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Review Article

Association of Guillain-Barre syndrome with COVID-19 infection: An updated systematic review

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ABSTRACT

Objective: The systematic review aimed to determine demographic characteristics, clinical features, lab evaluation, management and complications of the studies focusing on Guillain-Barre syndrome (GBS) as a sequele of novel coronavirus (COVID-19) infection.

Methods: After protocol registration, PubMed, Web of Science and Cumulative Index to Nursing & Allied Health Literature (CINHAL) databases were searched for relevant articles using MeSH key-words and imported into referencing/review softwares. The data, regarding demographic and clinical characteristics, diagnostic workup and management, was analyzed in International Business Machines (IBM) Statistics SPSS 21. Many statistical tests, such as *t*-test and the Mann–Whitney *U* test, were used. $P < 0.05$ was considered significant.

Results: We identified 64 relevant articles. The mean age of the patients was 56 ± 16 years; the majority were males (64.9%). Among the neurological findings, paresthesia was the most typical symptom (48.9%). Most of the patients had been diagnosed by reverse transcriptase-polymerase chain reaction (RT-PCR) (69.2%). Two-third of the patients received immunoglobulins (IVIg) (77.7%). Although functions recovered in most patients, there were four patients with facial diplegia during follow-up (4.26%). Acute inflammatory demyelinating polyneuropathy (AIDP) was more likely to be associated with paresis of the lower extremity ($p < 0.05$) and higher levels of glucose on cerebrospinal fluid (CSF) analysis ($p < 0.05$). These patients were more likely to receive IVIg ($p < 0.05$) and develop respiratory insufficiency, subsequently ($p < 0.05$).

Conclusions: GBS is being recognized as one of the many presentations of the COVID-19 infection. Although the common form is AIDP that might lead to complications, other variants are possible as well, and more studies are needed to focus on those subvariants.

1. Introduction

Guillain Barre Syndrome (GBS) was first described by French neurologists Guillain, Barré, and Strohl as acute paralysis with areflexia with increased protein concentration and normal white blood cell count in cerebrospinal fluid (CSF) (van Doorn, 2013). GBS is most likely known to be a sequela of upper or lower respiratory infection or gastroenteritis with symptoms beginning from pain and progressing to maximal weakness over four weeks (van Doorn, 2013). Both GBS and Acute Motor Axonal Neuropathy (AMAN) have been described after SARS- and MERS-CoV infections (Kim et al., 2017; Tsai et al., 2005). Ongoing pandemic with novel coronavirus (COVID-19) has also led to the development of GBS as one of the many neurological complications. Several mechanisms ranging from direct spread through the cribriform plate, angiotensin converting enzyme (ACE2) receptor upregulation on glial tissues increasing the susceptibility to viral invasion, S-spike viral

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protein-mediated damage, and altered exosomal transport viral particles to glial tissues have been postulated (Hamming et al., 2004; Wu and Zheng, 2020). However, the inflammatory cytokine surge produced in response to COVID-19 infection resulting from activation of CD + 4 cells is one of the most promising mechanisms explaining indirect damage to the neuronal pathways that can manifest as a slowly increasing and subsequently, resolving weakness (Chen and Wherry, 2020).

Many variants of the syndrome might occur in COVID-19 induced sequelae or at initial presentation. The clinical spectrum of GBS includes a classic sensorimotor form, Miller Fisher syndrome (MFS), bilateral facial palsy with paraesthesia, pure motor, pure sensory, paraparetic, pharyngeal–cervical–brachial variants, polyneuritis cranialis (GBS–MFS overlap), and Bickerstaff brainstem encephalitis. Based on electrophysiological features, three main GBS subtypes are recognized: AIDP, AMAN, and acute motor-sensory axonal neuropathy (AMSAN) (Donofrio, 2017).

The spectrum of presenting features related to COVID-19 induced GBS can vary from respiratory symptoms specific to COVID-19 illness and neurological features which could be sequelae due to development of GBS in the setting of preceding COVID-19 infection. These include fever, dyspnea, cough, headache, diarrhoea, weakness, dysphagia, altered sensations, loss of reflexes (Abu-Rumeileh et al., 2021). Atypical features such as dysautonomia, asymmetrical pain distribution, and ataxia might also lead to initial suspicion (Abu-Rumeileh et al., 2021). Apart from current diagnostic criteria, other important features such as encephalitis, transverse myelitis, and acute myelitis should be ruled out using CSF examination and electrophysiological studies, especially for further subtypes identification. Considering the association of COVID-19 infection in the setting of current pandemic and the spectrum of GBS, it is vital to understand the common symptoms that would raise suspicion of GBS, time to presentation, and intervention for better outcomes, outcomes in general, and treatment modalities most frequently used to combat the problem.

