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ORIGINAL ARTICLE

Incidence and characteristics of Guillain–Barré syndrome in Taiwan before and during the COVID-19 pandemic: A 12-year single-center experience

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Abstract

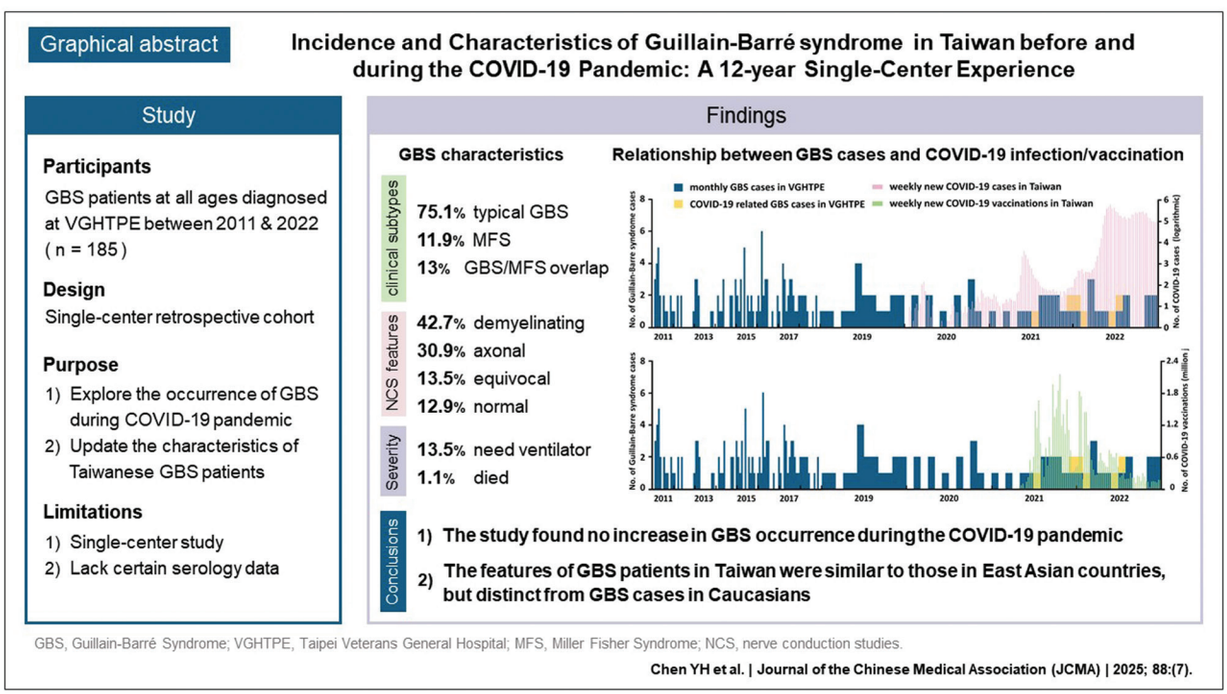
Background: There is substantial regional disparity in the presentation of Guillain–Barré syndrome (GBS), and coronavirus disease 2019 (COVID-19) possibly influences the development of GBS, but the association remains uncertain. This study aimed to investigate the incidence of GBS before and during the COVID-19 pandemic and delineate the clinical profile of GBS in Taiwanese patients.

Methods: Medical records of 185 ascertained GBS cases at Taipei Veterans General Hospital between 2011 and 2022 were reviewed. Patients were analyzed based on age, clinical subtypes, and electrophysiological findings. A multivariable ordinal logistic regression was conducted to identify factors related to outcomes measured by the GBS disability scale (GBS-DS), which ranges from 0 to 6, with higher scores indicating greater disability.

Results: The single-center incidence (SCI) of GBS, defined as the number of GBS cases relative to the total number of outpatient and emergency department visits per year, remained stable during the COVID-19 pandemic (14.3 cases per year) compared with the prepandemic period (15.8 cases per year). COVID-19 infection or vaccination was reported as a preceding event in six cases, five of which had good outcomes (GBS-DS ≤2). In our cohort, 12% were diagnosed with Miller-Fisher syndrome (MFS), 13% had GBS/MFS overlap, and the remaining patients had typical GBS. One-third had axonal GBS, associated with significantly worse outcomes compared with demyelinating GBS. The overall mortality rate was 1.1%. Old age, low Medical Research Council sum score, ventilator dependency, and autonomic dysfunction were independent predictors of high GBS-DS scores.

