Guillian--Barre' Syndrome in Patients with SARS-CoV-2: A Multicentric Study from Maharashtra, India

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Abstract

Background: Guillian--Barre' Syndrome (GBS) has been shown to be associated with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection. The aim of our study was to study the clinical profile and outcomes of GBS in COVID-19 from the Western region of India, the State of Maharashtra. **Methods:** This was a retrospective, multicenter observation study from different hospitals in Maharashtra beginning from March 2020 until November 2020. **Results:** We report 42 patients with COVID-19 GBS. Mean age was 59 years (range, 24--85 years). 31/42 (73.8%) were men. GBS was the presenting symptom in 14/42 (33%), while six of them remained asymptomatic for COVID-19 despite positive SARS-CoV-2 on nasopharyngeal swab reverse transcriptase polymerase chain reaction. The median interval between COVID-19 and GBS was 14 days (SD + 11), with minimum of 1 and maximum 40 days. Clinical presentation was like that of typical GBS. Electrophysiological studies showed a predominant demyelinating pattern in 25/42 (59.5%). Inflammatory markers were elevated in 35/42 (83.3%) and 38/42 (90.5%) had an Abnormal high-resolution CT (HRCT) chest. 14/42 (33.3%) patients required a ventilator, with nine deaths. Intravenous immunoglobulin was the mainstay of treatment for GBS. Majority had a good outcome and were walking independently or with minimal support at discharge. In subgroup analysis, the postinfectious group had a better outcome than the parainfectious group. **Conclusion:** GBS in COVID-19 occurs as both parainfectious and postinfectious GBS. Parainfectious GBS needs more rigorous monitoring and may benefit from COVID-19 specific treatment. Routine screening for SARS-CoV-2 should be implemented in patients with GBS in view of the ongoing pandemic.

Keywords: Coronavirus, COVID-19, Guillian--Barre' Syndrome, neuropathy, SARS-CoV-2

INTRODUCTION

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic has continued to mystify us with its varied clinical presentations. It was designated as coronavirus disease 2019 (COVID-19) in February 2020 by WHO. The clinical spectrum appears to range from asymptomatic infection, mild viral syndrome with fever, myalgia or cough to severe pneumonia requiring ventilator with rapid deterioration and early death.[1] Similar to other coronaviruses, severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East respiratory syndrome coronavirus (MERS), SARS-CoV-2 has been found to have central and peripheral nervous system manifestations.[2,3] Guillian--Barre' Syndrome (GBS), an autoimmune polyradiculoneuropathy has been reported with previous outbreaks of viruses such as Zika virus, MERS, West Nile virus, H1N1, Swine flu, and Chikungunya. The very first case of GBS associated with SARS-CoV-2 virus or COVID-19 was reported from Wuhan, China, in a lady who developed acute lower extremity weakness because of demyelinating neuropathy (GBS) and improved after intravenous immunoglobulin (IVIG). Thereafter, various single case reports of GBS associated with COVID-19 have been reported, the recent largest case series from Italy has reported 30 cases.[4-10] At the time of writing this paper, 73 cases of GBS with COVID-19 have been reported from at least 52 manuscripts worldwide.[11] These cases raise the concern of a possible association of GBS and SARS-CoV-2. The aim of the present study was to evaluate the clinical profile and outcome in a series of 42 patients of GBS associated with COVID-19 from the state of Maharashtra in India.

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Methods

Study design

This is a multicenter, retrospective observational study. All neurologists from the Western region of India, the state of Maharashtra were invited to contribute their cases of GBS who were detected to have SARS-CoV-2 infection between March 2020 and October 2020. 15 centers participated in the study. The study protocol was approved by the Fortis Hospital Institutional Academic Ethics Committee. Data was anonymized and waiver of written consent for patients was granted.