2. Materials and methods

2.1. Protocol development and systematic review registration

The protocol for current systemic review was designed after thorough literature review and then it was registered on PROSPERO International prospective register of systematic reviews and study with the database (ID CRD42020208187) before initiation of search of the articles.

2.2. Search strategy

Keywords (including all commonly used abbreviations of these terms) used in the search strategy were as follows: (((coronavirus OR “corona virus” OR coronaviridae OR coronaviridae OR betacoronavirus OR covid19 OR “covid 19” OR ncov OR “CoV 2” OR CoV2 OR sarscov2 OR 2019nCoV OR “novel CoV”) OR "Coronavirus"[Mesh] OR "Coronavirus Infections"[Mesh] OR "COVID-19"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "Betacoronavirus"[Mesh])) AND 2019/12[PDAT] : 2030 [PDAT]) and ("Guillain-barre syndrome"[MeSH Terms] OR "guillain barre syndrome"[Text Word] OR "Miller Fisher Syndrome"[Mesh]).

2.3. Data extraction (selection and coding)

We screened PubMed, Web of Science and CINAHL databases for all case descriptions of GBS associated with COVID-19 articles published from January 1st 2020 to September 15th 2020. After the initial search, duplicates were removed and imported all included search study into EndNote online software. Two independent reviewers screened remaining studies for the inclusion based on inclusion criteria, and researchers were blinded to each others’ decisions. Rayyan software and Mendeley desktop were used. The screening was done via reading the abstract and if needed by reading full-text articles. Studies published in the English language or with English translation available, were included in the initial review. Once the initial screening is done, two independent reviewers reviewed full-text article for final inclusion. Reviewers were blinded to each others’ decisions, and a third reviewer resolved any dispute.

Data was extracted from study documents, including information about study design and methodology, participant demographics and baseline characteristics, study country, publication journal, clinical presentation, symptoms, laboratory data, imaging data, intervention, treatment, clinical outcomes, morbidity and mortality.

One reviewer did data extraction, and another reviewer cross-checked the extracted data for accuracy and completeness. Any disagreements between individual judgements were resolved via the third reviewer. Attempts were made to obtain any missing data from study corresponding investigators via email. If data could not be obtained, that study was excluded from the analysis on a case-by-case basis. Publications that were not peer-reviewed were excluded from this study. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria were applied (Fig. 1). The preliminary data was entered and recorded in an excel spreadsheet [Supplementary file 1; Supplementary Tables 1 to 5].

2.4. Risk of bias (quality) assessment

Quality assessment of all the included studies was assessed using the methodological quality and synthesis of case series and case reports described by Murad et al. (2018) [Tables 1 and 2].

According to this tool, four broad perspectives to assess the quality:

1. Selection of the study groups
2. Ascertainment of the observed outcome
3. Causality of the observed outcome
4. Case reporting.

2.5. Strategy for data synthesis

For statistical analysis, we used IBM SPSS Statistics version 21 (IBM, Armonk, NY, USA). Based on the distribution of values, continuous data were expressed as mean ± standard deviation or median and interquartile range (IQR). Depending on the number of groups and data distribution, we applied the *t*-test, the Mann–Whitney *U* test or the Kruskal–Wallis test (followed by Dunn–Bonferroni post hoc test). We adopted the Chi-square test for categorical variables. Differences were considered statistically significant at $p < 0.05$.

3. Results

A total of 64 studies were analyzed. The details of each article are mentioned in Supplementary Material 2. There were a total of 94 patients whose data were included in the study. The clinical characteristics of the 94 patients are shown in Table 3. The patients’ mean age was 56 ± 16 years, and most of the patients were male (61/94, 64.89%). Comorbid conditions, particularly malignancy, chronic lung diseases such as chronic obstructive pulmonary disease (COPD), chronic vascular disease (dyslipidemia and peripheral artery disease), metabolic disease (obesity and type 2 diabetes mellitus), and heart disease (coronary heart disease and hypertension) were present in 28 patients (28/94, 29.78%) (Table 3). Many patients had presented with other co-morbid conditions such as dyslipidemia (6/94, 6.38%), cancer (4/94, 4.26%), obesity (3/94, 3.19%), coronary artery disease (2/94, 2.13%), and COPD (2/94, 2.13%) and peripheral artery disease (1/94, 1.06%). The most common time from symptom onset to the clinical presentation was 0 to 10 days (34/94, 36.17%) (Table 3).