Conclusion: This single-center study found no increase in GBS occurrence during the COVID-19 pandemic. In Taiwan, GBS is characterized by a higher occurrence of MFS and GBS/MFS overlap and more frequent axonal GBS, highlighting geographical variations in GBS features between Asian and Western countries.

Keywords: COVID-19; Guillain–Barré syndrome; Miller Fisher syndrome; Vaccines



Lay Summary: Guillain–Barré syndrome (GBS) presents with varying characteristics across different regions, and the association between GBS and COVID-19 remains uncertain. We investigated the incidence of GBS before and during the COVID-19 pandemic and the clinical profile of GBS in Taiwanese patients by reviewing 185 GBS cases at Taipei Veterans General Hospital between 2011 and 2022. COVID-19 infection or vaccination was reported as a preceding event in six cases, five of which had good outcomes. The single center incidence (SCI) of GBS, defined as the number of GBS cases relative to the total number of outpatient and emergency department visits per year, remained steady during the COVID-19 pandemic (14.3 cases/year) compared to the pre-pandemic period (15.8 cases/year). In Taiwan, GBS is characterized by a higher occurrence of MFS and GBS/MFS overlap and more frequent axonal GBS, highlighting geographical variations in GBS features between Asia and Western countries.

1. INTRODUCTION

Guillain–Barré syndrome (GBS) is an acute-onset immune-mediated disease of the peripheral nervous system. After Miller-Fisher syndrome (MFS) and other regional subtypes were recognized as GBS variants,[1,2] GBS now comprises a spectrum of clinical subtypes characterized by varying degrees of weakness, sensory abnormalities, and autonomic dysfunction.[3,4] With more phenotypes being defined, the diagnosis of GBS can be made clinically in the early stages before abnormal findings on nerve conduction studies (NCS) and cerebrospinal fluid (CSF) analysis. Among the clinical subtypes, the term "typical GBS" specifically describes patients with flaccid paralysis with or without sensory symptoms, "MFS" describes patients with ophthalmoplegia and/or ataxia, and "Guillain–Barré/Miller Fisher overlap syndrome (GBS/MFS overlap)" refers to patients presenting with both GBS and MFS features.[4,5]

An antecedent event, such as an infection or vaccination, often precedes the onset of GBS. Transient surges in cases of GBS had sought global attention on multiple occasions over the past century, notably the 1976 swine flu vaccine program in the United States and the 2015-2016 Zika virus outbreak in Latin America.[3] In the wake of the coronavirus disease 2019 (COVID-19) pandemic, the medical community and policymakers have focused on the relationship between GBS, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and COVID-19 vaccines. Although few studies have hinted that a COVID-19 infection increases the risk of GBS,[6–8] others suggested no causal link between GBS and COVID-19 infection.[9–11] The epidemiological association between GBS and COVID-19–related events remains inconclusive and particularly understudied in Taiwan.

More importantly, the clinical characteristics of GBS vary across geographical regions.[12] MFS, GBS/MFS overlap, and axonal GBS are more frequently encountered in East Asia than in Western countries.[12–15] Studies of Taiwanese GBS patients conducted more than two decades ago could not take advantage of the new 2014 diagnostic classification that encompasses the full spectrum of GBS.[4,16,17] This resulted in a lack of information on the frequencies, clinical characteristics, and outcomes among GBS patients with different subtypes in Taiwan. Therefore, the present study was conducted to investigate the clinical and epidemiological features of Taiwanese patients with GBS, including (i) the trend of GBS cases before and during the COVID-19 pandemic era, (ii) the frequencies and differences between GBS clinical subtypes, and (iii) the factors that predict unfavorable outcomes.

