Treatment Options for COVID-19–Related Guillain-Barré Syndrome

A Systematic Review of Literature

Sogand Goudarzi, MD, Shooka Esmaeeli, MD,†‡ Juan D. Valencia, MD,† Maegan E. Lu, BS,‡ Riley R. Hales, BS,‡ Corey R. Fehnel, MD, MPH,§ Christopher M. Conley, MD,‡ Sadeq A. Quraishi, MD, MHA, MMSc,‖ and Ala Nozari, MD, PhD‡*

Background: Central nervous system complications are reported in an increasing number of patients with Coronavirus Disease 2019 (COVID-19). COVID-19–related Guillain-Barré syndrome (GBS) is of particular importance given its association with higher mortality rates and prolonged respiratory failure.

Review Summary: We conducted a systematic review of published cases for COVID-19–related GBS, and provide a summary of clinical management strategies for these cases. Sixty-three studies, including 86 patients, were included. Seventy-six cases with reported outcome data were eligible for the outcome analysis. Ninety-nine percent of patients were diagnosed with COVID-19 before diagnosis of GBS (median: 14 d prior, interquartile range: 7 to 20). Intravenous immunotherapy (intravenous immunoglobulin: 0.4 g/kg/d for 5 d) was the most frequently used treatment approach. The review indicated that the outcome was not favorable in 26% of cases (persistent neurological deficits). A mortality rate of 3.5% was observed in patients with COVID-19–related GBS.

Conclusions: Although evidence to support specific treatments is lacking, clinicians should consider the benefits of immunotherapy and plasma exchange in addition to the standard antimicrobial and supportive therapies for patients who meet the diagnostic criteria for acute sensory and motor polyradiculoneuritis. Intravenous immunoglobulin treatment alone is not shown to result in improved outcomes or mortality. More extensive studies aimed at exploring the neurological manifestations and complications of COVID-19 and distinctive treatment options for COVID-19–related GBS are warranted.

Key Words: COVID-19, coronavirus, Guillain-Barré syndrome, plasma exchange, intensive care units, immunotherapy, IVIG

(*The Neurologist* 2021;26:196–224)

An increasing body of evidence has emerged to establish the link between Coronavirus Disease 2019 (COVID-19) infection and major neurological complications such as cerebrovascular accidents, acute transverse myelitis, encephalitis, and Guillain-Barré syndrome (GBS).

Angiotensin-converting enzyme 2 (ACE2) has been identified as an important severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) receptor, mediating its entry into the cell.[1] ACE2 receptors are widely expressed in the lungs, heart, and brain.[2] The expression of the ACE2 receptors on the endothelial cells of the blood-brain barrier facilitates the viral binding and entry into the central nervous system (CNS).[3–6] ACE2 receptors are highly expressed in the ventrolateral medulla and the nucleus of the solitary tract.[5] In addition to the direct viral binding and cell entry, activation of inflammatory mediators is thought to result in a proinflammatory state within the CNS.[7] In addition, COVID-19 is suggested to trigger a molecular mimicry phenomenon on the affected endothelial cells, where cross-reactions occur between antibodies and a large number of proteins present on the plasma membrane surface due to COVID-19 induced stress.[8,9] As a result of the above mechanisms various pathways within the CNS can lead to direct injury to nerve tissue, in addition to a cytokine storm across the blood-brain barrier, hypoxia from COVID-19–related lung injury, and an uncontrolled immune response.[6,10–13] Figure 1 demonstrates different mechanisms through which SARS-CoV-2 may cause neuronal injuries.

Neurological manifestations are reported in up to 36% of patients with COVID-19. Among COVID-19-associated CNS conditions, GBS has emerged in an increasing number of case reports as an additional hazard with a significant risk of mortality or prolonged respiratory failure.[4,11,12,14–20]

We herein present an in-depth systematic review of COVID-19–related GBS cases with analysis. The purpose of this systematic review is to recapitulate the available treatments for COVID-19–related GBS and to provide a summary of clinical management strategies for this complication. We explore management obstacles in the intensive care unit (ICU) for COVID-19–related GBS patients during the pandemic.

METHODS

Search Strategy and Selection Criteria

All articles in English and Spanish languages, including adult patients, and published in PubMed-indexed scientific journals were considered eligible. Randomized controlled trials, prospective and retrospective cohorts, case series, and case reports, as well as cross-sectional studies involving patients with COVID-19–related GBS were eligible for inclusion.

We performed a systematic search on databases PubMed, EMBASE, and Web of Science to identify studies with the

From the *Division of Cardiovascular Medicine; Departments of †Anesthesiology, Critical Care, and Pain Medicine; §Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School; ‡Department of Anesthesiology, Boston Medical Center, Boston University School of Medicine; and ‖Department of Anesthesiology and Perioperative Medicine, Tufts Medical Center, Tufts University School of Medicine, Boston, MA.

S.G. and S.E. contributed equally.

The authors declare no conflict of interest.

Correspondence to: Ala Nozari, MD, PhD, Department of Anesthesiology, Boston Medical Center, Boston University School of Medicine, Boston, MA. E-mail: ala.nozari@bmc.org.

ISSN: 2331-2637/21/2605-0196
DOI: 10.1097/NRL.0000000000000342

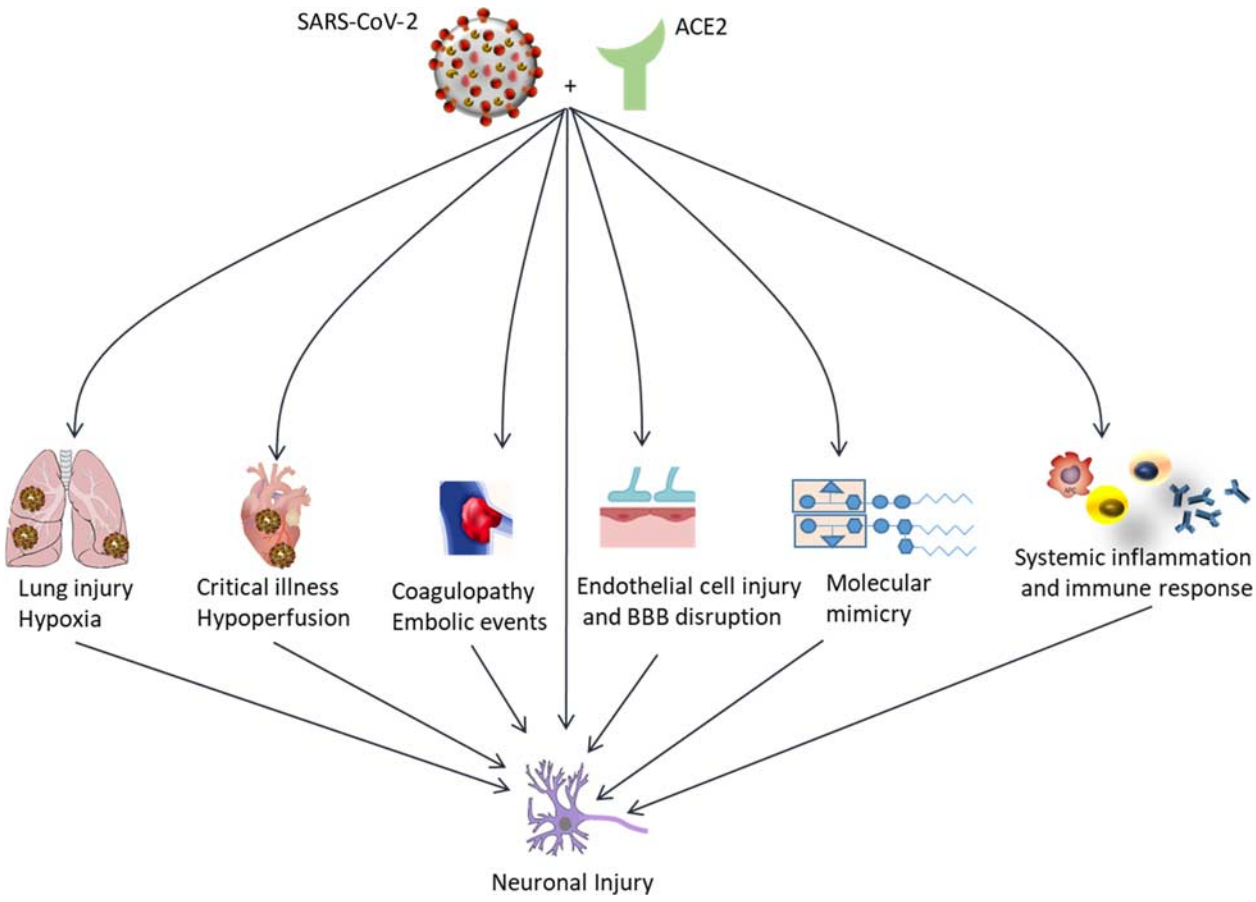

FIGURE 1. ACE2-binding SARS-CoV-2 causes various complications in different organs that can lead to neurological complications. ACE2 indicates angiotensin-converting enzyme 2; BBB, blood-brain barrier; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

following subject heading terms: "COVID" OR "Coronavirus" AND "Guillain-Barre." We extracted the data from reports, with adherence to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline.[21] Details of the patient population, COVID-19 symptoms and management, GBS symptoms, management, and outcomes were recorded. The search occurred from May 19, 2020, through January 31, 2021 which captured a total of 99 studies. Thirteen additional reports were captured from reference lists of retrieved reports and Google Scholar searches. At the time of conducting this study there were no published randomized trials or cross-sectional studies. We identified 3 systematic reviews, 1 cohort, and 1 observational study. All case reports and case series were included in the analysis. There were also 3 correspondence letters eligible for inclusion in the qualitative synthesis (Table 1).

Data Analysis

Descriptive statistics were tabulated for the analytic cohort. Continuous data were reported as median with interquartile ranges and compared using the Kruskal-Wallis test or Wilcoxon rank test. Categorical data were expressed as proportions and compared using the χ^2 test. The published outcome data for each case were classified into 2 categories. Clinical improvement, defined as neurological or autonomic, or respiratory symptoms improvement, weaning off the ventilator, or improvement of oxygen requirement and inflammatory markers. No improvement is defined as no sign of clinical improvement, worsening of the neurological examination, hemodynamic instability, and death. All analyses were conducted using R (The R Foundation for Statistical Computing, Vienna, Austria).[24] *P*-values <0.05 were considered to be significant.

RESULTS

To graphically summarize the studies' inclusion processes, we constructed a PRISMA diagram (Fig. 2) which demonstrates the selection mechanism of among the total of 99 discovered publications.[21] From a total of the final 63 publications (55 case reports and 8 case series), 86 cases were included in this study. Most of the cases were reported from Italy (30%), the United States (19%), and Spain (9%) (Fig. 3). The reported in-hospital mortality rate among a total of 86 patients were 3.5%. Seventy-six cases reported the outcome of their management and were included in the final analysis; among them, 74% reported clinical improvement, while 26% reported no improvement. Demographic and clinical data stratified by patients' outcome are shown in Table 2. Patients with no improvement were older ($P = 0.003$) and had a higher incidence of quadriplegia ($P = 0.02$), areflexia ($P = 0.02$) and respiratory failure ($P = 0.004$) (Table 2).

TABLE 1. COVID-19–Related GBS Correspondence Letters

References	Title	Question	Conclusion
Gupta et al[22]	Is COVID-19–related Guillain-Barré syndrome different?	How does COVID-19–related Guillain-Barré syndrome compare against other presentations of GBS?	Anti-ganglioside antibody was not found in patients with COVID-19– and Zika virus–related GBS. The neuropathy in viral infections–related GBS could be due to other autoantibodies that are not detected as yet or the viruses produced nerve damage due to other neurotoxic effects
Cappello[8]	COVID-19 and molecular mimicry: the Columbus' Egg?	Does molecular mimicry explain both the acute pulmonary embolism and the multi-organ microvascular thrombosis that some patients experience?	It would be appropriate if this Journal would stimulate the scientific community on the fact that molecular mimicry phenomena can occur in SARS-CoV-2 It is also urgent to start the search for human epitopes that turn into autoantigens, and to remind this risk to all those who are currently working on vaccines
Gigli et al[23]	Guillain-Barré syndrome in the COVID-19 era: just an occasional cluster?	Compare the frequency of GBS cases during the March-April months of the last 3 y and to admissions for GBS during the same months of the current year in Friuli Venezia-Giulia, Italy	Compared with years 2017-2019, the increase of GBS cases in 2020 is 5.41-fold The suspicion that this striking difference could be due to the pandemic curve in our region is, therefore, legitimate

COVID-19 indicates Coronavirus Disease 2019; GBS, Guillain-Barré syndrome; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

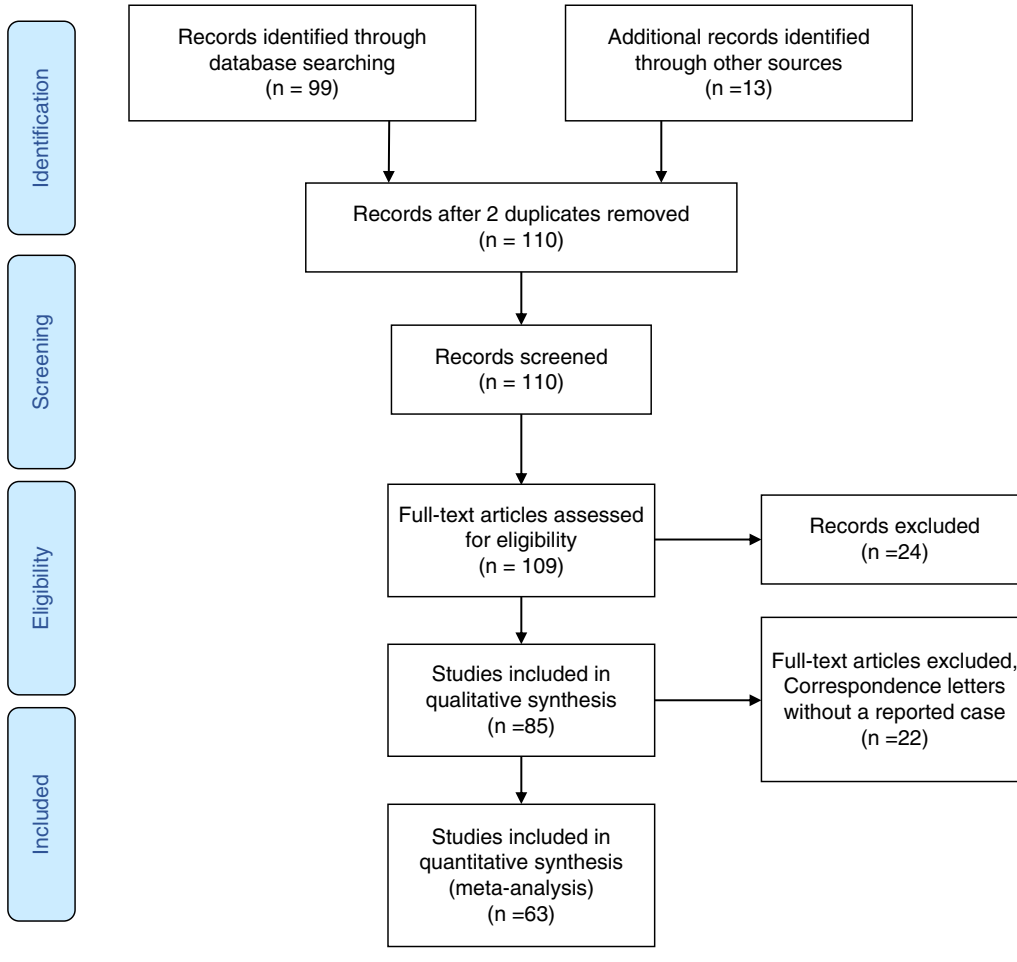

FIGURE 2. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.