Inclusion criteria

i.   Patients diagnosed as GBS by the treating Neurologist according to the diagnostic criteria,[12] based on clinical, electrophysiological and/or supportive cerebrospinal fluid analysis (CSF), who had SARS-CoV-2 infection. A clinical diagnosis of GBS was accepted in those in whom electrophysiological studies or CSF studies could not be done because of the restrictions of the pandemic or the affordability.
ii. SARS-CoV-2 infection was identified by a positive reverse transcriptase polymerase chain reaction of nasopharyngeal swab (SARS-CoV-2 RT-PCR) or COVID-19 antibody positive result.

Exclusion criteria

i.   Mimickers of GBS such as critical illness neuromyopathy or other neuromuscular conditions in patients with SARS-CoV-2 infection.
ii. Patients with GBS who tested negative for SARS-CoV-2 infection.

Patient information was collected from various sites by reviewing electronic medical records or paper charts and shared via an end-to-end encrypted email or a phone review provided by the treating Neurologist. Clinical, demographic, laboratory, radiologic, electrophysiologic, and treatment details were collected. It was noted if patients presented with GBS or with COVID-19 symptoms at the onset. Time interval between onset of symptoms of COVID-19 and GBS was procured from the data. Those who presented with GBS, we noted the time they developed symptoms consistent with COVID-19. Those patients who were positive for SARS-CoV-2 at the time of presentation with GBS and developed symptoms of COVID-19, or had elevated inflammatory markers or HRCT chest suggestive of SARS-CoV-2 interstitial pneumonia or were treated for the same, were defined as parainfectious GBS. Patients who developed GBS after recovery from COVID-19, or had negative SARS-CoV-2 by RT-PCR but had positive antibodies against SARS-CoV-2 were defined as postinfectious GBS. Electrophysiologic studies were conducted in the respective hospitals by trained electrophysiologists and interpreted by the treating neurologists. Based on the electrophysiologic study, GBS was classified into subtypes as acute inflammatory demyelinating polyradiculoneuropathy (AIDP) and acute motor/sensorimotor axonal polyradiculoneuropathy (AMAN, AMSAN) or mixed in whom both features were present. Miller--Fisher variant was identified based on clinical characteristics of ataxia, ophthalmoplegia, and areflexia. Anti-ganglioside antibodies were used as supportive criteria if present. Cerebrospinal fluid (CSF) analysis data was collected from those who underwent the procedure, which included cell count and routine chemistry and CSF SARS-CoV-2 RT-PCR. Inflammatory markers associated with COVID-19 such as C-reactive protein (CRP), serum lactate dehydrogenase (LDH), and serum ferritin and chest radiograph or HRCT chest findings were obtained if available. Detailed information on treatment of GBS and COVID-19 was procured. Use of specific medications for COVID-19 such as remdesvir, tocilizumab, or convalescent plasma therapy in addition to the supportive treatment for COVID-19 was tabulated. Primary outcome was either death or discharge from the hospital. Secondary outcome was functional status at the time of discharge. Also, we studied the outcomes in the subset of patients who presented with GBS alone who were asymptomatic for COVID 19, however were incidentally detected to have SARS-CoV-2 virus.

Statistical analysis

We used descriptive statistics to summarize and visualize patient data. For categorical variables, we used frequency and calculated proportions using the number of patients with data available as the denominator. The Shapiro--Wilk test was used to test the normality of data distribution. Continuous variables were reported as mean ± SD or as median with IQR, respectively, for normal and non-normal distributions, whereas categorical variables were presented as counts and percentages. Statistical analyses were performed using SPSS (the statistical package for social sciences) IBM Corp. Released in 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp).

Results

A total of 42 patients from 15 participating centers were included in the study for analysis. Table 1 summarizes the demographic and clinical characteristics of these patients. There were 31 (73.8%) male and 11 (26.2%) female patients. The mean age was 58 years (SD ± 14) (median age 59 years; range, 24--85 years). The median time interval between the onset of SARS-CoV-2 and GBS was 14 days (SD ± 11), (range 1--40 days). 6 patients with GBS who were positive for SARS-CoV-2 RT-PCR remained asymptomatic for COVID-19. Common clinical features were that of typical GBS, ascending paralysis with symmetric quadriparesis and areflexia seen in 24 (57.1%) patients, 13 (31%) patients had predominant lower extremity weakness, and only one had upper extremity weakness with facial diplegia. Miller--Fisher with Guillian--Barre' Overlap syndrome (MFS-GBS) with ophthalmoplegia, areflexia, and ataxia and generalized weakness was clinically evident in 3/42 (7.14%) patients. They tested negative for anti-ganglioside antibody. Cranial nerve involvement was seen with ophthalmoplegia (3/42 patients), bifacial weakness (5/42 patients), and dysphagia (1/42 patient).