2. METHODS

2.1. Patients and data collection

This study was based in part on data from the Big Data Center, Taipei Veterans General Hospital. A total of 928 patients were identified using International Classification of Diseases codes for a discharge diagnosis of GBS or polyneuropathy (Supplementary Table 1, https://links.lww.com/JCMA/A333) at Taipei Veterans General Hospital between January 2011 and December 2022. After reviewing the medical records of the patients, the diagnoses of GBS and MFS were ascertained in 185 patients based on the diagnostic guideline of the European Academy of Neurology/Peripheral Nerve Society.[5] The level of diagnostic certainty proposed by the Brighton Collaboration and a clinical subtype of GBS were assigned to each patient based on their key clinical characteristics, CSF analyses, and electrophysiological findings (Supplementary Table 2, https://links.lww.com/JCMA/A333).[4,18]

Demographics, clinical characteristics, CSF examinations, associated treatments, and antecedent events within 4 weeks before the GBS diagnosis were obtained. We used the Guillain–Barré syndrome disability scale (GBS-DS), ranging from 0 (healthy) to 6 (dead),[19] at nadir during hospitalization, upon discharge, and at the last available follow-up up to 6 months to measure the functional status of the patients. An "unfavorable outcome" at the last follow-up was defined as a GBS-DS score ≥3 (unable to walk 10 m without assistance), whereas a "good outcome" was defined as a GBS-DS score ≤2.[20] Medical Research Council (MRC) sum score, evaluating global muscle strengths by manual testing of six muscle groups on both sides,[21] was also obtained. Results of NCS of the upper and lower limbs were analyzed and classified into four categories (demyelinating, axonal, equivocal, and normal) using Hadden's criteria.[22] When serial NCS data during hospitalization were available, the latest dataset was analyzed. The study was approved by the Institutional Review Board of Taipei Veterans General Hospital (No. 2023-06-028CC). The board waived the requirement of written informed consent for participation.

2.2. COVID-19 data

COVID-19 vaccination status, including the brand, the dose, the date of vaccination, and the history of COVID-19 infection, were collected. Any COVID-19 vaccination that was taken within 8 weeks and COVID-19 infections that occurred within 4 weeks before the admission date were considered an antecedent event of GBS.[3,7] The nationwide numbers of confirmed COVID-19 cases and vaccine doses administered are publicly available data from the Taiwan Centers for Disease Control, Ministry of Health and Welfare.

2.3. Statistical analysis

The annual single-center incidence (SCI) of GBS was defined as the number of confirmed GBS cases versus the total number of outpatient and emergency department visits at Taipei Veterans General Hospital in the same year. Categorical variables are described as frequencies and percentages (%), whereas continuous variables are shown as the median with interquartile range (IQR). The characteristics of study

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participants were compared between GBS cases diagnosed in the prepandemic era (2011-2019) and those diagnosed during the pandemic (2020-2022). Further subclassifications were made based on distinct clinical subtypes (typical GBS, GBS/MFS overlap, MFS), different age groups (<12, 12-17, 18-65, >65 years), as well as NCS results suggesting demyelinating and axonal neuropathies. Mann-Whitney *U* test or Kruskal-Wallis *H* test was conducted to compare continuous variables where appropriate, whereas Pearson's χ^2 test, Fisher's exact test, or the generalized Fisher-Freeman-Halton test was performed for categorical variables. Ordinal logistic regression, given its greater power to account for the shift in distribution along an ordinal scale,[23] was applied to the analysis of the GBS-DS score. A stepwise, multivariable ordinal logistic regression analysis was later carried out to determine factors independently related to the clinical outcome (ie, GBS-DS scores at discharge and the last follow-up) and to calculate the corresponding odds ratio (OR) and 95% confidence interval (CI). Factors that showed significance in univariate analyses as well as those known to be related to prognosis in the literature were included in the multivariate regression model. All analyses were performed using Jamovi 2.5 (The Jamovi project, Sydney, Australia) and a two-tailed *p* value <0.05 was considered statistically significant.