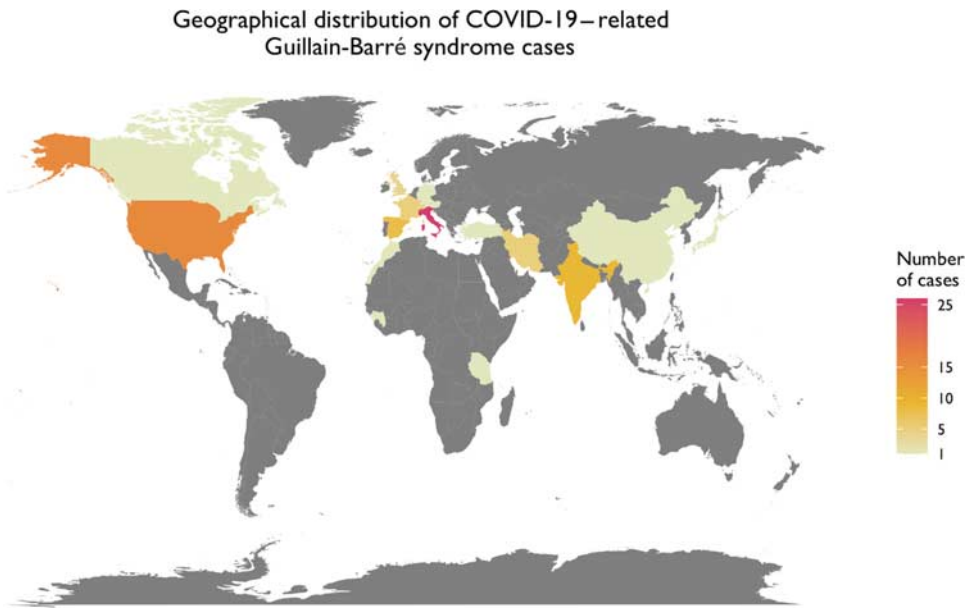

FIGURE 3. Geographical distribution of the Coronavirus Disease 2019 (COVID-19)-related Guillain-Barré syndrome cases.

Demographic data of published cases, as well as the reported clinical data for each COVID-19 case, is demonstrated in Table 3. Among a total of 86 cases, the most-reported comorbidity was hypertension (20%) and type 2 diabetes or prediabetes (9%). Cough (70%), fever (63%), dyspnea (24%), anosmia or ageusia (17%), diarrhea (16%), pharyngitis or upper respiratory infection (URI) symptoms (15%), and fatigue, myalgia, or arthralgia (12%) were the first COVID-19 infection symptoms reported among the patients, respectively. A majority of the cases (83%) were diagnosed using the reverse transcription-polymerase chain reaction technique; and 86% of the specimens were collected through nasopharyngeal (NP) swab. Forty-five percent of the cases reported cerebrospinal fluid polymerase chain reaction for COVID-19 results with no positive report. Seventy-eight percent of the cases reported their choice of treatment for COVID-19. These treatments included hydroxychloroquine (45%), antibiotics (34%), lopinavir/ritonavir (25%), darunavir and antiretroviral therapy (7%), umifenovir (3%), oseltamivir (3%), tocilizumab (1%), and corticosteroids (16%). There was no reported use of remdesivir among the cases we reviewed. Similarly, the use of Regeneron monoclonal antibodies against SARS-CoV-2 (casirivimab with imdevimab) has not been reported in any cases with COVID-19–related GBS; the only reported monoclonal antibody in this population was tocilizumab, a monoclonal antibody against the interleukin-6 receptor. One case reported at the *Chest* annual meeting reported the use of tocilizumab together with convalescent plasma, but the patient did not improve and remained dependent on ventilatory support. Among 92% of the cases that reported ventilator support status, 48% reported failure of weaning trials during the treatment period.

Ninety-nine percent of the patients were diagnosed with COVID-19 before GBS symptoms were recorded, with 1 patient who had GBS symptoms 7 days before the COVID-19 diagnosis. The median interval between COVID-19 diagnosis and the first recorded neurological symptoms was 14 (interquartile range = 7 to 20) days. Paresthesia (41%), quadriparesis (28%), areflexia (27%), paraparesis (26%), dysphagia (15%), facial paresis (14%), ataxia (12%), asthenia (12%), hypoesthesia (10%), respiratory failure (7%), facial diplegia (6%), paraplegia (3%), and quadriplegia (3%) were the GBS symptoms reported among the patients respectively. Forty-four percent of the cases reported performing biological tests for other viral infections. Among these patients, human immunodeficiency virus (68%), followed by influenza viruses (21%) were the most common tested viruses. Nineteen percent of the cases reported performing magnetic resonance imaging. Twelve percent of these cases did not detect any GBS-related findings. However, 31% reported enhancement of caudal nerve roots, and 12% reported abnormal enhancement of facial nerve. A motor nerve conduction study was performed in 76% of the cases. Among these cases, the most frequently examined nerves for velocity assessment were tibial nerve (54%), common peroneal nerve (37%), and the median nerve (37%). For those cases in which the tibial nerve was tested, 49% showed bilateral absent or decreased velocity, 26% showed unilateral decreased velocity, and 17% showed normal velocity at the tibial nerve. Among cases who reported common peroneal nerve testing, 71% had bilateral absent or decreased velocity, 21% had normal velocity, and 8% had unilateral decreased velocity at the common peroneal nerve. For cases with reported median nerve testing, 50% had bilateral absent or decreased velocity, 25% had normal velocity, and 25% had unilateral absent or decreased velocity at the median nerve. Sixty-five percent of the cases reported the type of GBS; among them, 54% were acute inflammatory demyelinating polyneuropathy (AIDP), 32% were acute motor-sensory axonal neuropathy (AMSAN), 11% were MFS and 4% had isolated facial diplegia. Almost all of the cases (98%) reported their choice of GBS management. Intravenous immunoglobulin (IVIG) (87%) was the most used treatment approach followed by plasma exchange (8%). Four percent of patients who received IVIG also underwent plasmapheresis; 2% received low molecular weight heparin (LMWH) or enoxaparin, and 1% Gabapentin. Two percent of patients were treated only with prednisone, and 5% received no specific GBS treatments. Detailed GBS clinical and management data are demonstrated in Table 4 and diagnostic data in Table 5.

TABLE 2. Demographic and Clinical Features of the Cases With Reported Outcome (N = 76)

	Clinical Improvement (N = 57)	No Improvement (N = 21)	*P*
Age (y)	55 (49-64)	66.5 (55-72)	**0.003**
Sex*			
Female	17 (30)	8 (40)	0.6
Male	39 (70)	12 (60)	
Comorbidities†			
Yes	20 (61)	9 (82)	0.3
No	13 (39)	2 (18)	
COVID-19 symptoms			
Fever	35 (61)	15 (71)	0.4
Cough	35 (61)	17 (81)	0.2
Dyspnea	13 (22)	4 (20)	0.5
Anosmia/ageusia	14 (24)	1 (4)	0.05
GBS subtype‡			
AIDP	20 (54)	5 (31)	0.5
AMSAN	9 (24)	6 (35)	
FDP	1 (3)	1 (6)	
MFS	4 (11)	1 (6)	
GBS symptoms			
Tetraparesis	15 (27)	8 (40)	0.4
Paresthesia	23 (41)	11 (55)	0.4
Hypoesthesia	7 (12)	2 (10)	1
Ataxia	8 (14)	1 (5)	0.4
Areflexia	11 (20)	10 (50)	**0.02**
Quadriplegia	0	3 (15)	**0.02**
Paraplegia	1 (2)	2 (10)	0.3
Paraparesis	17 (30)	4 (20)	0.8
Facial paresis	8 (14)	3 (15)	1
Facial diplegia	4 (7)	1 (5)	1
Respiratory failure	1 (2)	5 (23)	**0.004**
Time from onset of COVID-19 diagnosis to GBS (d)§	14 (10-20)	10 (6-14)	0.1
Time from neurological symptoms to hospital admission (d)‖	3 (2-4)	1 (1-3)	0.2
Ventilator support	22 (39)	16 (80)	**0.004**
Time from hospital admission to ICU admission (d)¶	3 (2-3)	2 (1.5-3.5)	0.6
COVID-19 treatment#			
Hydroxychloroquine	20 (43)	8 (47)	1
Lopinavir/ritonavir	9 (20)	7 (41)	0.1
Remdesivir	0	0	1
Antiviral agents	15 (32)	7 (41)	1
Antibiotics	14 (30)	7 (41)	0.7
Corticosteroids	8 (17)	3 (18)	1
Convalescent plasma	0	0	1
Tocilizumab (the only reported monoclonal antibody)	4 (8)	0	0.4
GBS treatment**			
IVIG	49 (87)	13 (65)	0.6
Plasmapheresis	3 (5)	1 (5)	1
Plasmapheresis and IVIG	1 (2)	2 (10)	0.3
Prednisone	0	2 (10)	0.1
No treatment	2 (4)	1 (5)	1
In-hospital mortality	0	3 (15)	**0.02**
Time from neurological symptoms to start of IVIG treatment (d)††	4 (2-7)	3 (3-4)	0.6
IVIG days‡‡	5 (5-5)	5 (5-5)	0.4
IVIG dose§§			
0.40 g/kg/d for 5 d	34 (81)	10 (83)	1
2 g/kg for 5 d	6 (14)	2 (17)	1
30 g for 5 cycles	2 (5)	0	1
Hospital length of stay (d)‖‖	12.5 (9-23.7)	7 (4-31)	0.6
ICU length of stay (d)¶¶	0 (0-5)	4 (1-14)	**0.02**

Bold values are indicates statistically significant.

Data are presented as median (interquartile range), or n (%), and compared using Kruskal-Wallis test, or Wilcoxon signed-rank test and χ^2 test, respectively.

*76 cases reported patients' sex.

†44 cases reported comorbidities.

‡54 cases reported the GBS subtype.

§70 cases reported time from onset of COVID-19 diagnosis to GBS.

‖47 cases reported time from neurological symptoms to hospital admission.

¶23 cases reported time from hospital admission to ICU admission.

#64 cases reported their COVID-19 managements.

**75 cases reported their GBS treatments.

††32 cases reported time from neurological symptoms to start of IVIG treatment.

‡‡56 cases reported IVIG days.

§§54 cases reported exact used IVIG dose.

‖‖37 cases reported hospital length of stay.

¶¶41 cases reported ICU length of stay.

AIDP indicates acute inflammatory demyelinating polyneuropathy; AMSAN, acute motor and sensory axonal neuropathy; COVID-19, Coronavirus Disease 19; FDP, facial diplegia; GBS, Guillain-Barré syndrome; ICU, intensive care unit; IVIG, intravenous immunoglobulin; MFS, Miller-Fisher syndrome.

DISCUSSION

In this systematic review of reported COVID-19 cases, we did not identify a consensus on the diagnostic approach and treatment of patients with superimposed GBS. The most commonly reported treatment was IVIG, in addition to therapies aimed at the COVID-19 infection such as antibiotics and antiviral agents. Our findings confirm that quadriplegia, areflexia, and respiratory failure are associated with poor outcome among COVID-19–related GBS patients ($P = 0.02$, 0.02, and 0.004, respectively), but GBS subtypes and treatment strategies including IVIG and systemic steroids are not. Moreover, this review indicated a mortality rate of 3.5% in patients with COVID-19–related GBS, which is more than twice the WHO reported mortality rate of 2.2% among general COVID-19 cases.[80] We also found a significantly higher rate of acute respiratory failure requiring mechanical ventilation in this population (47% vs. 16% in the general COVID-19 cases[81]) and persistent neurological deficits (26% vs. 18.3%[82]). Although available case reports do not provide evidence of causation, the poor outcome and high mortality rate in COVID-19–related GBS patients underscores the importance of early diagnosis and effective treatment of neurological complications in this population.

GBS Diagnosis in COVID-19 Patients

Clinical diagnosis of GBS can be particularly challenging in patients with severe COVID-19 symptoms.[2,20] A considerable variety of early neurological symptoms have been reported after the onset of COVID-19 symptoms. The interval between the first reported signs of viral infection and the onset of neurological symptoms ranged from 0 to 60 days, with 1 case reporting GBS symptoms 7 days before COVID-19 symptoms occurred.[27]

Types of GBS in COVID-19 Patients

The geographical distribution of reported COVID-19–related GBS resembles the worldwide distribution[80] of COVID-19 infections at the time of this report (Fig. 3). The most commonly

Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.

diagnosed type of GBS in this population is reported to be AIDP, as is typical in dengue or Zika virus–related GBS. However, one study reported that COVID-19–related GBS patients were mainly diagnosed with acute motor axonal neuropathy (AMAN) and AMSAN. The authors further stated that patients with AIDP had better outcomes than those diagnosed with AMAN or AMSAN.[22] We could not corroborate these findings, nevertheless, and failed to validate an association between GBS types and patient outcomes in this review. Gupta and colleagues also speculated that COVID-19–related GBS may have a different pathogenetic mechanism compared with other types of GBS. However, the findings reported in this review indicate a common clinical and pathogenetic characteristics between COVID-19–related GBS and other types of GBS.[22]

General Treatments for COVID-19

Management of the COVID-19 infection is overshadowed by many epidemiological, clinical and social factors and a lack of effective therapies and accepted treatment protocols. While several experimental strategies have been used to treat patients with significant symptoms, current management of COVID-19 primarily focuses on providing supportive therapies including mechanical ventilation.[83] Recent experimental therapies have shown some promise, including antiviral agents such as the adenosine analogue remdesivir and the protease inhibitors lopinavir and ritonavir.[84–88] Chloroquine and hydroxychloroquine have been shown to inhibit COVID-19 in vitro and were widely used in patients with COVID-19 until newer studies proved their lack of clinical efficiency.[84,89] While hydroxychloroquine has largely fallen out of favor as a primary therapeutic option for COVID-19,[90] a significant percentage of existing case studies in our review have documented its use in treatment. In the COVID-19-GBS cases included in this review, 25% were treated with lopinavir or ritonavir, and 43% were treated with hydroxychloroquine.[14,15,17–20,25,27,29] Further, antibiotics such as azithromycin and amoxicillin were also used in 33% of the cases we analyzed.[14,19,20,26,28,29] The body of evidence is increasing in support of the use of monoclonal antibodies (tocilizumab, casirivimab, and imdevimab) in general COVID-19 patients,[91,92] but given the limited data available in patients with COVID-19–related GBS, it is impossible to determine their clinical importance and outcome effects in this population.