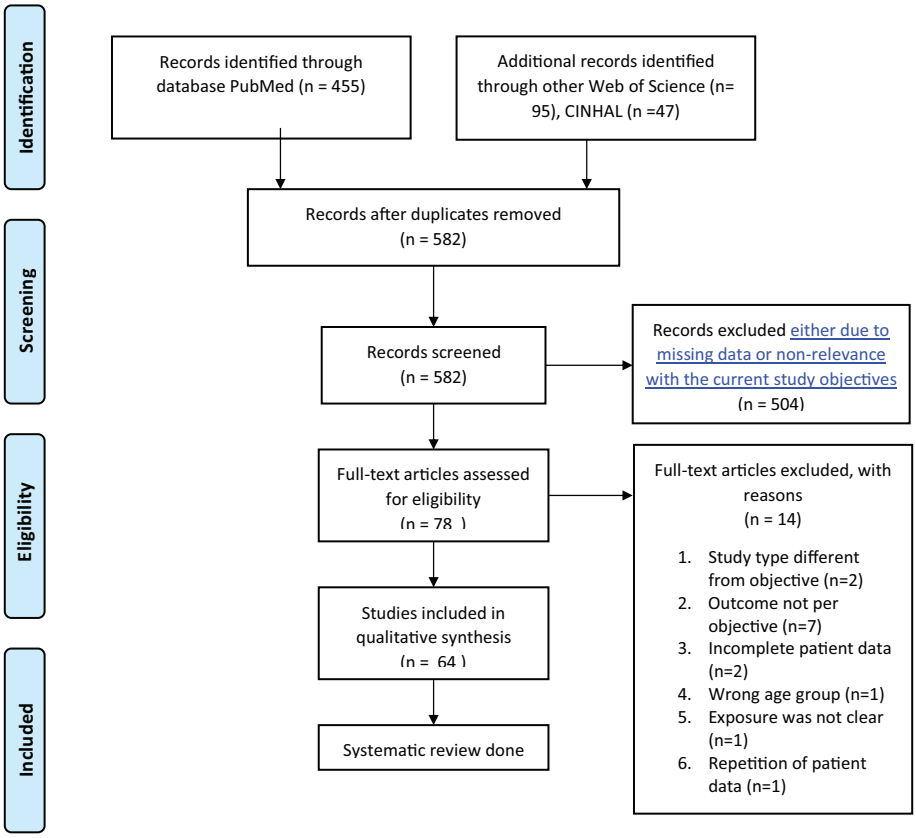

Fig. 1. PRISMA flow chart.

Table 1
Tool used to evaluate the methodological quality of included case reports and case series.

Domain	Leading explanatory questions	The question used in the evaluation
Selection	1. Does the patient(s) represent(s) the whole experience of the investigator (center) or is the selection method unclear to the extent that other patients with similar presentation may not have been reported?	Yes
Ascertainment	2. Was the exposure adequately ascertained?	Yes
	3. Was the outcome adequately ascertained?	Yes
Causality	4. Were other alternative causes that may explain the observation ruled out?	Yes
	5. Was there a challenge and/or re-challenge phenomenon?	No
	6. Was there a dose-response effect?	No
	7. Was follow-up long enough for outcomes to occur?	Yes
Reporting	8. Is the case(s) described with sufficient details to allow other investigators to replicate the research or to allow practitioners make inferences related to their own practice?	Yes

Table 2
Quality assessment of the included studies ($n = 64$).

Judgment	%	N	Case study ($n = 52$)	Case series ($n = 12$)
Good	98.4	63	52	11
Fair	1.6	1	0	1
Poor	0.0	0	0	0

3.1. Clinical symptoms and COVID-19 status

All 94 patients were presented with both non-neurological and neurological findings. The neurological presentation was preceded by respiratory symptoms in 68 patients (72.35%) while gastrointestinal symptoms in 18 patients (19.15%). There was a significant overlap of presenting symptoms. Among the neurological findings, paresthesia was the commonest symptom (46/94, 48.93%) followed by paresis of the lower extremity (39/94, 41.49%) and upper extremity (21/94, 22.34%). Bulbar symptoms were present in 20/94 patients (21.28%), ataxia and gait disturbance were present in 21/94 patients (22.34%) whereas 11/94 patients (11.70%) reported eye symptoms including eyelid ptosis (2/11; 18.18%), diplopia (6/11; 54.55%), retroorbital pain (1/11; 9.09%) and ophthalmoplegia (2/11; 18.18%).