Table 1: Association between clinical demographic variables with mortality outcome

Characteristics	Total (*n*=42) %	Discharged (*n*=33) %	Death (*n*=9) %
Age			
<60 years	22 (52.4)	18 (54.5)	4 (44.4)
>60 year	20 (47.6)	15 (45.5)	5 (55.6)
Sex			
Female	11 (26.2)	9 (27.3)	2 (22.2)
Male	31 (73.8)	24 (72.7)	7 (77.8)
Comorbidities			
None	22 (52.38)	18 (54.5)	4 (44.4)
Yes	20 (47.6)	15 (45.5)	5 (55.5)
Hypertension	10	7	3
Diabetes Mellitus II	5	1	4
Chronic kidney disease	2	2	2
Ischemic heart disease	1	1	1
Presenting symptoms			
GBS	14 (33.3)	13 (39.4)	1 (11.1)
COVID-19 symptoms	28 (66.7)	20 (60.6)	8 (88.9)
Preceding febrile illness			
Yes	22 (52.4)	20 (60.6)	2 (22.2)
No	20 (47.6)	13 (39.4)	7 (77.8)
Time interval between GBS and COVID 19			
≤7 days	10 (23.8)	4 (12.1)	6 (66.7)
8-14 days	10 (23.8)	8 (24.2)	2 (22.2)
15-21 days	6 (14.2)	5 (15.1)	1 (11.1)
>21 days	8 (19.0)	8 (24.2)	0 (0)
Asymptomatic for Covid-19	6 (14.3)	6 (14.3)	0 (0)
Unable to determine	2 (4.8)	0 (0)	(0)
Post infectious or parainfectious			
Parainfectious	26 (61.9)	17 (51.5)	9 (100)
Post infectious	16 (38.1)	16 (48.5)	0 (0)
Neurological Presentation			
Generalized weakness	24 (57.14)	18 (54.5)	6 (66.7)
Lower extremity weakness	11 (26.2)	10 (33.3)	1 (11.1)
Upper extremity weakness	1 (2.38)	1 (3.03)	0 (0)
MFS-GBS overlap syndrome	3 (7.14)	2 (6.06)	1 (11.1)
Admitted for COVID-19, difficulty weaning from ventilator	5 (11.90)	3 (9.09)	2 (22.2)
GBS subtype based on NCS			
Demyelinating	25 (59.5)	20 (60.6)	5 (55.5)
Axonal	9 (21.4)	7 (21.2)	2 (22.2)
Mixed	5 (11.90)	4 (12.1)	1 (11.1)
CSF findings			
Albuminocytological dissociation	26 (61.9)	18 (54.5)	8 (88.8)
Normal	8 (19.04)	8 (24.2)	0 (0)
Not done	8 (19.04)	7 (21.2)	1 (11.1)
Nasopharyngeal swab for SARS CoV-2 RT - PCR			
Detected	38 (90.5)	29 (87.9)	9 (100)
Not detected	4 (9.5)	4 (12.1)	0 (0)
Inflammatory markers for COVID 19			
(CRP, LDH, serum ferritin)			
Elevated	35 (83.3)	26 (78.8)	9 (100)
Normal	5 (11.9)	5 (15.1)	0 (0)
NA	2 (4.8)	2 (6.1)	0 (0)
HRCT chest findings			
Abnormal*	38 (90.5)	29 (87.9)	9 (100)

Contd...

Table 1: Contd...