Steroids for COVID-19–Related GBS

Steroids were administered to 12% of the cases that were included in our analysis.[20,29,83] Recent guidelines on the management of critically ill adults with COVID-19 recommends against routine use of steroids in mechanically ventilated adults without acute respiratory distress syndrome; however, they can be used in the presence of acute respiratory distress syndrome and in patients experiencing a refractory shock.[93] Studies suggest that corticosteroids may lead to prolonged viral shedding, hence the need to limit their routine use.[12,94] Available literature argues, nevertheless, that steroids could mitigate the fatal immune system activation seen in COVID-19,[83] based on their positive effects during the Ebola epidemic and as the first-line therapy for the postviral autoimmune response to herpes virus encephalitis.[83,95–97] A recent study showed that intravenous dexamethasone therapy for 10 days was associated with decreased 28-day mortality in COVID-19 patients receiving respiratory support but no benefit in those who did not require respiratory support. These findings suggest that the benefits of diminished immunopathologic activation may outweigh possible prolonged viral shedding in the subset of COVID-19 patients requiring ventilatory support.[98]

The effects of steroid use during the management of typical GBS patients has also been widely studied.[99] Consistent with earlier reports from GBS in general population,[99] our review indicates that systemic steroids does not affect the outcome, defined as mortality or ICU admission, in patients with COVID-19–related GBS.

IVIG Treatment for COVID-19–Related GBS

IVIG was used in 87% of the GBS cases included in our review. When treating the parainfectious form of GBS that co-occurs with COVID-19, IVIG, or plasma exchange may not only mitigate the neuroinflammatory response but may also prove beneficial in controlling the associated systemic inflammation and sepsis.[12,100,101] In this setting, however, a clinical concern is related to the association between IVIG and the risk of thromboembolism.[102] COVID-19 is commonly associated with a prothrombotic state, as evident from an increase in the D-dimer levels[103] and reported cases of venous thromboembolism and embolic strokes.[104] Current guidelines support the use of thromboprophylaxis with low molecular weight heparin, in COVID-19 patients without contraindications. Those with clinical evidence of a venous thromboembolism should be treated with therapeutic doses of anticoagulation.[105]

The most common dose for IVIG was 0.4 g/kg/d for 5 days.[4,11,14–18,20] Overall, outcomes with these medications were greatly variable and unpredictable. In patients treated with IVIG and some combination of hydroxychloroquine, antivirals, and antibiotics, outcomes ranged from complete recovery[4] to persistent lower extremity weakness[20] to death from progressive respiratory failure.[17] Despite uncertainty regarding COVID-19 and GBS management, one report recommended antiviral agents and IVIG as a reasonable therapeutic strategy at this point.[14]

Convalescent Plasma and Plasma Exchange Therapy

Only 7 reported cases of COVID-19–associated GBS have been treated with plasmapheresis alone or in addition to IVIG.[28,47] A randomized controlled trial in 2014 suggested that IVIG and plasmapheresis are equally effective in treating GBS.[106] Some experts, however, believe that plasmapheresis may be a better therapeutic approach and should be considered before IVIG in GBS. Historically, IVIG has been more widely used because of its availability and simplicity; it requires no specialized equipment and has a relatively low risk of adverse events.[106] There is also no evidence at this time that a combination therapy with IVIG and plasmapheresis is associated with better long-term or short-term outcomes compared with standard therapy in GBS patients.[106–109] Although the Surviving Sepsis Campaign panel of experts recommend against routine use of IVIG in COVID-19 patients, it may be reasonable to consider these treatment options in the subgroup of COVID-19 patients with a suspected or confirmed GBS.

Out of the cases we reviewed, none reported the use of convalescent plasma therapy in the treatment of COVID-19–related GBS. However, the use of convalescent serum therapy for COVID-19 is a rapidly emerging but controversial area of research. Plasma is collected from previously infected individuals to passively transfer antibodies to an infected patient, with the goal to improve clinical symptoms and mortality.[110] Plasma exchange with convalescent serum could be an innovative approach to the management of COVID-19–associated GBS. While current randomized controlled trials have not shown a significantly beneficial or detrimental effect of convalescent plasma on mortality in COVID-19 patients, lower mortality rates have been associated with those who receive plasma containing higher concentrations of neutralizing antibodies. Some studies suggest convalescent exchange may have the greatest benefit

TABLE 3. Characteristic and COVID-19–Related Data Among COVID-19–Related GBS Cases

References	Age (y)	Sex	Medical History/Comorbidities	COVID-19 Symptoms	COVID-19 Dx Method	COVID-19 Management	ICU Required	Ventilation Required	Time
Alberti et al[17]	71	M	HTN AAA (T) Lung cancer (T)	Fever Dyspnea	RT-PCR NP swab	Lopinavir/ritonavir Hydroxychloroquine	Yes	Yes	< 24 h
Camdessanche et al[18]	64	M	Rotator cuff tear at admission	Fever Cough	RT-PCR NP swab	Paracetamol Lopinavir/ritonavir	Yes	Yes	12 d
El Otmani et al[19]	70	F	RA	Cough	RT-PCR OP swab	Hydroxychloroquine Azithromycin	No	No	NA
Juliao et al[25]	61	M	NR	Fever Cough	RT-PCR NP swab	Lopinavir/ritonavir Hydroxychloroquine	No	No	NA
Marta-Enguita et al[26]	76	F	None	Fever Cough	RT-PCR Site NR	Amoxicillin/clavulanate Azithromycin	Yes	Yes	4 h
Ottaviani et al[15]	66	F	HTN	Fever Cough Dorsal rash	RT-PCR NP swab	Lopinavir/ritonavir Hydroxychloroquine	Yes	Yes	NR
Padroni et al[16]	70	F	NR	Fever Cough	RT-PCR NP swab	Supportive	Yes	Yes	4 d
Scheidl et al[4]	54	F	None	Hypogeusia Hyposmia	RT-PCR OP swab	None	No	No	NA
Sedaghat and Karimi[14]	65	M	DM2	Fever Cough Dyspnea	RT-PCR OP swab	Lopinavir/ritonavir Hydroxychloroquine Azithromycin	No	No	NA
Zhao et al[27]	61	F	NR	Fever Cough	RT-PCR OP swab	Umifenovir Lopinavir/ritonavir	No	No	NA
Toscano et al[28]	77	F	NR	Fever Cough Ageusia	RT-PCR NP swab	Acetaminophen	Yes	Yes	NR
Toscano et al[28]	23	M	NR	Fever Pharyngitis	RT-PCR NP swab	Amoxicillin	No	No	NA
Toscano et al[28]	55	M	NR	Fever Cough	RT-PCR NP swab	Azithromycin	Yes	Yes	2d
Toscano et al[28]	76	M	NR	Cough Hyposmia	RT-PCR NP swab	NR	No	No	NA
Toscano et al[28]	61	M	NR	Cough Ageusia Anosmia	Serum IgG	NA	Yes	Yes	5 d
Gigli et al[23]	53	M	NR	Fever Diarrhea	IgM/IgG Serum and CSF	NR	NR	NR	NR
Galan et al[29]	43	M	NR	URTI Diarrhea	RT-PCR Site NR	Lopinavir/ritonavir Hydroxychloroquine Amoxicillin Corticosteroids	No	No	NA
Virani et al[20]	54	M	*Clostridium difficile* colitis	Fever Cough Dyspnea	RT-PCR NP swab	Amoxicillin Corticosteroids Hydroxychloroquine	Yes	Yes	NR
Coen et al[30]	70	M	None	Cough Fatigue Myalgia	RT-PCR NP swab	NR	No	No	NA

Rana et al[31]	54	M	*Clostridium difficile* colitis HLD RLS	Fever Rhinorrhea Odynophagia	RT-PCR Site NR	Amoxicillin Corticosteroids Hydroxychloroquine Azithromycin	Yes	Yes	< 24 h
Arnaud et al[32]	64	M	NR	Cough Dyspnea Diarrhea Fever	RT-PCR NP swab	Cefotaxime Azithromycin Hydroxychloroquine	No	No	NA
Chan et al[33]	58	M	None	None	RT-PCR OP swab	Ceftriaxone Azithromycin	No	No	NA
Molina et al[34]	55	F	Dyslipidemia, active smoking	Fever Nonproductive cough Dyspnea	RT-PCR NP swab	Hydroxychloroquine Ceftriaxone Azithromycin	Yes	No	2 d
Farzi et al[35]	41	M	DM2	Cough Dyspnea Fever	RT-PCR NP swab	Lopinavir/Ritonavir Hydroxychloroquine	No	No	NA
Helbok et al[36]	68	M	None	Dry cough Headache Fatigue Myalgia Fever Anosmia Ageusia	Antibody testing	Oral methylprednisolone C-reactive protein Elevated erythrocyte sedimentation Plasma exchange	Yes	Yes	36 h
Hutchins et al[37]	21	M	HTN, prediabetes, class I obesity	Fever Cough Dyspnea Diarrhea Nausea Headache Sinonasal congestion	RT-PCR NP/OP swab	Plasma exchange	No	No	NA
Lantos et al[38]	36	M	left eye strabismus (asymptomatic for 30 y)	Fever Chills Myalgia	RT-PCR NP swab	Hydroxychloroquine	No	No	NA
Lascano et al[39]	52	F	None	Dry cough Fever Odynophagia Arthralgia Diarrhea	IgM/IgG, followed by RT-PCR NP swab	None	No	Yes	NA
Lascano et al[39]	63	F	DM2	Dry cough Shivering Odynophagia Breathing difficulties Chest pain	RT-PCR NP swab	None	No	No	NA
Lascano et al[39]	61	F	None	Productive cough Fever Myalgia Vasovagal syncope Diarrhea Nausea Vomiting	RT-PCR NP swab	None	No	No	NA

TABLE 3. (*continued*)

References	Age (y)	Sex	Medical History/Comorbidities	COVID-19 Symptoms	COVID-19 Dx Method	COVID-19 Management	ICU Required	Ventilation Required	Time
Reyes-Bueno et al[40]	51	F	None	Diarrhea Odynophagia Cough	IgG	Gabapentin	No	No	NA
Su et al[41]	72	M	Coronary artery disease, HTN, alcohol abuse	Mild diarrhea Anorexia Chills	RT-PCR NP swab	Sulfamethoxazole-trimethoprim	Yes	Yes	3 d
Webb et al[42]	57	M	HTN and psoriasis	Cough Headache Myalgia Malaise Fever Diarrhea	RT-PCR NP swab	Co-amoxiclav	Yes	Yes	3 d
Bigaut et al[43]	48	M	NR	Cough Asthenia Myalgia in legs Anosmia Ageusia Diarrhea	RT-PCR NP swab	None	No	No	NA
Bigaut et al[43]	70	F	NR	Anosmia Ageusia Diarrhea Asthenia Myalgia	RT-PCR NP swab	None	Yes	Yes	3 d
Assini et al[44]	55	M	NR	Anosmia Ageusia Fever Cough	RT-PCR OP swab	Idrossichlorochine Arbidol Ritonavir Lopinavir	Yes	Yes	3 d
Assini et al[44]	60	M	NR	Fever Cough	RT-PCR NP swab	Hydroxychloroquine Antiretroviral therapy Tocilizumab	No	Yes	NA
Bracaglia et al[45]	66	F	None	None	RT-PCR NP swab	Ritonavir Darunavir Hydroxychloroquine	No	No	NA
Ebrahimzadeh et al[46]	46	M	NR	Fever Sore throat Dry cough Dyspnea	RT-PCR NP swab	Hydroxychloroquine	No	No	NA
Ebrahimzadeh et al[46]	65	M	NR	NR	RT-PCR NP swab	NR	No	No	NA
Chan et al[47]	68	M	NR	Fever Upper respiratory symptoms	RT-PCR NP swab	Plasmapheresis	No	No	NA
Chan et al[47]	84	M	NR	Fever	RT-PCR NP swab	Plasmapheresis	No	Yes	NA
Sancho-Saldaña et al[48]	56	F	NR	Fever Dry cough Shortness of breath	RT-PCR NP swab	NR	Yes	No	5 d

Kilinc et al[49]	50	M	None	Dry cough	Fecal PCR, serum IgM, IgG	None	No	No	NA
Oguz-Akarsu[50]	53	F	None	Fever	RT-PCR NP swab	Hydroxychloroquine Azithromycin	No	No	NA
Pfefferkorn et al[51]	51	M	NR	Fever Flu-like symptoms Fatigue Dry cough	RT-PCR NP swab	Plasma exchange	No	Yes	NA
Hirayama et al[52]	54	F	Asthma	Cough Fever	RT-PCR OP swab	Betamethasone	No	No	NA
Korem et al[53]	58	F	Cervical spondylosis and disk herniation	Fever Cough Back pain	NR	Azithromycin	No	No	NA
Tiet and AlShaikh[54]	49	M	Sinusitis	Dyspnea Headache Cough	RT-PCR OP swab	None	Yes	No	NR
Defabio et al[55]	70	F	Reflex sympathetic dystrophy Fibromyalgia GERD Hiatal hernia Asthma	Fever Dyspnea Cough	NR	NR	No	No	NA
Curtis et al[56]	8	M	None	Dyspnea Cough	NR	None	Yes	Yes	NR
Gale et al[57]	58	M	HTN Hypercholesterolemia Myocardial infarction	Coryzal symptoms	RT-PCR Tracheal aspirate	Dexamethasone	Yes	Yes	2
Ameer et al[58]	30s	M	None	Fever Cough	RT-PCR NP, OP swabs	None	No	No	NA
Manganotti et al[59]	72	M	NR	Fever Dyspnea Hyposmia Ageusia	RT-PCR NP swab	Hydroxychloroquine Oseltamivir Darunavir Methylprednisolone Tocilizumab	Yes	Yes	NR
Manganotti et al[59]	72	M	NR	Fever Cough Dyspnea Hyposmia Ageusia	RT-PCR NP swab	Hydroxychloroquine Lopinavir-ritonavir Methylprednisolone	Yes	Yes	NR
Manganotti et al[59]	49	F	NR	Fever Cough Dyspnea Hyposmia Ageusia	RT-PCR NP swab	Hydroxychloroquine Lopinavir-ritonavir Methylprednisolone	NR	No	NR
Manganotti et al[59]	94	M	NR	Fever Cough GI symptoms	RT-PCR NP swab	Methylprednisolone	NR	No	NR
Manganotti et al[59]	76	M	NR	Fever Cough Dysuria Hyposmia Ageusia	RT-PCR NP swab	Hydroxychloroquine Oseltamivir Darunavir Methylprednisolone Tocilizumab Meropenam Linezolid Clarithromycin, doxycycline Fluconazole	Yes	Yes	NR

TABLE 3. (*continued*)

