0000000000000322](https://doi.org/10.1097/cnd.0000000000000322)
82. Yaqoob H, Jain A, Epelbaum O. A unique case of Guillain-Barré syndrome related to COVID-19 infection. *Chest.* 2020;158:A771. doi: [10.1016/j.chest.2020.08.718](https://doi.org/10.1016/j.chest.2020.08.718)
83. Bueso T, Montalvan V, Lee J, et al. Guillain-Barre syndrome and COVID-19: a case report. *Clin Neurol Neurosurg.* 2021;200:2020–22. doi: [10.1016/j.clineuro.2020.106413](https://doi.org/10.1016/j.clineuro.2020.106413)
84. Manji HK, George U, Mkopi NP, Manji KP. Guillain-Barré syndrome associated with COVID-19 infection. *Pan Afr Med J.* 2020;35:118. doi: [10.11604/pamj.supp.2020.35.2.25003](https://doi.org/10.11604/pamj.supp.2020.35.2.25003)
85. Su XW, Palka S V., Rao RR, Chen FS, Brackney CR, Cambi F. SARS-CoV-2-associated Guillain-Barré syndrome with dysautonomia. *Muscle and Nerve.* 2020;62:E48–49. doi: [10.1002/mus.26988](https://doi.org/10.1002/mus.26988)
86. Velayos Galán A, del Saz Saucedo P, Peinado Postigo F, Botia Paniagua E. Guillain-Barré syndrome associated with SARS-CoV-2 infection. *Neurologia.* 2020;35:268–69. doi: [10.1016/j.nrl.2020.04.007](https://doi.org/10.1016/j.nrl.2020.04.007)
87. Barrachina-Esteve O, Palau Domínguez A, Hidalgo-Torrico I, Viguera Martínez ML. Síndrome de Guillain-Barré como forma de presentación de la infección por SARS-CoV-2. *Neurología.* 2020;35:710–12. doi: [10.1016/j.nrl.2020.07.001](https://doi.org/10.1016/j.nrl.2020.07.001)
88. Marta-Enguita J, Rubio-Baines I, Gastón-Zubimendi I. Síndrome de Guillain-Barré fatal tras infección por el virus SARS-CoV-2. *Neurología.* 2020;35:265–67. doi: [10.1016/j.nrl.2020.04.004](https://doi.org/10.1016/j.nrl.2020.04.004)
89. Gigli GL, Bax F, Marini A, et al. Guillain-Barré syndrome in the COVID-19 era: just an occasional cluster? *J Neurol.* 2020;0123456789:1–3. doi: [10.1007/s00415-020-09911-3](https://doi.org/10.1007/s00415-020-09911-3)
90. Manganotti P, Pesavento V, Buoite Stella A, et al. Miller Fisher syndrome diagnosis and treatment in a patient with SARS-CoV-2. *J Neurovirol.* 2020;26:605–606. doi: [10.1007/s13365-020-00858-9](https://doi.org/10.1007/s13365-020-00858-9)
91. Gale A, Sabaretnam S, Lewinsohn A. Guillain-Barré syndrome and COVID-19: association or coincidence. *BMJ Case Rep.* 2020;13:10–14. doi: [10.1136/bcr-2020-239241](https://doi.org/10.1136/bcr-2020-239241)

92. García-Manzanedo S, López de la Oliva Calvo L, Ruiz Álvarez L. Síndrome de Guillain-Barré tras infección por COVID-19. *Med Clin (Barc)*. 2020;155:366. doi:10.1016/j.medcli.2020.06.023
93. Raahimi MM, Kane A, Moore CE, Alareed AW. Late onset of Guillain-Barré syndrome following SARS-CoV-2 infection: part of “long COVID-19 syndrome”? *BMJ Case Rep*. 2021;14:1–4. doi: 10.1136/bcr-2020-240178
94. Bourque PR, Breiner A, Moher D, et al. Adult CSF total protein: higher upper reference limits should be considered worldwide. a web-based survey. *J Neurol Sci*. 2019;396:48–51. doi:10.1016/j.jns.2018.10.033
95. Tan CY, Razali SNO, Goh KJ, Shahrizaila N. Diagnosis of Guillain-Barré syndrome and validation of the Brighton criteria in Malaysia. *J Peripher Nerv Syst*. 2020;25:256–64. doi: 10.1111/jns.12398
96. Shang P, Zhu M, Baker M, Feng J, Zhou C, Zhang H-L. Mechanical ventilation in Guillain-Barré syndrome. *Expert Rev Clin Immunol*. 2020;16:1053–64. doi: 10.1080/1744666X.2021.1840355
97. Leonhard SE, Bresani-Salvi CC, Lyra Batista JD, et al. Guillain-barré syndrome related to Zika virus infection: a systematic review and meta-analysis of the clinical and electrophysiological phenotype. *PLoS Negl Trop Dis*. 2020;14:1–24. doi: 10.1371/journal.pntd.0008264