Characteristics	Total (*n*=42) %	Discharged (*n*=33) %	Death (*n*=9) %
Normal	1 (2.38)	1 (3.03)	0 (0)
Not done	3 (7.14)	3 (9.1)	0 (0)
Treatment			
Intravenous Immunoglobulin	31 (73.8)	23 (69.7)	8 (88.8)
Plasmapheresis	1 (2.38)	1 (3.03)	0 (0)
IV methylprednisolone	1 (2.38)	1 (3.03)	0 (0)
No treatment	9 (21.42)	8 (24.2)	1 (11.1)
Treatment specific for COVID 19			
Remdesvir	17 (40.5)	16 (48.5)	1 (11.1)
Remdesvir+Tocilizumab	2 (4.8)	1 (3)	1 (11.1)
Tocilizumab	1 (2.38)	1 (3)	0 (0)
Remdesvir+convalescent plasma	4 (9.5)	0 (0)	4 (44.4)
Favipiravir	1 (2.4)	1 (3)	0 (0)
Ventilator required			
Yes	14 (33.3)	5 (15.2)	9 (100)
Non-invasive ventilation	6 (14.28)	6 (18.2)	0 (0)
No	22 (52.4)	22 (66.7)	0 (0)

GBS: Guillian Barre' Syndrome, MFS-GBS overlap syndrome: Miller Fisher Guillian Barre' overlap syndrome, NCS: nerve conduction study, CSF: cerebrospinal fluid, CRP: C reactive protein, LDH: lactate dehydrogenase. *HRCT chest abnormal - consistent with COVID-19 pneumonia

Table 2: Neurological outcome at discharge

Neurological outcome at discharge	Percentage
Bedbound	16
Walking with moderate support	16
Walking with minimal support	24
Walking independently at discharge	44

The predominant subtype of GBS based on the electrophysiological study was demyelinating in 25 (59.5%) patients. CSF results were available in 34 patients. 26 (61.9%) patients had an elevated CSF protein with an albuminocytological dissociation. SARS-CoV-2 in CSF was tested in only two patients and was negative. Inflammatory markers for COVID-19 disease, CRP, LDH, and sr ferritin were elevated in the majority (83.3%). HRCT chest was abnormal in 38 patients (90.47%), 26 (61.9%) were compatible with COVID-19 interstitial pneumonia. Nasopharyngeal swab by RT-PCR for SARS-CoV-2 was positive in 38/42 (90.5%) patients. Majority of our patients were parainfectious (26/42; 61.90%), while others 16/42 (38.09%) were postinfectious GBS [Table 3].

31 patients (73.8%) received intravenous immunoglobulin (IVIG) for GBS. 14 patients (34.1%) required mechanical ventilation, 6 (14.6%) improved with non-invasive ventilation using BIPAP. 25 patients (59.52%) received COVID-19 specific treatment; 19 of which were discharged home and six died despite aggressive anti-COVID-19 measures. 33/42 (78.57%) patients were discharged. Death occurred in 9/42 (21.4%) patients. All deaths were seen in the parainfectious GBS group. The parainfectious GBS group required mechanical ventilator or non-invasive ventilation in 17/26 (65.38%) patients and were given COVID-19 specific treatment [Table 3].

DISCUSSION

Human coronaviruses can penetrate the central nervous system and cause varied symptoms.[13] Neurological manifestations were seen in 30% of the patients during the SARS pandemic. GBS or acute polyneuropathy was reported during SARS-CoV and MERS-CoV pandemics.[2,3,14-16] It was reported to occur 21--25 days after SARS-CoV infection.[14] GBS was also reported with betacoronavirus infection (HCV-OC43) in a child.[17] Several case reports of GBS with SARS-CoV-2 have been reported in different parts of the world.[4-11,18,19-23] We report a large series of 42 cases of GBS and SARS-CoV-2 infection from one region of India, most cases were from the city of Mumbai.