References	Age (y)	Sex	Medical History/Comorbidities	COVID-19 Symptoms	COVID-19 Dx Method	COVID-19 Management	ICU Required	Ventilation Required	Time
McDonnell et al[60]	54	M	DM2 Herniated nucleus pulposus at C6-C7, L2-L3, L3-L4, L4-L5 with disk bulges	Fever Ageusia	NP swab RT-PCR	Hydroxychloroquine 400 mg for 4 d	Yes	No	0
Diez-Porras et al[61]	54	M	HTN Obesity	Febrile syndrome Cough Myalgia	RT-PCR NP swab	Azithromycin, hydroxychloroquine, lopinavir/ritonavir	Yes	Yes	NR
Manji et al[62]	12	M	NR	Fever Cough Respiratory distress Hypoxia Tachycardia	RT-PCR NP swab	Empiric antibiotic coverage and other treatment modalities as required	Yes	Yes	NR
Bueso et al[63]	60	F	Migraines	Fever Cough Myalgia Dysgeusia Dyspnea	RT-PCR NP swab	Azithromycin Hydroxychloroquine	No	No	N/A
Zito et al[64]	57	M	NR	Dysgeusia Cough Fever	Positive serum SARS-CoV-2 IgG	NR	No	No	NA
Garnero et al[65]	65	M	NR	Pneumonia	NR	NR	NR	NR	NR
Garnero et al[65]	73	M	NR	Pneumonia	NR	NR	NR	NR	NR
Garnero et al[65]	55	M	NR	Pneumonia	NR	NR	NR	NR	NR
Garnero et al[65]	46	F	NR	Diarrhea	NR	NR	NR	NR	NR
Garnero et al[65]	60	M	NR	Pneumonia	NR	NR	NR	NR	NR
Garnero et al[65]	63	F	NR	Pneumonia	NR	NR	NR	NR	NR
Lowery et al[66]	45	M	Dyslipidemia HTN Crohn disease on adalimumab	Sinus congestion Cough Dyspnea	RT-PCR NP swab	200 mg hydroxychloroquine bid for 5 d	Yes	Yes	2
Hutchins et al[37]	21	M	HTN Prediabetes Obesity	Fever Cough Dyspnea Diarrhea Nausea, Headache Sinonasal congestion Dizziness Tachycardia	RT-PCR NP and OP swab	Supplemental O_2	No	No	NA
Atakla et al[67]	41	M	NR	Influenza syndrome Digestive disorder Anosmia Ageusia	RT-PCR NP swab	Azithromycin	Yes	Yes	NR
Abrams et al[68]	67	F	Breast cancer (T)	Cough Nausea	RT-PCR NP swab	NR	Yes	Yes	NR
Agha Abbaslou et al[69]	55	F	Unknown chronic lung disease	Cough Fever Chills Dyspnea	RT-PCR NP swab	Hydroxychloroquine (lopinavir/ritonavir)	Yes	Yes	2

Assini et al[70]	60	M	NR	Cough Fever	RT-PCR NP swab	Hydroxychloroquine Antiretroviral therapy Tocilizumab	Yes	Yes	3
Assini et al[70]	55	M	NR	Cough Fever Anosmia Ageusia	RT-PCR NP swab	Hydroxychloroquine Umifenovir Ritonavir Lopinavir	Yes	Yes	3
Chakraborty and Kumar[71]	75	M	NR	Dyspnea	RT-PCR NP swab	Culture-based antibiotics	Yes	Yes	< 1
Garcia-manzanedo et al[72]	77	M	HTN HLD COPD	NR	RT-PCR NP swab	Hydroxychloroquine lopinavir/ritonavir Piperacillin/tazobactam	Yes	Yes	NR
Liberatoret al[73]	49	M	HTN Testicular seminoma (T)	Cough Fever	RT-PCR NP swab	Hydroxychloroquine Lopinavir/ritonavir Ceftriaxone	Yes	Yes	4
Tard et al[74]	76	M	Isquemic cardiomyopathy AAA HTN HLD	Cough Asthenia	RT-PCR NP swab	NR	Yes	Yes	1
Dufour et al[75]	36	F	Obesity	Dyspnea Anosmia	RT-PCR NP swab	Supportive	No	No	NA
Nanda et al[76]	55	F	DM2 HTN CLT	Fever Abdominal pain	RT-PCR NP swab	NR	No	No	NA
Nanda et al[76]	72	M	HTN	Cough Fever	RT-PCR NP swab	Supportive	Yes	Yes	NR
Nanda et al[76]	55	M	DM2 HTN CKD	Cough Sore throat	RT-PCR NP swab	NR	No	No	NA
Nanda et al[76]	49	M	HTN	Fever	RT-PCR NP swab	NR	No	No	NA
Raahimi et al[77]	46	M	HTN	NR	RT-PCR NP swab	Supportive	No	Yes	NR

AAA indicates abdominal aortic aneurysm; CKD, chronic kidney disease; CLT, chronic lymphocytic thyroiditis; COPD, chronic obstructive pulmonary disease; COVID-19, Coronavirus Disease 19; CSF, cerebrospinal fluid; DM2, type 2 diabetes mellitus; Dx, diagnostic; F, female; GBS, Guillain-Barré syndrome; GERD, gastroesophageal reflux disease; GI, gastrointestinal; HLD, hyperlipidemia; HTN, hypertension; ICU, intensive care unit; M, male; MRI, magnetic resonance imaging; NA, not applicable; NE, not evocable; NP, nasopharyngeal; NR, not reported; OP, oropharyngeal; RA, rheumatoid arthritis; RLS, restless leg syndrome; RT-PCR, reverse transcription-polymerase chain reaction; T, treated; Time, time between hospital admission and ICU admission; URTI, upper respiratory tract infection.

TABLE 4. GBS-related Data Among COVID-19–Related GBS Cases

References	GBS Symptoms	ND	CN Involvement	AD Symptoms	Time	MRC and DTR	CSF	GBS Subtype	GBS Management	IVIG-D	Outcome
17	Paresthesia Tetraparesis Hypesthesia Areflexia	3	No	No	4	3/5 UE 2/5 LE DTR absent global (S)	P: 54 mg/dL L: 9 cells/μL	NR	IVIG (0.40 g/kg/d for 5 d)	3	Deceased (severe respiratory failure)
18	Paresthesia Tetraparesis Areflexia	9 (I)	Dysphagia	No	11	2/5 PUE 4/5 DUE 2/5 LE DTR absent global (S)	P: 166 mgl/dL L: NR	AIDP	IVIG (0.40 g/kg/d for 5 d); LMWH	3	ICU admission and mechanically ventilated (respiratory insufficiency)
19	Paresthesia Quadriplegia Areflexia	10	No	No	3	NR	P: 100 mg/dL L: NR	AMSAN	IVIG (2 g/kg for 5 d)	10	No significant neurological improvement after 1 wk of treatment
25	FDP	1	FDP	No	10	NR Absent blink reflex bilaterally (S)	P: 44 mg/dL L: absent	FDP	Prednisone	NA	Small improvement of symptoms bilaterally after 2 wk
26	Lumbago Paresthesia Tetraparesis Areflexia	10	Dysphagia	No	8	0/5 PUE 4/5 DUE 0/5 PLE 2-3/5 DLE DTR absent global (S)	P: NR L: NR	NR	None	NA	Deceased (severe respiratory failure)
15	Paraparesis Paraplegia Areflexia	3	Unilateral FNP	No	10	Initial 4/5 DUE(S)	P: 108 mg/dL L: absent	NR	IVIG (0.4 g/kg for 5 d)	3	Did not improve with treatment, progressively developed proximal weakness in all extremities, dysesthesia, and unilateral facial palsy
16	Paresthesia Tetraparesis Areflexia	1	No	No	24	4/5 DUE 4/5 DLE DTR absent global (S)	P: 48 mg/dL L: 1 cell/L	NR	IVIG (400 mg/die for 5 d)	3	Worsening of muscle weakness causing respiratory failure
4	Paresthesia Paraparesis Areflexia	10	Dysphagia	No	21	3/5 PLE 4/5 DLE DTR absent LE(S)	P: 140 g/L L: normal	AIDP	IVIG (0.40 g/kg/d for 5 d)	12	Almost complete recovery of neurological symptoms after the treatment
14	Tetraparesis FDP Areflexia	5	FDP	No	9	2/5 PUE 3/5 DUE 1/5 PLE 2/5 DLE Grade 3 HB DTR absent global (S)	Not performed	AMSAN	IVIG (0.40 g/kg/d for 5 d)	14	NR
27	Tetraparesis Areflexia	1	No	No	7(I)	4/5 PUE 4/5 DUE 3/5 PLE 3/5 DLE DTR absent LE(S)	P: 124 mg/dL L: 5 cells/dL	AIDP	IVIG (dose NR)	4	Normal muscle strength in both UE and LE and return of DTR in LE

27	Paresthesia Tetraplegia Facial paresis Areflexia	1	Dysphagia Tongue weakness	No	7	NR	P: 101 mg/dL L: 4 cells/mm^3	AMSAN	IVIG (2 cycles; dose NR)	2	Persistence of severe UL weakness, LL paraplegia and dysphagia
27	Paresthesia FDP Ataxia Areflexia	< 1	FDP	No	10	NR	P: 123 mg/dL L: absent	AMSAN	IVIG (1 cycle; dose NR)	1	Decreased ataxia, disappearance of limb paresthesia, and mild decrease of facial weakness
27	Tetraparesis Facial paresis Respiratory failure Areflexia	1	FDP	No	10	NR	P: 193 mg/dL L: absent	AMAN	IVIG (2 cycles; dose NR)	4	Neuromuscular respiratory failure, progression to flaccid tetraplegia. His condition remained critical after 1 mo of neurological onset
27	Tetraparesis Ataxia Areflexia	1	No	No	5	NR	P: normal L: absent	AIDP	IVIG (1 cycle; dose NR)	7	Mild motor improvement after treatment, more evident in UE. However, patient unable to stand 1 mo after symptoms onset
27	Facial paresis Paraplegia Respiratory failure	1	Facial paresis Dysphagia	No	7	NR	P: 40 mg/dL L: 3 cells/mm^3	AIDP	IVIG (1 cycle; dose NR); plasmapheresis	2	Neuromuscular respiratory failure with concomitant A*cinetobacter* pneumonia during IVIG treatment. Patient still tetraplegic and ventilation dependent 4 wk after neurological onset
28	Paresthesia Ataxia	NR	No	No	NR	NR	P: 1928 mg/dL L: 2.6 cells/μL	AIDP	NR	NA	NR
23	Tetraparesis Hypoesthesia Facial paresis Dysphagia Areflexia	NR	Facial paresis Dysphagia	No	10	3/5 PUE 3/5 PLE 4/5 DUE 4/5 DLE DTR absent global (S)	NR	NR	IVIG (dose NR)	NR	Worsening of motor function during the first 2 d of hospitalization, adding facial paresis and dysphagia to the previous symptoms. Slight improvement of neurologic and respiratory symptoms afterwards
29	Tetraparesis Areflexia	2	No	UR	8	3/5 UE 2/5 LE DTR absent global (S)	Not performed	NR	IVIG (0.40 g/kg/d for 5 d)	2	Improvement of respiratory symptoms and UE weakness. LE weakness persisted after treatment
20	Paraparesis Allodynia Areflexia	4	No	UR Constipation	10	MRC NR DTR absent global (S)	Albumin-cytologic dissociation. Levels not reported	AIDP	IVIG (0.40 g/kg/d for 5 d)	5	Rapid improvement of neurological symptoms after treatment
30	Tetraparesis Areflexia FDP	NR	FDP	UR Resting tachycardia	14	3/5 PUE 4/5 DLE 0-1/5 PLE 0-1/5 DLE(S)	Not performed	AIDP	IVIG (0.40 g/kg/d for 5 d)	NR	Improvement of respiratory symptoms. Worsening of neurological symptoms at follow up progressing to tetraparesis and FDP
31	Areflexia Paraparesis Decreased proprioception	4	No	No	21	NR	P: 1.65 g/L L: absent	NR	IVIG for 5 d (dose NR)	NR	NR

TABLE 4. (*continued*)

References	GBS Symptoms	ND	CN Involvement	AD Symptoms	Time	MRC and DTR	CSF	GBS Subtype	GBS Management	IVIG-D	Outcome
32	Areflexia FDP Dysarthria	NR	Yes	No	No COVID-19 symptoms at onset of neurological symptoms	NR	P: 1.00 g/L L: 4×10^6 cells/L	AIDP	IVIG (0.40 g/kg/d for 5 d)	2	The patient was discharged from hospital 2 d after completing IVIG. At that time, he had slight movements of his facial muscles, and the distal paresthesias of his lower extremities were unchanged
33	Paresthesias Quadriparesis FDP Dysphagia	1	Yes	No	14	2/5 left UE 3/5 right UE 4/5 LE DTR absent global (S)	P: 0.86 g/L L: 3 cells/mm^3	AMSAN	IVIG (0.40 g/kg/d for 5 d)	NR	After 5 d of ICU admission, she was discharged to the neurology ward for clinical improvement with a motor balance of 5/5 (right arm), 3/5 (left arm), and 4/5 (both legs), with paresthesias persisting
34	Hyporeflexia Hypoesthesia Decreased proprioception	7	No	No	10	4/5 UE 3/5 LE DTR absent LE(S)	NR	AIDP	IVIG (0.40 g/kg/d for 5 d)	7	On discharge patient could ambulate but with some residual weakness in lower extremities, so was referred for rehabilitation clinic
35	Hypoesthesia Dysesthesia Ataxia Paraparesis	2	No	No	14	2/5 PUE 4/5 DUE 2/5 PLE 4/5 DLE DTR absent global (S)	P: 64 mg/dL L: 2 cells/mm^3	AIDP	IVIG 30g total dose for 1 d, followed by 4 cycles of plasma exchange	3	The patient improved gradually and was transferred to a neurorehabilitation facility 4 wk after symptom onset, where he regained mobility without significant help another 4 wk later
36	Dysarthria Hypogeusia Facial paresis Hypoesthesia Paraparesis	1	Yes	No	16	4/5 PUE 4/5 PLE DTR absent global (S)	P: 46 mg/dL L: absent	Bifacial weakness with paresthesias (BFP)	5 cycles plasma exchange	NR	Tolerated plasma exchange well with slight improvement in facial weakness and paresthesia. Discharged to inpatient rehabilitation
37	Ophthalmoparesis Ataxia Hyporeflexia Hypoesthesia	NR	Yes	No	2	NR	NR	MFS	IVIG (dose and duration NR)	NR	Subsequent improvement of neurological symptoms after IVIG treatment. Patient was discharged after 4 d of hospitalization
38	Quadriparesis Ataxia Paresthesia Dysgeusia Cacosmia	NR	No	Yes	15	NR	P: 60 mg/dL L: 3 cells/mm^3	AIDP	IVIG (0.40 g/kg/d for 5 d)	2	At 5 d, improvement of tetraparesis. Able to stand up with assistance
38	Tetraparesis Paresthesia Areflexia	NR	No	No	7	NR	P: 40 mg/dL L: 2 cells/mm^3	AIDP	IVIG (0.40 g/kg/d for 5 d)	10	At 5 d, dismissal with full motor recovery. Persistence of lower limb areflexia and distal paresthesia
38	Facial diplegia Paresthesia Paraparesis Dysphagia Areflexia	NR	Yes	Yes	22	NR	P: 140 mg/dL L: 4 cells/mm^3	AIDP	IVIG (0.40 g/kg/d for 5 d)	2	At 5 d, improvement of tetraparesis and ability to walk with assistance. Persistence of neuropathic pain and distal paresthesia