Apart from the patients who had COVID-19 diagnosed at the facility where the cases were reported (Table 3), most of the patients had been transferred or had been already diagnosed with COVID-19 at a prior facility before the presentation (8/94, 8.51%). Majority of the patients had positive COVID-19 result through RT-PCR from a nasopharyngeal sample (65/94, 69.15%).

3.2. Neurological examination relevant to GBS spectrum

The clinical features were variable. The most common exam finding was reduced power (73.43%) in either the upper or lower extremities. It was symmetrical in some cases but was also asymmetric in some patients. Patients also had reduced sensations to pinprick, vibratory or proprioceptive stimuli. One patient had hyperreflexia, rather than areflexia which was noticed in most cases (65.63%).

Table 3
Baseline characteristics of 94 patients.

Variables	n (%)
Age in years (mean ± S·D)	56 ± 16
Gender	
Male (n, %)	61 (64.89)
Co-morbid conditions	
Hypertension	16 (17.02)
Type 2 diabetes mellitus	10 (10.60)
Others[a]	18 (19.15)
Time from onset of COVID symptoms to neurological symptoms	
0–10 days	34 (36.17)
11–20 days	29 (30.85)
21 days or more	25 (26.59)
Status of RT-PCR COVID sample	
Nasopharyngeal sample positive	65 (69.15)
Oropharyngeal sample positive	16 (17.00)
Serology (COVID-19 antibodies) positive	5 (5.30)
Presented to facility with diagnosed COVID-19	8(8.51)
Symptoms	
Fever	62 (65.95)
Respiratory symptoms	68 (72.34)
GI symptoms	18 (19.15)
Paresthesia	46 (48.93)
Paresis of lower and upper extremity	60 (63.83)
Findings on examination (n = 64)	
Reduced power in upper/lower extremities	47 (73.43)
Areflexia	42 (65.63)
Diminished sensation	23 (35.94)
Ataxia	07 (10.94)
Hyperreflexia	01 (1.56)

[a] Other co-morbid conditions include obesity, COPD, cancer, peripheral artery disease, dyslipidemia, and coronary artery disease.

3.3. Results of electrophysiological, CSF, and neuroimaging investigations

Electromyography/electroneurography results were available for 70/94 patients (74.47%). The most common finding was demyelination in 44/70 patients (62.86%) followed by associated sural sparing with demyelination in 7/70 patients (10.00%), mixed demyelination and axonal damage in 5/70 patients (7.14%), axonal motor and sensory changes in 3/70 patients (4.28%). (Table 4).

Abnormal CT-chest imaging was found in 35/94 patients (37.23%) with findings relevant to COVID-19 pneumonia, particularly ground-glass opacities. Abnormal MRI (brain and/or spine) was seen in 16/94 patients (17.02%) with findings suggestive of oedema of the cervical spine (1/16), cranial neuritis (3/16) and abnormal enhancement of cranial nerves (12/16).

Changes suggestive of albuminocytological disassociation such as elevated CSF proteins were present in 70/80 (87.50%), and normal CSF-WBC was present in 54/80 patients (67.50%). In CSF, three patients had oligobands, and two patients had anti-ganglioside antibodies.

3.4. Distribution of clinical and electrophysiological variants of GBS

Out of 94 patients, GBS subtypes were available for 83 patients. Seventy patients have been diagnosed based on electromyography (EMG) results and 13 patients were included based on clinical features. AIDP was found in 58/83 patients, AMSAN was found in 10/83 patients, ten patients had Miller Fisher syndrome, and five patients had AMAN (Fig. 2).

3.5. Management

Majority of the patients (50/94, 53.20%) had been treated on an inpatient basis (on the floor), and some patients (27/94, 28.70%) had to be transferred to intensive care unit (ICU) based on either isolation requirements or oxygen requirement (Table 5). The management options for the spectrum varied from immunoglobulins (IVIg) to antivirals. Majority of the patients received IVIg (73/94, 77.66%). There was a lot of overlap in management protocols in many patients.