3. RESULTS

3.1. Clinical characteristics of the Taiwanese cohort

Demographic and clinical features of the 185 patients with GBS are detailed in Table 1. The median (IQR) age at diagnosis was 54 (37-71) years, ranging from 1 to 91 years, and the male/female ratio was 1.53 (112 men and 73 women). Nearly three-fifths of the patients reported an event preceding the onset of GBS, with upper respiratory tract infections being the most common (27.0%), followed by gastrointestinal infection (11.4%), herpesvirus infection (5.4%), and influenza infection (4.9%). One patient (0.5%) had a COVID-19 infection 20 days before the onset of GBS (Table 2). Eight patients (4.3%) reported vaccination as a preceding event, including COVID-19 vaccination in five cases (Tables 1 and 2).

Most patients presented with limb weakness (82.7%) and sensory symptoms (68.1%), and more than half of the patients (53.5%) had cranial neuropathies. Autonomic dysfunction and ataxia were observed in around one-fifth of the patients. Among the 163 patients who underwent CSF analysis, 127 (77.9%) showed albumino-cytological dissociation, and the highest white blood cell count recorded was 49 cells/mm^3. Based on electrophysiological features of GBS, the most common subtype of GBS was demyelinating GBS (42.7%), followed by the axonal subtype (30.9%). NCS findings could not classify the GBS subtype as demyelinating or axonal in 13.5% of the patients, and normal studies in 12.9%. Twenty-five patients (13.5%) required mechanical ventilation, and two died during the study period, corresponding to a mortality rate of 1.1% (Table 1). In our cohort, the median (IQR) GBS-DS score at nadir and the last available follow-up was 4 (3-4) and 2 (1-3), respectively (Fig. 1A). In Taiwan, 41.9% of the GBS patients received plasmapheresis (PP), 35.3% were treated with intravenous immunoglobulin (IVIg), and 2.7% had methylprednisolone pulse therapy. Two-thirds of them received monotherapy, 6.5% received two types of treatments, and 27.0% underwent supportive care without immunotherapy (Table 1).

Table 1

Demographic and clinical characteristics of patients with Guillain–Barré syndrome in this study

	N (%) or median (IQR)	All (n = 185)
Demographics	Age at onset, y	54 (37-71)
	Sex, male	112 (60.5)
Antecedent events	Upper respiratory tract infections	50 (27.0)
	Gastrointestinal infections	21 (11.4)
	Influenza	9 (4.9)
	Herpesvirus infections[a]	10 (5.4)
	Operation	5 (2.7)
	Paraneoplastic	4 (2.2)
	Vaccination[b]	8 (4.3)
	Others[c]	3 (1.6)
Clinical manifestation	Limb weakness	153 (82.7)
	MRC sum score	47 (35-53)
	Hyporeflexia or areflexia	166 (89.7)
	Paresthesia or sensory deficit	126 (68.1)
	Consciousness disturbance	5 (2.7)
	Cranial neuropathy, any	99 (53.5)
	Facial nerve	40 (21.6)
	Bulbar involvement	49 (26.5)
	Ocular involvement	41 (22.2)
	Autonomic dysfunction	34 (18.4)
	Ataxia	33 (17.8)
Severity of illness	Length of hospital stay, d	17 (11-33)
	ICU admission	42 (22.7)
	Length of ICU stay, d	13 (5-20)
	Required mechanical ventilation	25 (13.5)
	Died	2 (1.1)
	GBS-DS at nadir	4 (3-4)
	GBS-DS at discharge	3 (2-3)
	GBS-DS at the last follow-up	2 (1-3)
Cerebrospinal fluid analysis (n = 163)	Increased protein level (>45 mg/dL)	127 (77.9)
	White blood cell count	1 (0-2)
Nerve conduction studies (n = 178)	Demyelinating	76 (42.7)
	Axonal	55 (30.9)
	Equivocal	24 (13.5)
	Normal	23 (12.9)
Treatment	No treatment	50 (27.0)
	IVIg	65 (35.3)
	PP	77 (41.9)
	MTP pulse therapy	5 (2.7)
	Any of PP, IVIg, or MTP pulse therapy methylprednisolone pulse therapy treatment, n (%)	123 (66.5)
	Two types of treatment[d]	12 (6.5)

COVID-19 = coronavirus disease 2019; GBS-DS = Guillain–Barré syndrome disability scale; ICU = intensive care unit; IQR = interquartile range; IVIg = intravenous immunoglobulin; MRC = Medical Research Council; MTP = methylprednisolone; PP = plasmapheresis.