39	Diplopia Paraparesis Facial paresis Areflexia	12	Yes	Yes	15	3/5 PLE 2/5 DLE DTR absent global (S)	P: 70 mg/dL L: 5 cells/mm^3	MFS	IVIG (0.40 g/kg/d for 5 d); gabapentin 900 mg/d	13	Progressive improvement in facial and limb paresis, diplopia and pain. Patient still on neurological rehabilitation
40	Paresthesia Quadriplegia Areflexia	1	No	Yes	6	3/5 PUE 3/5 PLE DTR absent global (S)	P: 313 mg/dL L: 1 cell/mm^3	AIDP	IVIG (2 g/kg divided over 3 d)	3	Transferred to ICU and intubated. Developed ventilator-associated pneumonia (*Stenotrophomonas maltophilia*). Remains in the ICU with severe weakness
41	Quadriparesis Hypoesthesia	1	No	No	6	4/5 UE 3/5 PLE 2/5 DLE DTR absent global (S)	P: 51 mg/dL L: normal cell counts	AIDP	IVIG (0.40 g/kg/d for 5 d)	2	Intubated and ventilated in the ICU. Treated for aspiration pneumonia. Oxygen requirements and inflammatory markers have improved; patient currently being weaned-off ventilation
42	Paresthesia Ataxia FNP	4	Yes	NR	21	4/5 UE 3/5 DLE DTR absent global (S)	P: 0.94 g/L L: normal cell count	NR	IVIG started on day 5 (2 g/kg)	5	Discharged home with progressive improvement
42	Tetraparesis Dyspnea FNP	3	Yes	NR	10	2/5 PLE 4/5 DLE DTR absent LE(S)	P: 1.06 g/L 6×10^6/L	NR	IVIG (2 g/kg) started day 4 of neurological symptoms	4	Condition improved slowly with physiotherapy, needing transfer to rehabilitation center
43	Dysphagia Facial paresis	NR	Yes	NR	20	NR	P: normal L: NR	GBS/MFS overlap syndrome	IVIG (0.4 g/kg/d for 5 d)	NR	Very rapid clinical response in swallowing, speech, tongue mobility and strength, and eyelid ptosis
44	Paraparesis	NR	NR	Paralytic ileus Loss of blood pressure control,	23	NR	P: normal L: NR	ASMAN	IVIG (0.4 g/kg/d for 5 d)	3	Autonomic symptomatology significantly improved—remission of gastroplegia and recovery of intestinal functions. Persistent osteotendinous hyporeflexia but slight improvement in foot drop
45	Hyposthenia Paresthesia Dysphagia Dysarthria FDP	NR	Yes	NR	0	4/5 PUE 3/5 DUE 2/5 PLE 1/5 DLE DTR absent global (S)	P: 245 mg/dL L: 13/mm^3	NR	IVIG for 5 d	NR	Immediately after IVIG, improved to MRC scale of 4/5 in distal upper limbs and 3/5 in both proximal and distal lower limbs, FDP developed, ultimately transferred to rehabilitaiton care
46	Paraparesis Paresthesia FNP	2	Yes	NR	18	4/5 UE 4/5 PLE 3/5 DLE DTR absent global (S)	P: 78 mg/dL L: 4/mm^3	NR	Did not receive treatment	NA	After 16 d of close monitoring, his muscle forces improved to near normal
46	Paraparesis Paresthesia	4	No	NR	10	4/5 UE 2/5 PLE 3/5 DLE DTR absent at LE, decreased at UE(S)	NR	NR	IVIG (dose NR)	NR	Discharged after 14 d, muscle forces were 4/5 in all extremities

TABLE 4. (*continued*)

References	GBS Symptoms	ND	CN Involvement	AD Symptoms	Time	MRC and DTR	CSF	GBS Subtype	GBS Management	IVIG-D	Outcome
47	Paraparesis Paresthesia Facial paresis Dysphagia Dysarthria	5	Yes	NR	18	4/5 PLE DTR absent at LE(S)	P: 226 mg/dL L: 3 cells/mm^3	NR	Plasmapheresis	NA	dysphagia has resolved and 28 d after GBS symptom onset, he can now ambulate with minimal assistance
47	Paraparesis Paresthesia Facial paresis Respiratory failure	7	Yes	NR	23	3/5 PUE 4/5 PLE DTR absent at LE(S)	P: 67 mg/dL L: 1 cell/mm^3	NR	IVIG (dose NR); plasmapheresis	NR	Underwent tracheostomy and 25 d after GBS symptom onset, he remains quadriparetic with intermittent autonomic dysfunction, but is slowly being weaned from the ventilator
48	Tetraparesis Paresthesia FNP Dysphagia	2 (I)	Yes	NR	15	2/5 all extremities DTR absent global (S)	P: 0.86 g/L L: 3 cells/mm^3	NR	IVIG (2 g/kg/5 d)	NR	Started recovering by day 7 after the onset of weakness
49	FDP Paraparesis	4	Yes	NR	28	MRC NR DTR absent global (S)	P: normal L: normal	AMSAN	IVIG (2 g/kg/5 d)	7	Recovery started within days of treatment. On day 14 the patient was discharged with a mild proximal weakness in the lower extremities and FDP
78	Dysarthria Paraparesis	3	Yes	NR	(I)# NR	4/5 LE DTR absent at LE(S)	P: 32.6 mg/dL L: normal	NR	Plasmapheresis	NA	Two weeks after the onset of symptoms, the neurological findings had improved markedly and she was able to walk without assistance
51	Tetraparesis Paresthesia FDP	2	Yes	NR	14	2-4/5 all extremities DTR absent global (S)	P: normal L: 9 cell/μL	AIPD	IVIG (30 g daily for 5 d)	< 1	Thirty-one days after admission signs of motor improvement with regressive facial and hypoglossal paresis but still needed mechanical ventilation
52	Paresthesia Asthenia	NR	No	NR	20	4/4 PLE 5/5 DLE 4/4 UE	NR	NR	Did not receive treatment	NA	Symptoms improved with discharge home on day 18
53	Paresthesia Asthenia Lumbago Ascending quadriparesis	NR	No	No	14	3/5 LE 4/5 UE	P: 117 mg/dL L: 2 cumm	NR	2 mg/kg IVIG for 4 d	NR	Symptoms improved significantly, discharged to acute rehabilitation facility
54	Paresthesia Facial diplegia Asthenia	NR	Facial diplegia	None	21	1/5 LE 3/5 PUE 2/5 DUE DTR absent global (S)	P: > 1.25 g/L L: 1×106 cells/L	AIDP	IVIG 0.4 g/kg for 5 d	NR	Gradually improved, able to mobilize unassisted with neurorehabilitation and 15 wk after IVIG treatment
55	Paresthesia Dysautonomia	NR	No	UR	3 mo	4/5 LE DTR absent LE (S)	P: 127 mg/dL L: 8/cmm	NR	IVIG	NR	Motor and sensation largely returned at discharge

56	Paraplegia Urinary retention	NR	Esotropia, dysconjugate gaze	UR	NR	3/5 UE 2/5 LE DTR absent global (S)	P: 620 mg/dL L: 1 cell/cumm	AIDP	IVIG 2 g/kg over 48 h	2	Extubated on hospital day 5, transferred to inpatient rehabilitation 3 wk after IVIG completion
57	Asthenia Paresthesia	2	Weak cough Dysphagia Dysarthria	Labile blood pressure Fecal retention	13	5/5 UE 4/5 LE	P: 1.5 g/L L: absent	AIDP	IVIG 0.4 g/kg	NR	Extubated on hospital day 18, discharged to community rehabilitation unit, then to home
58	Asthenia Areflexia Paresthesia	1	NR	NR	4	3/5 PUE 2/5 DUE 3/5 LE DTR absent global (S)	P: 1.14 g/L L: <1/mm^3	AMSAN	IVIG 0.4 g/kg/d for 5 d	NR	Discharged on hospital day 12, significant improvement with residual weakness in hands and feet
59	Tetraparesis	NR	Facial paresis	NR	18	MRC: NR DTR absent global (S)	P: 52 mg/dL L: 1 cell/mm^3	NR	IVIG cycle (0.4 g/kg for 5 d)	NR	Progressive improvement of tetraparesis after initiating IVIG therapy
59	Tetraparesis	NR	None	NR	30	MRC: NR DTR absent global (S)	P: 40 mg/dL L: 1 cell/mm^3	NR	IVIG cycle (0.4 g/kg for 5 d)	NR	Progressive improvement of asthenia after initiating IVIG therapy
59	Ophthalmoplegia Ataxia	NR	Ophthalmoplegia Facial hypoesthesia	NR	14	MRC: NR DTR absent global (S)	P: 72 mg/dL L: 5 cell/mm^3	NR	IVIG cycle (0.4 g/kg for 5 d)	NR	Progressive improvement of neurological symptoms after initiating IVIG therapy
59	Lower extremity Asthenia	NR	None	NR	33	MRC: NR DTR diminished global (S)	Not performed	NR	Methylprednisolone 60 mg for 5 d	NR	Stationary; no significant improvement of neurological symptoms after initiating IVIG therapy
59	Asthenia Facial paresis Diplopia	NR	Facial paresis Diplopia	NR	22	MRC: NR DTR absent global (S)	P: 53 mg/dL L: 2 cell/mm^3	NR	IVIG cycle (0.4 g/kg for 5 d)	NR	Progressive improvement of neurological symptoms after initiating IVIG therapy
60	Dysphagia Asthenia Paresthesias Facial diplegia Dysphagia Dysarthria	2	Facial diplegia and paresthesias Dysphagia Dysarthria	NR	1	4/5 UE 3/5 PLE DTR: +1 throughout	P: 74 mg/dL L: absent	Recurrent GBS secondary to COVID-19 infection or CIDP	IVIG cycle (0.4 g/kg for 5 d)	3	Residual asthenia and hypoxia resolved weeks after discharge; regained full muscle strength but severe persistent paresthesias of the medial left knee up to the medial thigh
61	Hypoesthesia Paraparesis	1	None	NR	5	2/5 left UE 3/5 right DUE DTR absent global (S)	P: 52 mg/dL L: absent	ADP	IVIG cycle (0.4 g/kg for 5 d)	NR	Discharged from ICU 14 d after intubation with residual severe flaccid tetraparesis, bilateral facial palsy, and dysphagia; underwent 7 wk of rehabilitation and now able to walk independently with support
62	Quadriparesis Facial paresis Asthenia	5	NR	NR	7	1/5 LE 2/5 UE DTR absent global (S)	NR	NR	IVIG cycle (0.4 g/kg for 5 d)	NR	Respiratory and neurological status improved 5 d after admission after course of IVIG; planned for weaning and extubation on day 6 but patient unintentionally self-extubated and expired from cardiac arrest

TABLE 4. (*continued*)

References	GBS Symptoms	ND	CN Involvement	AD Symptoms	Time	MRC and DTR	CSF	GBS Subtype	GBS Management	IVIG-D	Outcome
63	Paresthesias Asthenia Respiratory failure	NR	NR	Loss of blood pressure and heart rate control Fecal incontinence Urinary retention	22	2/5 LE 3/5 UE 3/5 neck flexion and extension DTR: absent in LE, diminished in UE	P: 197 mg/dL L: absent	NR	IVIG cycle (0.4 g/kg for 5 d), enoxaparin 30 mg bid	NR	Improvement in respiratory and neurological function; ambulating with assistance 2 mo after admission; persistent neuropathic pain in lower extremities
64	Paresthesias Asthenia Gait disturbance	13	No	No	18	3/5 right DLE 4/5 left DLE 4/5 DUE DTR: diminished global (S)	P: normal L: normal	AMSAN	IVIG cycle (0.4 g/kg for 5 d)	16	After IVIG, significant improvement in asthenia but persistent gait disturbance; patient transferred to rehabilitation and slowly regained ability to walk unassisted after 1 mo at discharge
65	NR	NR	NR	NR	NR	NR	NR	AIDP	IVIG	NR	NR
65	NR	NR	NR	NR	0	NR	P: 0.6 g/L L: NR	Classical GBS	IVIG	NR	NR
65	NR	NR	Yes	NR	20	NR	P: 0.3 g/L L: NR	NFS-GBS Overlap	IVIG	NR	NR
65	NR	NR	NR	NR	3	NR	P: 1 g/L L: NR	Classical GBS	IVIG	NR	NR
65	NR	NR	NR	NR	20	NR	P: 0.2 g/L L: NR	AMSAN	IVIG	NR	NR
65	NR	NR	NR	NR	15	NR	P: 0.9 g/L L: NR	AMSAN	IVIG	NR	NR
66	Ataxia Asthenia Paresthesias Dysphagia Quadriparesis Respiratory failure	NR	Bilateral ptosis, CN 3,4,6 deficits Dysphagia	NR	14	2/5 right UE, LE 0/5 left UE DTR absent global (S)	P: normal L: normal	MFS-GBS overlap	IVIG cycle (0.4 g/kg for 5 d)	4	5 wk after admission, transferred to LTAC for vent weaning and PT, now 5.5 postdiagnosis and tolerating few hours per day of pressure support; patient able to control head, some distal extremity, extraocular, and tongue movements
79		NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
67	FDP Pharyngeal paralysis Dysphagia Quadriparesis	4	FDP Pharyngeal paralysis Dysphagia	Urinary incontinence	5 to 10	2/5 PLE 1/5 DLE 3/5 UE DTR diminished global (S)	P: 64 mg/dL L: normal	AIDP	IVIG cycle (0.4 g/kg for 5 d)	NR	Marked neurological improvement on hospital day 16 with residual urinary incontinence; patient transferred to physiotherapy unit for rehabilitation
68	Paresthesia Tetraparesis	1	No	UR	5	3/5 UE 3/5 LE DTR absent global (S)	P: 222 mg/dL L: 0 cells/μL	NR	5 cycles plasma exchange	NA	Hospitalization subsequently complicated by streptococcal bacteremia requiring antibiotics. Discharged at day 30 with improved neurological condition

Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.