Table 4
Clinical characteristics of 94 patients.

Variables	n (%)
Abnormal CT imaging (chest)	35 (37.23)
Abnormal MRI (brain and/or spine)	16 (17.02)
Electromyography (EMG) ($n = 70$)	
Demyelination	44 (62.86)
Axonal motor and sensory with muscle/neurogenic damage	1 (1.43)
Demyelination with sural sparing	7 (10.00)
Axonal motor and sensory changes	3 (4.29)
Axonal changes	2 (2.86)
Mixed demyelination and axonal damage	5 (7.14)
Absent blink reflex	1 (1.43)
Mixed demyelination with sural damage	1 (1.43)
Demyelination with absent blink reflex	1 (1.43)
Axonal changes and sural sparing	1 (1.43)
Axonal motor, sensory changes and sural sparing	1 (1.43)
Axonal motor changes	3 (4.29)
Findings on CSF analysis ($n = 80$)	
CSF proteins elevated	70/80 (87.50)
CSF glucose levels elevated	19/80 (23.75)
CSF WBC count normal	54/80 (67.50)
Presence of oligobands in CSF	3/80 (3.75)
Presence of anti-ganglioside antibodies in CSF,	2/80 (2.50)
Mode of treatment	
Floor	50 (53.20)
ICU	8 (8.50)
Transferred to ICU	27 (28.70)
Transferred to floor from ICU	9 (9.60)
Treatment received	
Immunoglobulins	73 (77.66)
Steroids	15 (15.96)
Plasmapharesis	11 (11.70)
Hydroxychloroquine	27 (28.70)
Antibiotics	16 (17.02)
Antivirals	21 (22.34)
Oxygen requirements	
Invasive	33 (35.11)
Non-invasive	61 (64.89)
Mortality	5 (5.30)
Complications	
Respiratory insufficiency	23 (24.47)
Bulbar symptoms	12 (12.77)
Autonomic dysfunction	8 (8.51)
Tetraparesis	4 (4.26)

Many patients were given combination therapies to combat neurological problems. IVIG and steroids were administered to 10/94 patients (10.64%). IVIG and plasmapheresis were done in 2/94 patients (2.13%). Steroids and plasmapheresis were done in 2/94 patients (2.13%).

Other therapies received for COVID-19 management included hydroxychloroquine in 25/94 patients (26.60%) and antivirals in 21/94 patients (22.34%).

Complications were noted in 36 patients (Table 5)—many patients presented with more than one complication. Aspiration, bacteremia and heparin-induced thrombocytopenia in addition to respiratory insufficiency, was seen in one patient. One patient had gastroplegia and autonomic dysfunction. Patients also had bulbar and autonomic dysfunction (2/94, 2.12%), respiratory insufficiency and bulbar symptoms (2/94, 2.12%) as well as a triad of respiratory insufficiency, bulbar symptoms and tetraparesis in 3/94 patients (3.19%). Patients also had a trio of bulbar symptoms, autonomic dysfunction and tetraparesis in one patient. One patient had respiratory insufficiency and tetraparesis.

Sensorimotor function recovered in 20/94 patients (21.27%), improved in 18/94 patients (19.15%) and did not improve in 7/94 patients (7.45%). Four patients had facial diplegia at time of follow-up (4.26%).

A comparison of the clinical features of patients presenting with AIDP to other variants is shown in Table 5. AIDP was more likely to be associated with paresis of the lower extremity ($p < 0.05$). EMG changes were more frequent in cases of AIDP when compared to other variants

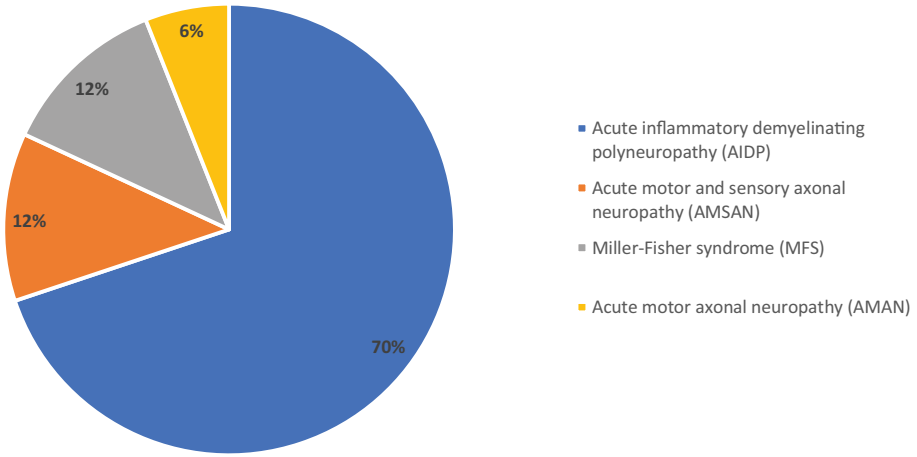

Fig. 2. Variants of Guillain Barre Syndrome (GBS).