Clinical features

Majority of the patients in our study were elderly men as seen in the previous descriptions of GBS and COVID-19. [4-11] This reflects the gender prevalence of COVID-19.[24] Underlying comorbidities were seen in 47.61% patients. Despite these comorbidities, 75% (15/20) of them had a good outcome and were discharged from the hospital. Classically, about two-thirds of all GBS associated with other virus or bacterial infections are postinfectious, triggered by an infection that occurs up to 6 weeks preceding the illness.[25] Zhao *et al*. reported a "parainfectious" association of GBS and COVID-19, similar to that seen in ZiKa virus infection.[4,11,19-21] Similar to the observation by Zhao *et al*., the majority of patients in our series were "parainfectious." GBS was observed at a median time of 14 days after COVID-19.[11,22,24] We observed that GBS was the initial presenting symptom in 14 (33.3%) patients, out of which six remained asymptomatic for COVID-19. They were diagnosed to have SARS-CoV-2 based on the positive nasopharyngeal swab for SARS-CoV-2 by RT-PCR or a

Table 3: Clinical features and outcomes of parainfectious and post-infectious GBS		
	Parainfectious (*n*=26) %	**Post-infectious (*n*=16) %**
Age (years)		
<60	14 (53.8)	8 (50)
≥60	12 (46.1)	8 (50)
Sex		
Female	7 (26.9)	4 (25)
Male	19 (73.0)	12 (75)
Preceding febrile illness		
Yes	8 (30.7)	14 (53.8)
No	18 (69.2)	2 (12.5)
Interval between GBS and COVID-19		
<14 days	16 (61.5)	4 (25)
≥14 days	4 (15.4)	10 (62.5)
Asymptomatic for covid-19	4 (15.4)	2 (12.5)
Unable to determine	2 (7.6)	0 (0)
Neurological presentation		
Generalized weakness	16 (61.5)	8 (50)
Lower extremity weakness	5 (19.2)	6 (37.5)
Upper extremity weakness	1 (3.8)	0 (0)
MFS-GBS overlap syndrome	3 (11.5)	0 (0)
Admitted for COVID-19, difficulty weaning from ventilator	5 (19.2)	0 (0)
Nasopharyngeal swab for RT-PCR		
Detected	25 (96.1)	13 (81.2)
Not detected	1 (3.8)	3 (18.7)
SARS - CoV-2 antibody positive	0 (0)	2 (12.5)
Inflammatory markers for COVID-19		
Elevated	24 (92.3)	11 (68.7)
Normal	2 (7.6)	3 (18.7)
Not done	0 (0)	2 (12.5)
HRCT chest		
Abnormal	23 (88.5)	15 (93.7)
Normal	1 (3.8)	0 (0)
Not done	2 (7.6)	1 (6.2)
Treatment		
Intravenous immunoglobulin	21 (80.8)	10 (62.5)
Plasmapheresis	0 (0)	1 (6.2)
Iv methylprednisolone	1 (3.8)	0 (0)
No treatment	3 (11.5)	6 (37.5)
Treatment specific for COVID-19		
Remdesvir	11 (42.3)	6 (37.5)
Remdesvir + Tocilizumab	1 (3.8)	1 (6.2)
Tocilizumab	1 (3.8)	0 (0)
Remdesvir + Convalescent plasma	4 (15.4)	0 (0)
Favipiravir	0 (0)	1 (6.2)
Ventilator required		
Yes	13 (50)	1 (6.2)
Non-invasive ventilation	4 (15.4)	2 (12.5)
No	9 (34.6)	13 (81.2)
Outcome		
Discharged	17 (65.3)	16 (100)
Death	9 (34.6)	0 (0)

positive SARS-CoV-2 antibody. The remaining developed symptoms of SARS-CoV-2 pneumonia 1--2 weeks later with worsening shortness of breath or increasing oxygen requirement.