69	Paraparesis	26 (I)	NR	No	31	3/5 LE DTR absent LE (S)	P: 48 mg/dL L: 0 cells/μL	AMSAN	IVIG (dose NR)	5	Deceased due to ARDS
70	Paraparesis	NR	NR	UR Loss of blood pressure control	20	MRC NR DTR absent global (S)	P: normal range L: NR	AMSAN	IVIG (0.4 g/kg/d)	NR	After 5 d, the vegetative symptomatology significantly improved, with the remission of gastroplegia and recovery of intestinal functions
70	Ptosis Dysphagia Dysphonia	20 (I)	Yes	No	20	5/5 both UE and LE DTR decreased (S)	P: normal L: NR	MFS	IVIG (0.4 g/kg/d) 5 d	NR	The first clinical improvements occurred during the fifth day of treatment, with progressively improving trend and complete remission on swallowing and feeding
71	Tetraparesis	1	NR	No	< 1	2/5 both UE and LE DTR decreased global (S)	P: 39 mg/dL L: 1 cell/μL	AIPD	IVIG (0.4 g/kg/d) 5 d	NR	Patient was extubated on the 17th day of illness. Subsequently, he was discharged from the hospital 24th day of illness with no residual muscle weakness
72	FDP Dysarthria Dysphagia	< 1	Yes	No	7	5/5 both UE and LE	P: 77 mg/dL L: NR	AIPD	IVIG (0.4 g/kg/d) 5 d	NR	Progressive clinical improvement was observed after 2nd dose of IVIG, leading to discharge
73	Paraparesis	27 (I)	Yes	Hypertensive crisis Tachyarrhythmia-bradyarrythmia	36	3/5 UE 4/5 LE DTR decreased global (S)	P: 48 mg/dL L: 0 cells/μL	AIPD	Supportive	NA	Forty days from fever the patient showed a spontaneous improvement of the clinical picture, at day 56 after admission only mild weakness of the deltoid bilaterally and left biceps was evident
74	Tetraplegia Paresthesis FDP	< 1	Yes	No	10	Initial MRC NR DTR absent global (S)	P: 1 g/dL L: 0 cells/μL	NR	IVIG (0.4 g/kg/d) 5 d Plasma exchange (4 cycles)	NR	Following IVIG and steroids, a partial clinical improvement was seen. Two months after onset, FDP was still severe but improvements in muscle strength continued in axial, proximal and distal segments
75	Paraparesis	3	No	No	21	5/5 UE 3/5 LE DTR absent at LE (S)	P: 20 mg/dL L: 0 cells/μL	NR	IVIG (0.4 g/kg/d) 5 d	NR	After 1 wk of hospitalization, her strength began to improve. She was eventually discharged home after 10 d in the hospital. A follow-up phone call after 3 wk, found that that patient was already ambulating short distances with minor help
76	Tetraparesis	3	No	No	10	4/5 UE 2/5 LE DTR absent global (S)	P: 54 mg/dL L: 5 cells/μL	AMAN	IVIG (0.4 g/kg/d) 5 d	NR	Patient was discharged after 10 d of hospital stay with grade 4/5 power in both lower limbs and grade 4+/5 power in both upper limbs

TABLE 4. (*continued*)

References	GBS Symptoms	ND	CN Involvement	AD Symptoms	Time	MRC and DTR	CSF	GBS Subtype	GBS Management	IVIG-D	Outcome
76	Tetraparesis	3	No	No	6	3/5 UE 2/5 LE DTR absent global (S)	P: 74 mg/dL L: 0 cells/μL	AMSAN	IVIG (0.4 g/kg/d) 5 d	NR	Worsening respiratory distress, patient expired after 7 d of hospitalization
76	Tetraparesis	3	No	No	7	4/5 UE 3/5 LE DTR absent at LE (S)	P: 84 mg/dL L: 5 cells/dL	AMSAN	IVIG (0.4 g/kg/d) 5 d	NR	Good improvement (able to walk independently at discharge)
76	FNP Paraparesis	4	Yes	No	10	5/5 UE 3/5 LE DTR absent at LE	P: 52 mg/dL L: 5 cells/dL	AMAN	IVIG (0.4 g/kg/d) 5 d	NR	Good improvement (able to walk independently at discharge)
77	Paraparesis Parestesis	7	No	No	53	5/5 UE 3/5 LE DTR absent at LE	P: 127 mg/dL L: <2 cells/dL	AIDP	IVIG (0.4 g/kg/d) 5 d	NR	Three months after his hospital discharge, he has been able to walk independently, occasionally using a stick for longer distances

AAA indicates abdominal aortic aneurysm; AD, autonomic dysregulation; AIDP, acute inflammatory demyelinating polyradiculoneuropathy; AMAN, acute motor axonal neuropathy; AMSAN, acute motor-sensory axonal neuropathy; ARDS, acute respiratory distress syndrome; CN, cranial nerve; COVID-19, Coronavirus Disease 19; CSF, cerebrospinal fluid; DLE, distal lower extremities; DTR, deep tendon reflexes; DUE, distal upper extremities; FDP, facial diplegia; FNP, facial nerve palsy; GBS, Guillain-Barré syndrome; HB, House-Brackmann Facial Paralysis Scale; (I), symptoms started inversely; ICU, intensive care unit; IVIG, intravenous immunoglobulin; IVIG-D, days between neurological symptom's onset and the start of IVIG treatment; L, leukocytes; LE, lower extremities; LMWH, low–molecular-weight heparin; LTAC, Long-term acute care; MFS, Miller-Fisher syndrome; MRC, Medical Research Council Scale for Muscle Strength; NA, not applicable; ND, days between neurological symptoms and hospital admission; NR, not reported; P, protein; PLE, proximal lower extremities; PT, physical therapy; PUE, proximal upper extremities; (S), symmetric; Time, days between the onset of COVID-19 symptoms and onset of neurological symptoms; UE, upper extremities; UR, urinary retention.

TABLE 5. GBS Diagnostic Data Among COVID-19–Related GBS Cases

References	Antigangliosides Antibodies in Serum	CSF PCR Analysis for COVID-19	Motor nerve Conduction Study (*V, F Waves*)	Biological Test for Infections Other Than COVID-19	MRI Findings Related to GBS
17	NR	Negative	*V* = decreased at CPN, RN Absent at TN *F waves* = not performed at UE and LE	NR	Not performed
18	Negative	NR	*V* = decreased at right MN, as well as bilateral UN, CPN, and TN *F waves* = absent at CPN, TN bilaterally	Negative for *Campylobacter jejuni*, *Mycoplasma pneumoniae*, *Salmonella enterica*, CMV, EBV, HSV1, and 2, VZV, influenza virus A and B, HIV, and hepatitis E	Not performed
19	NR	Negative	*V* = normal in all extremities *F waves* = NR Marked reduction or absence of EP in both motor and sensory nerves	NR	Not performed
25	NR	Negative	Not performed	NR	None
26	NR	NR	Not performed	NR	Not performed
15	Negative	Negative	*V* = decreased at left TN and left CPN *F waves* = absent at left TN, CPN and right MN	NR	Not performed
16	NR	NR	*V* = decreased at MN, UN and TN bilaterally, NE at CPN bilaterally *F waves* = absent at MN, UN, TN, and CPN bilaterally	Negative for *Mycoplasma pneumoniae, Legionella pneumophila*, *Streptococcus pneumoniae*, HSV, VZV, EBV, CMV, HIV-1, *Borrelia burgdorferi*	Not performed
4	NR	NR	*V* = normal at TN, MN, UN bilaterally *F waves* = normal at TN with pathologic intermediate latency responses (complex A-waves) bilaterally	Negative for Lyme disease, *Campylobacter jejuni*, HIV	None
14	NR	NR	*V* = No response at MN, UN and CPN *F waves* = no response at TN	NR	None
27	NR	NR	*V* = normal in UE and LE *F waves* = absent at left UN, and TN bilaterally	NR	Not performed
28	Negative	NR	*V* = normal at UN and TN *F waves* = absent at UN and TN	NR	Enhancement of caudal nerve roots
28	NR	NR	*V* = decreased at TN *F waves* = absent at TN	NR	Enhancement of FN bilaterally
28	Negative	NR	*V* = normal at UN and TN *F waves* = absent at UN and TN	NR	Enhancement of caudal nerve roots
28	NR	NR	*V* = decreased at TN *F waves* = = normal at UN and TN	NR	None
28	Negative	NR	*V* = decreased at TN *F waves* = absent at TN	Negative for *Campylobacter jejuni*, EBV, CMV, HSV, VZV, influenza, HIV Patient developed Acinetobacter pneumonia during ICU stay	None
23	Negative	Negative	NR	Negative for influenza virus A and B, *Borrelia* and TBE	NR
29	NR	NR	*V* = decreased, nerves NR *F waves* = increased minimal latency at right L5 and S1 roots	NR	Not performed

TABLE 5. (*continued*)

References	Antigangliosides Antibodies in Serum	CSF PCR Analysis for COVID-19	Motor nerve Conduction Study (*V, F Waves*)	Biological Test for Infections Other Than COVID-19	MRI Findings Related to GBS
20	NR	NR	Not performed	Positive for Rhinovirus (NP swab)	None
30	Negative	Negative	*V* = NR *F waves* = decreased persistence or absence in tested nerves Nerves NR	NR	None
31	NR	NR	*V* = decreased Nerves NR *F waves* = absent Nerves NR	Negative for Influenza virus A and B	None
32	Negative	Negative	*V* = decreased in bilateral MN, UN, TN, CPN *F waves* = Absent in all 4 limbs	Negative for *Campylobacter jejuni*, HIV, syphilis, CMV, and EBV	Not performed
33	NR	Negative	*V* = NR *F waves* = Absent in the left TN	NR	Bilateral facial nerve enhancement involving the labyrinthine segment, tympanic segment, mastoid segment, and extracranial facial nerve
34	NR	Negative	*V* = NR *F waves* = Absent in the bilateral TN and UN	NR	Slight leptomeningeal enhancement at the brainstem and cervical cord
35	NR	NR	*V* = Decreased at left TN, bilateral MN and UN *F waves* = Absent in the bilateral TN and CPN	NR	NR
36	Negative	Negative (positive for anti-SARS-CoV-2-antibodies)	*V* = Normal at right MN, UN, CPN, TN *F waves* = Absent in right CPN and right TN	Negative for CMV, EBV, influenza virus A/B, respiratory syncytial virus, *Chlamydia pneumonia*, *Mycoplasma pneumonia*	None
37	Negative	NR	*V* = Decreased at left MN, CPN *F waves* = NR	Positive for HSV Negative for adenovirus, influenza a/b, parainfluenza 1/2/3/4, *Chlamydia pneumonia*, *Mycoplasma pneumonia*, bocavirus, coronavirus, respiratory syncytial virus A/B, metapneumovirus, rhinovirus/enterovirus	Abnormal enhancement of the facial (CNVII) and abducens (CNVI) nerves bilaterally, as well as the right oculomotor nerve (CNIII)
38	Negative	NR	*V* = NR *F waves* = NR	NR	Striking enlargement, prominent enhancement with gadolinium, and T2 hyperintense signal of the left cranial nerve (CN) III
39	Negative	Negative	*V* = Decreased at MN, UN, TN, CPN *F waves* = Absent	NR	Spinal cord: no nerve root gadolinium enhancement
39	NR	NR	*V* = Decreased at TN *F waves* = Absent	NR	Not performed
39	NR	Negative	*V* = Decreased at MN, UN, TN, CPN *F waves* = Absent	NR	None
40	Negative	NR	*V* = NR *F waves* = Anomalies in lower limbs	NR	NR
41	Negative	Negative	*V* = Decreased at TN, CPN, right UN *F waves* = Absent	Negative for JSV, VZV, and CMV	NR
42	Negative	Negative	*V* = Decreased at TN, CPN, right UN and MN *F waves* = Absent TN, CPN right MN	Negative for syphilis, HIV, HBV, and HCV	NR

TABLE 5. (*continued*)

References	Antigangliosides Antibodies in Serum	CSF PCR Analysis for COVID-19	Motor nerve Conduction Study (*V, F Waves*)	Biological Test for Infections Other Than COVID-19	MRI Findings Related to GBS
43	Negative	Negative	*V* = decreased at PN and TN bilaterally *F* = increased latency	Negative for HIV, Lyme disease, syphilis	Report shows multiple cranial neuritis, radiculitis, plexitis of both brachial and lumbar plexus
43	Negative	Negative	*V* = decreased at left MN *F waves* = NR	NR	Not performed
44	Negative	Negative	*V* = NR *F waves* = NR	NR	None
44	Negative	Negative	*V* = normal NR not reported *F waves* = NR	NR	NR
45	Negative	NR	*V* = decreased at left UN and bilateral PN *F waves* = absent at TN and PN bilaterally	Negative for HSV 1-2, EBV, VZV, CMV, HIV, *Mycoplasma pneumoniae*, *Borrelia*	NR
46	Negative	NR	*V* = decreased at UN bilaterally and right TN *F waves* = absent at MN, UN and TN bilaterally	Negative for *Campylobacter jejuni,* HIV, EBV, CMV, influenza virus (type A and B), and HCV	None
46	Negative	NR	*V* = decreased at TN bilaterally *F waves* = absent at MN, UN and TN bilaterally	Negative for *Campylobacter jejuni*, HIV, EBV, CMV, influenza virus (type A and B), and HCV	Not performed
47	Negative	NR	Not performed	Not performed	None
47	Positive	NR	Not performed	NR	NR
48	Negative	Negative	*V* = NR *F waves* = absent bilaterally	NR	Brainstem and cervical meningeal enhancement
49	Negative	Negative	*V* = NR *F waves* = NR	Negative for *Borrelia burgdorferi*, syphilis, *Campylobacter jejuni*, CMV, hepatitis E, *Mycoplasma pneumonia*, and EBV	None
50	NR	Negative	*V* = decreased at right UN and right PN *F waves* = normal minimal latencies with decreased persistence	Negative for HIV	Asymmetrical thickening and hyperintensity of postganglionic roots supplying the brachial and lumbar plexuses
51	Negative	Negative	*V* = decreased at left MN, left TN *F waves* = absent at UE and LE	NR	Symmetrical contrast enhancement of the spinal nerve roots at all levels of the spine including the cauda equina
52	Negative	NR	*V* = normal at left MN, UN, RN, CPN *F waves* = normal at left MN, UN	NR	Not performed
53	NR	NR	Not performed	NR	Moderate bilateral and moderate left-sided neural foraminal narrowing at L2-3 and L3-4
54	NR	Negative	*V* = Decreased at right MN, UN, TN *F waves* = NR	NR	NR
55	NR	NR	NR	Negative for meningitis, HSV, VZV, Lyme, VDRL, West Nile, Enterovirus, CMV, HIV	NR
56	NR	Negative	*V* = Decreased at left MN, CPN *F waves* = NR	Negative CSF Gram stain/culture, rapid meningitis-encephalitis multiplex panel; negative respiratory viral PCR and culture Negative blood, urine, stool cultures	Abnormal enhancement of posterior nerve roots from T11 through cauda equina

TABLE 5. (*continued*)