($p < 0.05$). CSF analysis of AIDP patients had chances of having greater levels of glucose ($p < 0.05$). These patients were more likely to receive immunoglobulins ($p < 0.05$). Respiratory insufficiency was more common in patients with AIDP ($p < 0.05$).

4. Discussion

In our systematic review, 94 cases had been included based on RT-PCR positive for COVID and findings suggestive of GBS that ultimately led to a working diagnosis of the condition or its subtype.

The mean age of the patients was 56 ± 16 years, and the majority of the patients were male (61/94, 64.89%). The age is comparatively lesser to another systematic review with patients' age varying from 23 to 76 years. Many studies have widely reported male predominances for COVID-19 induced GBS (Abu-Rumeileh et al., 2021; Carrillo-Larco et al., 2020; Caress et al., 2020). This is possibly attributed to males having higher levels of ACE2 in the circulation providing more receptors for interactions with COVID-19 resulting in uptake and infection (Jin et al., 2020).

The clinical features of GBS with COVID-19 were similar to classical GBS in the sense that patients presented with bilateral weakness of the legs and/or arms, paraesthesias or sensory loss, and decreased reflexes. Although, it was difficult to determine if the presenting symptom of weakness in the study had been progressive, paraesthesia had been the most typical symptom (46/94, 48.93%) followed by paresis of the lower extremity (39/94, 41.49%) and upper extremity (21/94, 22.34%). Areflexia had also been reported in many patients. Atypical presenting symptoms also include unsteady gait and symptoms pointing towards one particular variant. In our study, 21 patients had gait issues. There were 20 patients with bulbar symptoms and 11 patients with eye symptoms later diagnosed to have the Miller-Fisher variant of GBS as described in studies. The unusual features included the onset of fever and respiratory symptoms reported in 62 and 68 patients, respectively. As GBS is often a sequela of infectious etiology, it is not surprising that the literature does not explain these symptoms. Therefore, the symptoms are more specific to COVID-19 rather than GBS itself.

Fever is most likely to be caused by the upregulation of cytokines, leading to a cytokine storm as the body's last defense mechanism before succumbing to a vicious cycle of complications. Respiratory symptoms are most likely a result of viral invasion ending in interstitial inflammation evident on CT-scan as was the case in 35 patients (Dhama et al., 2020). Therefore, inflammatory neuropathy can be considered in patients who have radiological evidence of COVID-19 pneumonia in addition to other parameters, such as having a positive RT-PCR.

Electrophysiological studies reported that changes reflective of demyelination (44/94 patients). The fact that only two patients had anti-ganglioside antibodies in CSF analysis suggests that some other antibodies might be at play damaging myelin sheaths in addition to the theory that the damage is a result of inflammation. These antibodies could also target other components such as fibrinogen (α/β chains), transthyretin, and albumin, increasing significantly in the AIDP variant of GBS, resulting in extensive damage (Chiang et al., 2009; Zhang et al., 2012; Brettschneider et al., 2005). Another theory includes the alteration of immunoglobulin fragments after antigen-antibody complexes had targeted a lethal viral infection (Mallery et al., 2010).

The postulated mechanism of COVID-19 induced antibody production mediating myelin damage is also supported by the result that 11.70% of the patients responded to intravenous plasmapheresis, respectively, preventing an increase in mortality. Additionally, the theory of immunoglobulin alteration is supported by the fact that 77.66% of the patients had responded to intravenous immunoglobulins, combatting the altered response. Abnormal MRI findings had been found in 16 patients with 12/16 patients having enhancement of cranial nerves. This was an interesting feature because nerve root enhancement is considered a sensitive feature to include GBS in the differential for investigation in children and not adults (Gorson et al., 1996).