98. Rees JH, Hughes RAC. *Campylobacter jejuni* infection and Guillain-Barré syndrome. *N Engl J Med*. 1995;333:1374–9.
99. Katirji B, Ruff RL, Kaminski HJ. Neuromuscular disorders in clinical practice. Vol. 9781461465; 2014. doi: 10.1007/978-1-4614-6567-6
100. Piccione EA, Salame K, Katirji B. Guillain-Barré syndrome and related disorders BT – neuromuscular disorders in clinical practice. In: Katirji B, Kaminski HJ, Ruff RL, editors. *Neuromuscular Disorders in Clinical Practice*. New York: Springer; 2014, pp. 573–603. doi: 10.1007/978-1-4614-6567-6_28
101. Eastin C, Eastin T. Clinical characteristics of Coronavirus Disease 2019 in China: Guan W, Ni Z, Hu Y, et al. *N Engl J Med*. 2020 Feb 28 [Online ahead of print] DOI: 10.1056/NEJMoa2002032. *J Emerg Med*. 2020;58:711–12. doi: 10.1016/j.jemermed.2020.04.004
102. Rees JH, Soudain SE, Gregson NA, Hughes RAC. *Campylobacter jejuni* infection and Guillain-Barré syndrome. *N Engl J Med*. 1995;333:1374–79. doi: 10.1056/NEJM199511233332102
103. Keddie S, Pakpoor J, Mausele C, et al. Epidemiological and cohort study finds no association between COVID-19 and Guillain-Barré syndrome. *Brain*. 2021;144:682–93. doi: 10.1093/brain/awaa433
104. Liu H, Ma Y. Hepatitis E virus-associated Guillain-Barre syndrome: revision of the literature. *Brain Behav*. 2020;10:e01496. doi: 10.1002/brb3.1496
105. Hardy TA, Blum S, McCombe PA, Reddel SW. Guillain-Barré syndrome: modern theories of etiology. *Curr Allergy Asthma Rep*. 2011;11:197–204. doi: 10.1007/s11882-011-0190-y
106. Jahan I, Ahammad RU, Khalid MM, et al. Toll-like receptor-4 299Gly allele is associated with Guillain-Barré syndrome in Bangladesh. *Ann Clin Transl Neurol*. 2019;6:708–15. doi: 10.1002/actn.3.744
107. Jaramillo-Valverde L, Levano KS, Villanueva I, et al. Guillain-Barré syndrome outbreak in Peru: association with polymorphisms in IL-17, ICAM1, and CD1. *Mol Genet Genomic Med*. 2019;7:e00960. doi: 10.1002/mgg3.960
108. Nyati KK, Prasad KN, Verma A, et al. Association of TLR4 Asp299Gly and Thr399Ile polymorphisms with Guillain-Barré syndrome in Northern Indian population. *J Neuroimmunol*. 2010;218:116–19. doi: 10.1016/j.jneuroim.2009.10.018
109. Willison HJ, O’Hanlon GM. The immunopathogenesis of Miller Fisher syndrome. *J Neuroimmunol*. 1999;100:3–12. doi: 10.1016/S0165-5728(99)00213-1
110. Nagashima T, Koga M, Odaka M, Hirata K, Yuki N. Continuous spectrum of pharyngeal-cervical-brachial variant of Guillain-Barré syndrome. *Arch Neurol*. 2007;64:1519–23. doi: 10.1001/archneur.64.10.1519
111. Willison HJ, Yuki N. Peripheral neuropathies and anti-glycolipid antibodies. *Brain*. 2002;125:2591–625. doi: 10.1093/brain/awf272
112. Soliven B. Animal models of autoimmune neuropathy. *ILAR J*. 2014;54:282–90. doi: 10.1093/ilar/ilt054
113. Stathopoulos P, Alexopoulos H, Dalakas MC. Autoimmune antigenic targets at the node of Ranvier in demyelinating disorders. *Nat Rev Neurol*. 2015;11:143–56. doi: 10.1038/nrneuro.2014.260
114. Rodríguez Y, Rojas M, Pacheco Y, et al. Guillain-Barré syndrome, transverse myelitis and infectious diseases. *Cell Mol Immunol*. 2018;15:547–62. doi: 10.1038/cmi.2017.142
115. Safa A, Azimi T, Sayad A, Taheri M, Ghafouri-Fard S. A review of the role of genetic factors in Guillain-Barré syndrome. *J Mol Neurosci*. Published online 2020:1–19.
116. Guo L, Wang W, Li C, Liu R, Wang G. The association between HLA typing and different subtypes of Guillain Barré syndrome [in Chinese]. *Zhonghua Nei Ke Za Zhi*. 2002;41:381–3. Available at <http://europepmc.org/abstract/MED/12137599>
117. Hasan ZN, Zalzal HH, Mohammedsalih HR, et al. Association between human leukocyte antigen-DR and demyelinating Guillain-Barre syndrome. *Neurosciences (Riyadh)*. 2014;19:301–305.
118. Schirmer L, Worthington V, Solloch U, et al. Higher frequencies of HLA DQB1*05:01 and anti-glycosphingolipid antibodies in a cluster of severe Guillain-Barré syndrome. *J Neurol*. 2016;263:2105–13. doi: 10.1007/s00415-016-8237-6
119. Hu T, Liu Y, Zhao M, Zhuang Q, Xu L, He Q. A comparison of COVID-19, SARS and MERS. *PeerJ*. 2020;8:e9725–25. doi: 10.7717/peerj.9725
120. Tsai L-K, Hsieh S-T, Chang Y-C. Neurological manifestations in severe acute respiratory syndrome. *Acta Neurol Taiwan*. 2005;14:113–19.