The pattern of weakness seen was that of classical GBS with symmetric ascending weakness and generalized areflexia.[10,11,15,20,25] Dysautonomia was reported by Su *et al.*; however, is not a common feature of GBS and SARS-CoV-2

infection.[23] None of our patients were reported to have dysautonomia. 5 ICU patients with COVID-19 on ventilator were suspected to have GBS as they had difficulty weaning from the ventilator. Their ICU course was prolonged and the exact onset of GBS was unable to be determined. These patients may have developed critical illness neuromyopathy as the NCS showed mixed axon loss and demyelinating features. CSF albuminocytological dissociation was supportive of demyelinating GBS. Demyelinating GBS is the typical prototype of classic GBS, while axonal forms were more commonly reported with Zika and Dengue virus associated GBS.[26] Most prevalent subtype of GBS in COVID-19 was AIDP which was also seen in most our patients.[11,20,22] Acute motor axonal (AMAN) or motor sensory neuropathy (AMSAN) was seen in the Italian series.[5] MRI spine to evaluate the nerve roots was not done because of the pandemic and the restricted investigations being done at the participating centers. Albuminocytological dissociation was seen as in classic GBS with elevated CSF proteins and normal cell count.[25]

Association of GBS and COVID-19: Parainfectious or postinfectious?

It is debated how SARS-CoV-2 causes GBS and whether due to parainfectious or postinfectious pathogenesis. Determining whether GBS is para or postinfectious based on the temporal profile of GBS alone may not be accurate as patients with COVID-19 may remain asymptomatic or have minimal symptoms for even upto 14 days. HRCT chest findings persist beyond the acute infectious phase and may not help make the distinction. SARS-CoV-2 has not been detected so far in the CSF in the reported cases of GBS.[8-11,20,27] Hence, a direct nerve root invasion of the virus causing intrathecal replication is not a plausible explanation. A causal relationship between the two is difficult to establish but because of the temporal profile of GBS and COVID-19, possible pathogenetic mechanisms have been discussed such as molecular mimicry between the epitope on the surface of the virus and the membrane of sensory or motor neurons, or an antibody attack on the myelin sheath or axon. This may cause the typical postinfectious GBS after recovery from COVID-19. The absence of SARS-CoV-2 in the CSF and the clinical response to IVIG seems to support the postinfectious theory.[11,20,28] The paucity of testing and negative anti-ganglioside antibody questions its role in the pathogenesis of GBS associated with COVID-19. Anti-ganglioside antibodies have a pathogenic role in AMAN/AMSAN while most GBS cases reported with COVID-19 are demyelinating in nature. One patient had anti-GD1b antibody positive in COVID-19 related MFS.[29] We need larger testing for these antibodies and search for newer antibodies. Infact, we saw more parainfectious cases (26/42) than the typical postinfectious GBS (16/42) [Table 3]. The dysimmune or a hyperimmune process because of the massive cytokine storm may possibly explain the parainfectious nature of COVID-19 associated GBS.[11,20,28,30,31] This may also be responsible for the stormy clinical course with lung and multiorgan involvement resulting in poor outcomes and increased mortality as compared to better outcomes seen in the postinfectious GBS associated with COVID-19. Case reports from China,[4] Italy,[5] and those from Europe and the United States were likely more parainfectious cases as time interval between GBS and COVID-19 was less than 14 days in a series of 24 cases by Finsterer *et al*.[8,10,11] A direct neurotoxic effect on nerves is also postulated, however, the response to intravenous immunoglobulins does not support this.[8,20,28] The recent paper by Keddie *et al*. finds no association of GBS with COVID-19 because of the overall decrease in the incidence of cases of GBS seen in the UK.[32] Although we were not able to determine the incidence of GBS in our region or in India, our experience was similar with lesser GBS during the monsoon season this year possibly because of decreased incidence of common infections. However, the number of GBS cases seen in patients with SARS-CoV-2 worldwide suggests a possible pathogenic link between the two.