References	Antigangliosides Antibodies in Serum	CSF PCR Analysis for COVID-19	Motor nerve Conduction Study (*V, F Waves*)	Biological Test for Infections Other Than COVID-19	MRI Findings Related to GBS
57	NR	NR	*V* = Decreased at MN, UN *F waves* = NR	Positive IgG and IgM to *Campylobacter jejuni* Negative CSF PCR analysis of fungal, viral, bacterial pathogens, negative HBV	None
58	Negative	Negative	*V* = Decreased right TN *F waves* = NR	Negative HSV1, HSV2, VZV, enterovirus in CSF, negative serum HBV, HCV, HIV, syphilis, CMV, EBV, *Mycoplasma*, Lyme, *Legionella*, pneumococcus	Not performed
59	Negative	Negative	*V* = decreased at both MN and CPN bilaterally *F waves* = normal	Negative for HIV, HCV, HBV	Not performed
59	Negative	Negative	*V* = decreased at both MN and CPN bilaterally *F waves* = absent at CPN bilaterally	Negative for HIV, HCV, HBV	Negative
59	Negative	Negative	*V* = normal at both UE and LE bilaterally *F waves* = normal	Negative for HIV, HCV, HBV	Negative
59	Not performed	Not performed	*V* = NR *F waves* = Absent at CPN bilaterally	Negative for HIV, HCV, HBV	Not performed
59	Negative	Negative	*V* = normal at CPN bilaterally *F waves* = decreased at CPN bilaterally	Negative for HIV, HCV, HBV	Not performed
60	Negative	NR	NR	Negative for Lyme, HIV, viral hepatitis, ANA, RF	NR
61	Positive IgM for GM2 and GD3, weak IgG band for GT1b	NR	conduction blocks, absence of *F waves* in right ulnar and axon potentials in the F response of the right tibial nerve	NR	NR
62	NR	NR	NR	NR	NR
63	NR	NR	NR	NR	NR
64	Negative anti-GM1, anti-GD1b, anti-GQ1b IgG and IgM	NR	*V* = not evocable at TN bilaterally and CPN *F waves* = absent at LE bilaterally	Positive anti-EBV, anti-CMV, and anti-*Mycoplasma pneumoniae* IgG Negative HIV, syphilis, CMV, EBV, *Mycoplasma pneumoniae*	NR
65	Negative	NR	NR	NR	NR
65	Negative	Negative	NR	NR	NR
65	Negative	Negative	NR	NR	NR
65	Negative	Negative	NR	NR	NR
65	Negative	Negative	NR	NR	NR
65	Negative	NR	NR	NR	NR
66	Positive anti-GQ1B antibodies	Not performed	NR	Tracheal aspirate grew beta-lactamase resistant *Haemophilus influenzae*	Intrathecal caudal-equina enhancement consistent with GBS
79	NR	NR	NR	NR	NR
67	NR	Negative	*V* = normal at MN, UN and TN *F waves* = TN F-wave latencies with pathologic intermediate latency responses of complex A-wave bilaterally	Patient treated amoxicillin and ciprofloxacin for a GI disorder related to salmonellosis around 2 wk before admission	MRI C-spine showed no pathologic findings
68	Negative	Negative	Not performed	Negative antibodies for Lyme, and HIV	None

TABLE 5. (*continued*)

References	Antigangliosides Antibodies in Serum	CSF PCR Analysis for COVID-19	Motor nerve Conduction Study (*V, F Waves*)	Biological Test for Infections Other Than COVID-19	MRI Findings Related to GBS
69	NR	Not performed	*V* = absent at TN and CPN bilaterally *F waves* = NR	NR	NR
70	Negative	Negative	*V* = decreased in both UE and LE bilaterally *F waves* = NR	NR	NR
70	Negative	Negative	*V* = NR *F waves* = NR	NR	None
71	NR	NR	*V* = decreased at UN and MN, TN, and CPN unexcitable bilaterally *F waves* = absent at UN, MN, TN, and CPN bilaterally	NR	NR
72	NR	NR	*V* = NR *F waves* = NR	NR	None
73	Negative	Negative	*V* = normal at both UE and LE *F waves* = normal at both UN and TN	Negative for herpesviruses	None
74	Negative	Negative	*V* = decreased at both UE and LE *F waves* = NR	NR	None
75	Positive	NR	NR	NR	None
76	NR	NR	*V* = NR *F waves* = NR	Negative for HIV, HBV, HCV	None
76	NR	NR	*V* = NR *F waves* = NR	Negative for HIV, HBV, HCV	None
76	NR	NR	*V* = NR *F waves* = NR	Negative for HIV, HBV, HCV	None
76	NR	NR	*V* = NR *F waves* = NR	Negative for HIV, HBV, HCV	None
77	NR	Negative	*V* = decrease at TN and CPN bilaterally *F waves* = NR	Negative for HIV, syphilis and Lyme disease	None

ANA indicates antinuclear antibody; CMV, cytomegalovirus; COVID-19, Coronavirus Disease 19; CPN, common peroneal nerve; CSF, cerebrospinal fluid; EBV, Epstein-Barr virus; EMG, electromyography; EP, electrical potential; FN, facial nerve; GBS, Guillain-Barré syndrome; GI, gastrointestinal; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; HSV, herpes simplex virus; HTN, hypertension; ICU, intensive care unit; Ig, immunoglobulin; LE, lower extremities; MN, median nerve; MRI, magnetic resonance imaging; NE, not evocable; NR, not reportable; PCR, polymerase chain reaction; RF, rheumatoid factor; RN, radial nerve; SN, sural nerve; TBE, tick-borne encephalitis; TN, tibial nerve; UE, upper extremities; UN, ulnar nerve; V, conduction velocity (m/s); VZV, varicella zoster virus.

when initiated early in the disease course before complications of the infection occur.[111] A study of patients with severe COVID-19 pneumonia showed no difference in 30-day mortality or clinical status between those assigned to convalescent plasma versus placebo.[112] In regard to possible adverse effects, the largest safety study to date has noted transfusion reactions occurring in <1% of patients and causing death in 0.3%. Possible reactions include transfusion-associated circulatory overload, transfusion-related acute lung injury, and severe allergic reaction.[113]

While the use of convalescent plasma has not demonstrated significant effects on mortality in general COVID-19 patients, further research is needed to assess its impact on COVID-19–related GBS.[114] One case report has documented the use of convalescent plasma in a patient COVID-19–related GBS; however, its efficacy is unclear as the patient developed worsening respiratory failure and was unable to be weaned from ventilatory support at time of publication.[115] In addition, addressing the use of convalescent plasma in COVID-19–related GBS presents unique challenges apart from its use in general COVID-19 patients. One study reported deferring the use of convalescent plasma out of concern for potential parainfectious antibody-mediated peripheral nerve damage from donor plasma.[68] Due to the ambiguity of current evidence in this subset of COVID-19 patients, further research is needed to assess its efficacy in this population. It should be noted, however, that the most recent guidelines suggest using convalescent plasma in the management of COVID-19 patients only in the setting of a clinical trial.[113]

Critical Care in COVID-19 Patients With GBS

In our study, patients with poor outcomes or who showed no clinical improvement were associated with longer ICU stays ($P = 0.02$, Table 2). The ICU management of COVID-19-related GBS presents a unique set of challenges and obstacles. Poorer outcomes and longer ICU admissions highlight the increased mortality risk in this population and the potential burden on hospital resources. As mentioned above and presented in Table 1, there is a highly variable temporal relationship between the development of neurological and respiratory symptoms of GBS and COVID-19. In particular, evidence from several case reports suggests that possible symptom overlap portends more considerable obstacles in its management.[17,28] As both diagnoses may be complicated by severe respiratory failure and the need for early respiratory support,

ICU admission is often indicated but may not be feasible in some centers given the scarcity of resources during a pandemic.[17]

It is unclear if the development of ventilator-dependent respiratory failure in reported patients is caused by the sequelae of GBS-related neuromuscular dysfunction or COVID-19 respiratory symptoms. Out of the cases we analyzed, 47% required mechanical ventilation and ICU admission, highlighting the need for critical care resources in these patients.[15–18,20,26,28,31] A retrospective study in Wuhan, China reported that 71% of 52 COVID-19 patients with unspecified GBS status admitted to the ICU required mechanical ventilation.[116] Similarly, a retrospective study of 76 GBS patients admitted to the ICU showed that 78% required mechanical ventilation.[117] Although the precise pathophysiology of respiratory failure in COVID-19 patients with GBS remains unclear, the increased prevalence of ventilator dependency among cases we reviewed suggests a possible synergistic response associated with a worst outcome ($P = 0.004$), which warrants further investigation. Indeed, recent literature does support this hypothesis and suggest that the presence of significant respiratory symptoms in the acute phase of COVID-19 may be associated with more severe forms of GBS.[4] As such, respiratory complications in COVID-19 patients with GBS, including prolonged ventilator dependence and bacterial superinfection, pose a significant obstacle to patient recovery, particularly in areas with limited ICU resources. Current guidelines advise managing mechanically ventilated adults with COVID-19 similar to patients with other causes of acute respiratory failure. These ventilation strategies include low tidal volume ventilation at 4 to 8 mL/kg of predicted body weight, titrated positive end-expiratory pressure and reduction of barotrauma by restricting the peak and plateau inspiratory pressures.[94] However, the efficacy of other mechanical ventilation strategies in COVID-19 patients, as well as COVID-19–related GBS patients, has not yet been extensively investigated. The documented association between mechanical ventilation and no clinical improvement in this review ($P = 0.007$) underscores the need for carefully designed studies of ventilation strategies among this group of patients.

Study Limitations

The main limitation of the current systematic review of the literature is the low number of available cases worldwide and an even lower number of cases with the reported outcome. To facilitate further studies, we suggest that while reporting cases, authors report the outcome of the case as well. Despite the limitations, this systematic review and analysis is the first systematic study that rigorously assesses the effect of treatment outcomes and discusses the ICU challenges and management of COVID-19–related GBS patients during the COVID-19 pandemic.

CONCLUSIONS

To conclude, GBS should be considered as a potential high-risk complication in critically ill COVID-19 patients with early-onset weakness and pulmonary findings that are inconsistent with the severity of their respiratory status. Although evidence to support specific treatments are lacking, clinicians should consider the benefits of immunotherapy and plasma exchange, in addition to standard antimicrobial and supportive therapies, if the diagnostic criteria for an acute sensory and motor polyradiculoneuritis are met. This review indicated that IVIG treatment alone did not result in improved outcomes or mortality. Hence, the effects of more aggressive treatment options including plasmapheresis and convalescent plasma exchange should be examined further for this group of high-risk patients. More extensive studies aimed at exploring neurological manifestations and complications of COVID-19, together with distinctive treatment options for COVID-19–related GBS are warranted.

REFERENCES

1. Verdecchia P, Cavallini C, Spanevello A, et al. The pivotal link between ACE2 deficiency and SARS-CoV-2 infection. *Eur J Intern Med*. 2020;76:14–20.
2. Whittaker A, Anson M, Harky A. Neurological manifestations of COVID-19: a review. *Acta Neurol Scand*. 2020;142:14–22.
3. Vonck K, Garrez I, De Herdt V, et al. Neurological manifestations and neuro-invasive mechanisms of the severe acute respiratory syndrome coronavirus type 2. *Eur J Neurol*. 2020;27:1578–1587.
4. Scheidl E, Canseco DD, Hadji-Naumov A, et al. Guillain-Barre syndrome during SARS-CoV-2 pandemic: a case report and review of recent literature. *J Peripher Nerv Syst*. 2020;25:204–207.
5. Montalvan V, Lee J, Bueso T, et al. Neurological manifestations of COVID-19 and other coronavirus infections: a systematic review. *Clin Neurol Neurosurg*. 2020;194:105921.
6. Bridwell R, Long B, Gottlieb M. Neurologic complications of COVID-19. *Am J Emerg Med*. 2020;38:1549.e3–1549.e7.
7. Wu Y, Xu X, Chen Z, et al. Nervous system involvement after infection with COVID-19 and other coronaviruses. *Brain Behav Immun*. 2020;87:18–22.
8. Cappello F. COVID-19 and molecular mimicry: the Columbus' egg? *J Clin Neurosci*. 2020;77:246.
9. Cappello F. Is COVID-19 a proteiform disease inducing also molecular mimicry phenomena? *Cell Stress Chaperones*. 2020;25:381–382.
10. Dehghani Firouzabadi M, Dehghani Firouzabadi F, Goudarzi S, et al. Has the chief complaint of patients with COVID-19 disease changed over time? *Med Hypotheses*. 2020;144:109974.
11. Singh AK, Bhushan B, Maurya A, et al. Novel coronavirus disease 2019 (COVID-19) and neurodegenerative disorders. *Dermatol Ther*. 2020;33:e13591.
12. Needham EJ, Chou SHY, Coles AJ, et al. Neurological implications of COVID-19 Infections. *Neurocrit Care*. 2020;32:667–671.
13. Firouzabadi FD, Firouzabadi MD, Ghalehbaghi B, et al. Have the symptoms of patients with COVID-19 changed over time during hospitalization? *Med Hypotheses*. 2020;143:110067.
14. Sedaghat Z, Karimi N. Guillain Barre syndrome associated with COVID-19 infection: a case report. *J Clin Neurosci*. 2020;76:233–235.
15. 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;41:1351–1354.
16. Padroni M, Mastrangelo V, Asioli GM, et al. Guillain-Barré syndrome following COVID-19: new infection, old complication? *J Neurol*. 2020;267:1877–1879.
17. Alberti P, Beretta S, Piatti M, et al. Guillain-Barré syndrome related to COVID-19 infection. *Neurol Neuroimmunol Neuroinflamm*. 2020;7:e741.
18. Camdessanche JP, Morel J, Pozzetto B, et al. COVID-19 may induce Guillain-Barré syndrome. *Rev Neurol (Paris)*. 2020;176:516–518.
19. El Otmani H, El Moutawakil B, Rafai MA, et al. Covid-19 and Guillain-Barré syndrome: more than a coincidence!. *Rev Neurol (Paris)*. 2020;176:518–519.
20. Virani A, Rabold E, Hanson T, et al. Guillain-Barré syndrome associated with SARS-CoV-2 infection. *IDCases*. 2020;20:e00771.
21. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement (Chinese edition). *J Chinese Integr Med*. 2009;7:889–896.
22. Gupta A, Paliwal VK, Garg RK. Is COVID-19-related Guillain-Barré syndrome different? *Brain Behav Immun*. 2020;87:177–178.
23. Gigli GL, Bax F, Marini A, et al. Guillain-Barré syndrome in the COVID-19 era: just an occasional cluster? *J Neurol*. 2020;268:1195–1197.
24. R Core Team. *R: A Language and Environment for Statistical Computing*. Vienna, Austria: R Foundation for Statistical Computing; 2018.