Most patients had elevated protein levels in our study, and normal white blood cell counts suggestive of albuminocytologic disassociation. In a study, 50% of the patients with COVID-19 associated GBS had normal protein levels and only a few cases had albuminocytologic disassociation (Espíndola et al., 2020). These cases had initially presented with tetraplegia compared to the patients in our study who had given with paresis in the upper or lower extremities.

Dysautonomia has been reported as a common presenting feature (Van Den Berg et al., 2014). However, in our review, few patients had autonomic dysfunction (8.51%) as a complication suggesting long-lasting consequences of the initial autoimmune process.

Our review's major strengths are the inclusion of all relevant cases to date and an in-depth comparison of clinical, radiological, and diagnostic features of COVID-19 and concomitant GBS AIDP variant with other possible variants. The limitations include a lack of division of data to further subcategories as a result of missing information in some articles. Also the data is presented only for the group as a whole, and is not broken down into groups for closer analysis of cases. Additionally majority of included studies were case reports.

5. Conclusion

In conclusion, based on the systematic review of 94 cases, we showed that the clinical picture of COVID-19-associated GBS has a few clinical characteristics that increase suspicion of diagnosis in addition to the attributes of classic GBS. Furthermore, the response to plasmapheresis,

Table 5
Clinical characteristics of AIDP compared to other variants.

Variables	AIDP	Other	*p*-Value
Age in years (mean ± S·D)	54 ± 15	53 ± 17	0.68
Gender			
Male (n, %)	42 (50.60)	18 (21.69)	0.82
Female (n, %)	21 (25.30)	12 (14.46)	
RT-PCR COVID-19 positive	32 (38.55)	13 (15.66)	0.35
Serology positive	5 (6.02)	0 (0.00)	
Symptoms			
Fever	35 (42.17)	17 (20.48)	0.19
Respiratory symptoms	41 (49.40)	18 (21.69)	0.79
GI symptoms	13 (15.66)	3 (3.61)	0.55
Paresthesia	31 (37.35)	9 (14.29)	0.47
Paresis of lower/upper extremity	45 (54.22)	8 (9.63)	<0.05
Abnormal MRI (brain and spine)	12 (14.46)	4 (4.82)	0.28
Electromyography (EMG) ($n = 69$)			
Demyelination	42 (60.87)	2 (2.90)	0.00
Axonal motor and sensory with muscle/ neurogenic damage	0 (0.00)	1 (1.45)	
Demyelination with sural sparing	7 (10.14)	0 (0.00)	
Axonal motor and sensory changes	0 (0.00)	3 (4.35)	
Axonal changes	0 (0.00)	2 (2.90)	
Mixed demyelination and axonal damage	1 (1.45)	1 (1.45)	
Mixed demyelination with sural damage	1 (1.45)	0 (0.00)	
Demyelination with absent blink reflex	1 (1.45)	0 (0.00)	
Axonal changes and sural sparing	0 (0.00)	1 (1.45)	
Axonal motor, sensory changes and sural sparing	0 (0.00)	1 (1.45)	
Axonal motor changes	0 (0.00)	3 (4.35)	
Findings on CSF analysis ($n = 73$)			
CSF proteins elevated	46 (58.23)	17 (23.29)	0.37
CSF glucose levels elevated	10 (13.70)	6 (8.22)	0.01
CSF WBC count normal	33 (45.21)	14 (19.18)	0.43
Presence of oligobands	2 (2.74)	1 (1.37)	0.27
Presence of anti-ganglioside antibodies	0 (0.00)	1 (1.37)	0.12
Treatment received			
Immunoglobulins	50 (60.24)	18 (21.69)	0.02
Steroids	8 (9.63)	3 (3.61)	0.34
Plasmapharesis	6 (7.22)	3 (3.61)	0.89
Mortality	3 (3.61)	1 (1.20)	0.82
Complications			
Respiratory insufficiency	13 (15.66)	3 (3.61)	<0.01
Bulbar symptoms	9 (14.29)	2 (2.41)	0.38
Autonomic dysfunction	4 (4.82)	3 (3.61)	0.53
Tetraparesis	2 (2.41)	1 (1.20)	0.48

intravenous immunoglobulins, elevated protein in CSF, and lack of COVID-19 virus detection in CSF may suggest an immune response rather than an inflammatory or infectious one. Further analyses are required to address a few issues including essential features of other variants, protocols in asymptomatic patients, and protocols for electrophysiological studies to streamline the diagnosis.

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Declaration of Competing Interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jneuroim.2021.577577.

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