Treatment and outcomes

Majority 31/42 (73.8%) of our patients were treated with intravenous immunoglobulin (IVIG) with a favorable response. No complications such as thrombotic events were documented despite its prothrombotic risk which may pose a concern with COVID-19. IVIG was chosen as the modality of treatment because of the ease of administration. Only 1 patient underwent plasmapheresis. Cost of IVIG and plasmapheresis can be a major limiting factor in developing countries.[33] Plasmapheresis can be challenging with COVID-19, with underlying thrombocytopenia or sepsis. It also increases the risk of exposure of an additional healthcare worker to the virus. IVIG seems a reasonable practical treatment of GBS with COVID-19. Additionally, IVIG may benefit both GBS and COVID-19 pneumonia. Convalescent plasma therapy from patients who have recovered from SARS-CoV-2 infection may increase the chance of neutralizing the virus by providing specific antibodies and possibly treat the other immunologic effects of the virus as well. The use of convalescent plasma therapy or IVIG has been evaluated in the treatment of COVID-19.[34,35] The recent randomized control trial failed to show a significant difference between IVIG and placebo in improving the clinical outcomes or 30-day mortality in patients with severe COVID-19 pneumonia.[36]

Steroids in the form of intravenous methylprednisolone or dexamethasone was given to those who required oxygen for COVID-19 pneumonia. In the initial days of the COVID-19 pandemic, remdesvir, tocilizumab, and convalescent plasma was not used as it was not available. Mechanical ventilator was required in 14/42 (33.3%) patients out of which nine patients died. Death was because of the underlying COVID-19 pneumonia leading to ARDS, sepsis, or multiorgan failure. The neurological outcomes at discharge are summarized in Table 2. Majority of the patients had good outcomes at discharge, walking independently or with minimal support. We compared outcomes of para and postinfectious GBS separately [Table 3]. Parainfectious GBS as compared to postinfectious GBS had more lung involvement, requiring ventilator and COVID-19

specific treatments. As we discussed these were likely the effect of the hyperimmune effect of SARS-CoV-2 in the acute phase. Postinfectious GBS behaved like the typical postinfectious GBS seen with other infections and had good outcome.

It is important to screen patients for SARS-CoV-2 who present with GBS and are asymptomatic for SARS-CoV-2. We observed that these patients may require prolonged monitoring even in an intensive care unit (ICU) as they may become symptomatic for COVID-19 pneumonia 1-2 weeks later. 6 patients in our series presenting with GBS who were detected to have SARS-CoV-2 by RT-PCR remained asymptomatic for COVID-19. Nasopharyngeal swab for SARS-CoV-2 by RT-PCR or COVID-19 antibody was tested because of the ongoing pandemic. 3 of them were parainfectious and 3 were postinfectious with anti-COVID-19 antibodies detected in two. All of them received IVIG and had good outcome at discharge.

The limitation of our study was the retrospective nature. Being a multicenter study, there was difficulty in collating the data from different centers as it lacked uniformity. Information such as detailed clinical parameters including respiratory rate, oxygen requirement, laboratory parameters, HRCT chest findings that could help determine the severity of COVID-19 disease were not available in all the patients. Other viral infections were not tested in the CSF. Anti-ganglioside antibody test was not available to identify possible autoimmune targets of GBS. Despite the above limitations, this was a study that included relatively a good number of cases of GBS and COVID-19 from a small region of India which provides a comparative data with the reported series in other parts of the world. The true incidence of GBS in COVID-19 is difficult to ascertain.

Conclusion

Overall, the clinical presentation, nerve conduction studies, CSF studies were consistent with the typical non-COVID-19 GBS. In addition, the postinfectious GBS we observed more cases of parainfectious GBS in the setting of COVID-19. Routine testing of patients presenting with GBS for SARS-CoV-2 by nasopharyngeal swab RT-PCR, HRCT chest, or COVID-19 antibody detection in those with high index of suspicion will help prevent inadvertent viral transmission among close contacts and healthcare workers. Patients with COVID-19 in the ICU who develop GBS may be missed because of the lack of timely neurology consultations. GBS is a treatable disease and needs to be differentiated from critical illness myoneuropathy. With upcoming vaccines for COVID-19, vaccine associated GBS is a concern. Further data and larger case studies are needed to study the pathophysiology and correlation between GBS and COVID-19 and characterize the clinical pattern of GBS in the context of the pandemic. A worldwide registry for GBS and Neuromuscular diseases with COVID-19 is being undertaken and hopefully will provide more useful insights.[37]

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Conflicts of interest
There are no conflicts of interest.

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