25. 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;77:230–232.
26. Marta-Enguita J, Rubio-Baines I, Gastón-Zubimendi I. Síndrome de Guillain-Barré fatal tras infección por virus SARS-CoV2 [Fatal Guillain-Barre syndrome after infection with SARS-CoV-2]. *Neurologia*. 2020;35:265–267.
27. Zhao H, Shen D, Zhou H, et al. Guillain-Barré syndrome associated with SARS-CoV-2 infection: causality or coincidence? *Lancet Neurol*. 2020;19:383–384.
28. Toscano G, Palmerini F, Ravaglia S, et al. Guillain–Barré syndrome associated with SARS-CoV-2. *N Engl J Med*. 2020;382:2574–2576.
29. Galán AV, Saucedo PDS, Postigo FP, et al. Guillain-Barré syndrome associated with SARS-CoV-2 infection. *Neurologia*. 2020;35:268–269.
30. Coen M, Jeanson G, Culebras Almeida LA, et al. Guillain-Barré syndrome as a complication of SARS-CoV-2 infection. *Brain Behav Immun*. 2020;87:111–112.
31. Rana S, Lima AA, Chandra R, et al. Novel coronavirus (COVID-19)-associated Guillain-Barré syndrome: case report. *J Clin Neuromuscul Dis*. 2020;21:240–242.
32. Arnaud S, Budowski C, Ng Wing Tin S, et al. Post SARS-CoV-2 Guillain-Barré syndrome. *Clin Neurophysiol*. 2020;131:1652–1654.
33. Chan JL, Ebadi H, Sarna JR. Guillain-Barré syndrome with facial diplegia related to SARS-CoV-2 infection. *Can J Neurol Sci*. 2020;47:852–854.
34. Esteban Molina A, Mata Martínez M, Sánchez Chueca P, et al. Guillain-Barré syndrome associated with SARS-CoV-2 infection. *Med Intensiva*. 2020;44:513–514.
35. Farzi MA, Ayromlou H, Jahanbakhsh N, et al. Guillain-Barré syndrome in a patient infected with SARS-CoV-2, a case report. *J Neuroimmunol*. 2020;346:577294.
36. Helbok R, Beer R, Löscher W, et al. Guillain-Barré syndrome in a patient with antibodies against SARS-COV-2. *Eur J Neurol*. 2020;27:1754–1756.
37. Hutchins KL, Jansen JH, Comer AD, et al. COVID-19-associated bifacial weakness with paresthesia subtype of Guillain-Barré syndrome. *AJNR Am J Neuroradiol*. 2020;41:1707–1711.
38. Lantos JE, Strauss SB, Lin E. COVID-19-associated Miller Fisher syndrome: MRI findings. *AJNR Am J Neuroradiol*. 2020;41:1184–1186.
39. Lascano AM, Epiney JB, Coen M, et al. SARS-CoV-2 and Guillain-Barré syndrome: AIDP variant with favorable outcome. *Eur J Neurol*. 2020;27:1751–1753.
40. Reyes-Bueno JA, García-Trujillo L, Urbaneja P, et al. Miller-Fisher syndrome after SARS-CoV-2 infection. *Eur J Neurol*. 2020;27:1759–1761.
41. Su XW, Palka SV, Rao RR, et al. SARS-CoV-2-associated Guillain-Barré syndrome with dysautonomia. *Muscle Nerve*. 2020;62:E48–E49.
42. Webb S, Wallace VC, Martin-Lopez D, et al. Guillain-Barré syndrome following COVID-19: a newly emerging post-infectious complication. *BMJ Case Rep*. 2020;13:e236182.
43. Bigaut K, Mallaret M, Baloglu S, et al. Guillain-Barré syndrome related to SARS-CoV-2 infection. *Neurol Neuroimmunol Neuroinflamm*. 2020;7:e785.
44. Assini A, Benedetti L, Di Maio S, et al. New clinical manifestation of COVID-19 related Guillain-Barrè syndrome highly responsive to intravenous immunoglobulins: two Italian cases. *Neurol Sci*. 2020;41:1657–1658.
45. Bracaglia M, Naldi I, Govoni A, et al. Acute inflammatory demyelinating polyneuritis in association with an asymptomatic infection by SARS-CoV-2. *J Neurol*. 2020;267:3166–3168.
46. Ebrahimzadeh SA, Ghoreishi A, Rahimian N. Guillain-Barré syndrome associated with the coronavirus disease 2019 (COVID-19). *Neurol Clin Pract*. 2020;11:e196–e198.
47. Chan M, Han SC, Kelly S, et al. A case series of Guillain-Barré syndrome following COVID-19 infection in New York. *Neurol Clin Pract*. 2020. DOI: 10.1212/CPJ.0000000000000880.
48. Sancho-Saldaña A, Lambea-Gil Á, Liesa JLC, et al. Guillain–Barré syndrome associated with leptomeningeal enhancement following SARS-CoV-2 infection. *Clin Med (Lond)*. 2020;20:e93–e94.
49. Kilinc D, van de Pasch S, Doets AY, et al. Guillain-Barré syndrome after SARS-CoV-2 infection. *Eur J Neurol*. 2020;27:1757–1758.
50. Oguz-Akarsu E, Ozpar R, Mirzayev H, et al. Guillain-Barré syndrome in a patient with minimal symptoms of COVID-19 infection. *Muscle Nerve*. 2020;62:E54–E57.
51. Pfefferkorn T, Dabitz R, von Wernitz-Keibel T, et al. Acute polyradiculoneuritis with locked-in syndrome in a patient with COVID-19. *J Neurol*. 2020;267:1883–1884.
52. Hirayama T, Hongo Y, Kaida K, et al. Guillain-Barré syndrome after COVID-19 in Japan. *BMJ Case Rep*. 2020;13:e239218.
53. Korem S, Gandhi H, Dayag DB. Guillain-Barré syndrome associated with COVID-19 disease. *BMJ Case Rep*. 2020;13:e237215.
54. Tiet MY, AlShaikh N. Guillain-Barré syndrome associated with COVID-19 infection: a case from the UK. *BMJ Case Rep*. 2020;13:e236536.
55. Defabio AC, Scott TR, Stenberg RT, et al. Guillain-Barré syndrome in a patient previously diagnosed with COVID-19. *Am J Emerg Med*. 2020. [Epub ahead of print].
56. Curtis M, Bhumbra S, Felker MV, et al. Guillain-Barré syndrome in a Child With COVID-19 infection. *Pediatrics*. 2020:e2020015115.
57. Gale A, Sabaretnam S, Lewinsohn A. Guillain-Barré syndrome and COVID-19: association or coincidence. *BMJ Case Rep*. 2020;13:e239241.
58. Ameer NA-O, Shekhda KA-O, Cheesman A. Guillain-Barré syndrome presenting with COVID-19 infection. *BMJ Case Rep*. 2020;13:e236978.
59. 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*. 2021;93:766–774.
60. McDonnell EP, Altomare NJ, Parekh YH, et al. COVID-19 as a trigger of recurrent Guillain-Barré syndrome. *Pathogens*. 2020;9:965.
61. Diez-Porras L, Vergés E, Gil F, et al. Guillain-Barré-Strohl syndrome and COVID-19: case report and literature review. *Neuromuscul Disord*. 2020;30:859–861.
62. Manji HK, George U, Mkopi NP, et al. Guillain-Barré syndrome associated with COVID-19 infection. *Pan Afr Med J*. 2020;35(suppl 2):118.
63. Bueso T, Montalvan V, Lee J, et al. Guillain-Barre syndrome and COVID-19: a case report. *Clin Neurol Neurosurg*. 2021;200:106413.
64. Zito A, Alfonsi E, Franciotta D, et al. COVID-19 and Guillain-Barré syndrome: a case report and review of literature. *Front Neurol*. 2020;11:909.
65. Garnero M, Del Sette M, Assini A, et al. COVID-19-related and not related Guillain-Barré syndromes share the same management pitfalls during lock down: the experience of Liguria region in Italy. *J Neurol Sci*. 2020;418:117114.
66. Lowery MM, Taimur Malik M, Seemiller J, et al. Atypical variant of Guillain Barre syndrome in a patient with COVID-19. *J Crit Care Med*. 2020;6:231–236.
67. Atakla HG, Noudohounsi M, Sacca H, et al. Acute Guillain-Barré polyradiculoneuritis indicative of COVID-19 infection: a case report. *Pan Afr Med J*. 2020;35(suppl 2):150.
68. 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;26:797–799.
69. Agha Abbaslou M, Karbasi M, Mozhdehipanah H. A rare axonal variant of Guillain-Barré syndrome as a neurological complication of COVID-19 infection. *Arch Iran Med*. 2020;23:718–721.
70. Assini A, Benedetti L, Di Maio S, et al. Correction to: New clinical manifestation of COVID-19 related Guillain-Barrè syndrome highly responsive to intravenous immunoglobulins: two Italian cases. *Neurol Sci*. 2020;41:2307.
71. Chakraborty N, Kumar H. Intravenous Immunoglobulin may reverse multisystem inflammation in COVID-19 pneumonitis and Guillain-Barré syndrome. *Indian J Crit Care Med*. 2020;24:1264–1268.
72. García-Manzanedo S, López de la Oliva Calvo L, Ruiz Álvarez L. Guillain-Barré syndrome after COVID-19 infection. *Med Clin (Barc)*. 2020;155:366.
73. Liberatore G, De Santis T, Doneddu PE, et al. Clinical reasoning: a case of COVID-19-associated pharyngeal-cervical-brachial

variant of Guillain-Barré syndrome. *Neurology*. 2020;95: 978–983.
74. 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;50:397–399.
75. Dufour C, Co TK, 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.
76. Nanda S, Handa R, Prasad A, et al. COVID-19 associated Guillain-Barre syndrome: contrasting tale of four patients from a tertiary care centre in India. *Am J Emerg Med*. 2021;39:125–128.
77. Raahimi MM, Kane A, Moore CE, et al. Late onset of Guillain-Barré syndrome following SARS-CoV-2 infection: part of 'long COVID-19 syndrome'? *BMJ Case Rep*. 2021;14:e240178.
78. Oguz-Akarsu E, Ozpar R, Mirzayev H, et al. Guillain–Barré syndrome in a patient with minimal symptoms of COVID-19 infection. *Muscle Nerve*. 2020;62:E54–E57.
79. Foresti C, Servalli MC, Frigeni B, et al. COVID-19 provoking Guillain-Barré syndrome: the Bergamo case series. *Eur J Neurol*. 2020. [Epub ahead of print].
80. Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. *Lancet Infect Dis*. 2020;20:533–534.
81. Tzotzos SJ, Fischer B, Fischer H, et al. Incidence of ARDS and outcomes in hospitalized patients with COVID-19: a global literature survey. *Crit Care*. 2020;24:516.
82. Pilotto A, Cristillo V, Piccinelli SC, et al. COVID-19 severity impacts on long-term neurological manifestation after hospitalisation. *medRxiv*. 2021;2020:12.
83. Neri P, Pichi F. COVID-19 and the eye immunity: lesson learned from the past and possible new therapeutic insights. *Int Ophthalmol*. 2020;40:1057–1060.
84. Carod-Artal FJ. Complicaciones neurológicas por coronavirus y COVID-19 [Neurological complications of coronavirus and COVID-19]. *Rev Neurol*. 2020;70:311–322.
85. Cao B, Zhang D, Wang C. A trial of lopinavir–ritonavir in COVID-19. *N Engl J Med*. 2020;382:e68.
86. Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the treatment of COVID-19—final report. *N Engl J Med*. 2020;383: 1813–1826.
87. Kalil AC, Patterson TF, Mehta AK, et al. Baricitinib plus remdesivir for hospitalized adults with COVID-19. *N Engl J Med*. 2020;384:795–807.
88. Stone JH, Frigault MJ, Serling-Boyd NJ, et al. Efficacy of tocilizumab in patients hospitalized with COVID-19. *N Engl J Med*. 2020;383:2333–2344.
89. Khan S, Siddique R, Shereen MA, et al. Emergence of a novel coronavirus, severe acute respiratory syndrome coronavirus 2: biology and therapeutic options. *J Clin Microbiol*. 2020;58:e00187-20.
90. Singh B, Ryan H, Kredo T, et al. Chloroquine or hydroxychloroquine for prevention and treatment of COVID-19. *Cochrane Database Syst Rev*. 2021;2:CD013587.
91. Salama C, Han J, Yau L, et al. Tocilizumab in patients hospitalized with COVID-19 pneumonia. *N Engl J Med*. 2021;384:20–30.
92. Weinreich DM, Sivapalasingam S, Norton T, et al. REGN-COV2, a neutralizing antibody cocktail, in outpatients with Covid-19. *N Engl J Med*. 2021;384:238–251.
93. Alhazzani W, Møller MH, Arabi YM, et al. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with Coronavirus Disease 2019 (COVID-19). *Intensive Care Med*. 2020;46:854–887.
94. Russell CD, Millar JE, Baillie JK. Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. *Lancet*. 2020;395:473–475.
95. Xu J, Tan DY, Fau YY, et al. Do corticosteroids have a role in treating Ebola virus disease? *Sci China Life Sci*. 2015;58:111–113.
96. Stahl JP, Mailles A. Herpes simplex virus encephalitis update. *Curr Opin Infect Dis*. 2020;32:239–243.
97. Shang L, Zhao J, Hu Y, et al. On the use of corticosteroids for 2019-nCoV pneumonia. *Lancet*. 2020;395:683–684.
98. RECOVERY Collaborative Group, Horby P, Lim WS, Emberson JR, et al. Dexamethasone in hospitalized patients with COVID-19. *N Engl J Med*. 2020;384:693–704.
99. Hughes R. Corticosteroids for treating Guillain-Barré syndrome. *Cochrane Database Syst Rev*. 2000;2:CD001446.
100. Rimmer E, Houston BL, Kumar A, et al. The efficacy and safety of plasma exchange in patients with sepsis and septic shock: a systematic review and meta-analysis. *Crit Care*. 2014;18:699.
101. Busani S, Damiani E, Cavazzuti I, et al. Intravenous immunoglobulin in septic shock: review of the mechanisms of action and meta-analysis of the clinical effectiveness. *Minerva Anestesiol*. 2016;82:559–572.
102. Stiehm ER. Adverse effects of human immunoglobulin therapy. *Transfus Med Rev*. 2013;27:171–178.
103. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395:1054–1062.
104. Oxley TJ, Mocco J, Majidi S, et al. Large-vessel stroke as a presenting feature of COVID-19 in the young. *N Engl J Med*. 2020;382:e60–e60.
105. Spyropoulos AC, Levy JH, Ageno W, et al. Scientific and Standardization Committee communication: clinical guidance on the diagnosis, prevention, and treatment of venous thromboembolism in hospitalized patients with COVID-19. *J Thromb Haemost*. 2020;18:1859–1865.
106. Hughes RA, Swan AV, van Doorn PA. Intravenous immunoglobulin for Guillain-Barré syndrome. *Cochrane Database Syst Rev*. 2014;2014:CD002063.
107. van den Berg B, Walgaard C, Drenthen J, et al. Guillain-Barré syndrome: pathogenesis, diagnosis, treatment and prognosis. *Nat Rev Neurol*. 2000;10:469–489.
108. Farcas P, Avnun L, Frisher S, et al. Efficacy of repeated intravenous immunoglobulin in severe unresponsive Guillain-Barré syndrome. *Lancet*. 2000;350:1747.
109. Kapur S, Zipursky R, Jones C, et al. Relationship between dopamine D2 occupancy, clinical response, and side effects: a double-blind PET study of first-episode schizophrenia. *Am J Psychiatry*. 2000;157:514–520.
110. Rajendran KA-O, Krishnasamy N, Rangarajan J, et al. Convalescent plasma transfusion for the treatment of COVID-19: Systematic review. *J Med Virol*. 2000;92:1475–1483.
111. Libster R, Pérez Marc G, Wappner D, et al. Early high-titer plasma therapy to prevent severe COVID-19 in older adults. *N Engl J Med*. 2021;384:610–618.
112. Simonovich VA, Burgos Pratx LD, Scibona P, et al. A randomized trial of convalescent plasma in COVID-19 severe pneumonia. *N Engl J Med*. 2020;384:619–629.
113. Bhimraj A, Morgan RL, Shumaker AH, et al. Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19. *Clin Infect Dis*. 2020:ciaa478. [Epub ahead of print].
114. Food and Drug Administration. Recommendations for investigational COVID-19 convalescent plasma; 2020.
115. Yaqoob H, Jain A, Epelbaum O. A unique case of Guillain-Barré syndrome related to COVID-19 infection. *Chest*. 2020;158:A771.
116. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med*. 2020;8:475–481.
117. Siow WT, Liew MF, Shrestha BR, et al. Managing COVID-19 in resource-limited settings: critical care considerations. *Crit Care*. 2020;24:167.