[a]Cytomegalovirus infections (n = 6), Epstein-Barr virus infections (n = 2), varicella-zoster virus infection (n = 2).

[b]COVID-19 vaccines (n = 5), Influenza vaccines (n = 2), Zoster vaccine (n = 1).

[c]Urinary tract infections (n = 1), COVID-19 infections (n = 1), nivolumab-induced (n = 1).

[d]IVIg + PP (n = 9), IVIg + MTP pulse therapy (n = 2), PP + MTP pulse therapy (n = 1).

3.2. SCI of GBS during the COVID-19 pandemic

Across the 12-year study period, the estimated SCI of GBS in Taipei Veterans General Hospital ranged between 0.23 and 0.90 per 100,000 person-years with the median (IQR) of 0.67 (0.48-0.79) (Supplementary Table 3, https://links.lww.com/JCMA/A333). There was no apparent secular trend over the past decade. Fig. 2A and B illustrates the number of GBS cases per month in our hospital before and during the COVID-19 pandemic. The number of confirmed COVID-19 cases and the person-doses of COVID-19 vaccine administered in Taiwan increased drastically

Table 2

GBS cases with antecedent events associated with COVID-19 infection or vaccination

Patient	Events, days before admission	Sex	Age, y	Clinical subtypes	Facial diplegia	GBS-DS		Treatment
						Nadir	Last	
A	COVID-19 infection, 20 d	M	48	Classic sensorimotor	Y	2	0	PP
B	Vaccine (Moderna, booster), 31 d	M	51	BFP	Y	2	1	IVIg
C	Vaccine (Moderna, booster), 28 d	F	83	Classic sensorimotor	N	3	3	None
D	Vaccine (AZ, 1st dose), 32 d	F	85	GBS/MFS overlap	Y	4	2	IVIg
E	Vaccine (Moderna, 2nd dose), 44 d	F	42	Miller Fisher syndrome	N	2	1	IVIg
F	Vaccine (Moderna, 2nd dose), 56 d	F	43	PCB	N	2	1	None

AZ = Oxford–AstraZeneca; BFP = bifacial weakness with paresthesia; COVID-19 = coronavirus disease 2019; F = female; GBS = Guillain–Barré syndrome; GBS-DS = Guillain–Barré syndrome disability scale; GBS/MFS overlap = Guillain–Barré/Miller Fisher overlap syndrome; IVIg = intravenous immunoglobulin; M = male; N = no; PCB = pharyngeal-cervical-brachial variant; PP = plasmapheresis; Y = yes.

between 2020 and 2022, but GBS incidence in our hospital during the pandemic remained similar to that of the preceding years. The number of GBS cases was 15.8 per year before the pandemic and 14.3 per year during the pandemic years ($p = 0.690$) (Supplementary Table 4, https://links.lww.com/JCMA/A333). In six GBS cases, COVID-19–related histories were noted as preceding events, including one case of COVID-19 infection and five in which COVID-19 vaccinations were administrated (four Moderna [Cambridge, MA, USA; mRNA-1273] and one Oxford–AstraZeneca [Cambridge, UK; ChAdOx1]) (Table 2). The intervals between COVID-19 vaccination and GBS onset were 28 to 56 days. None of the patients with GBS related to COVID-19 infection or vaccination required intensive care or mechanical ventilation during hospitalization. Except for one patient with a GBS-DS score of 3 at the last follow-up, the other five patients had good outcomes (Table 2).

The frequency of GBS patients reporting upper respiratory tract infections as antecedent events during the COVID-19 pandemic era was significantly lower than that reported by GBS patients in the prepandemic years ($p = 0.009$) (Fig. 2C; Supplementary Table 4, https://links.lww.com/JCMA/A333). There were no other considerable changes in clinical features between GBS patients from the prepandemic era and those during the pandemic (Supplementary Table 4, https://links.lww.com/JCMA/A333). We also analyzed the seasonality of GBS and found that the occurrence of GBS increased in spring (35.1%), mildly decreased in summer (21.1%) and winter (25.4%), and further declined in autumn (18.4%) (Supplementary Table 5, https://links.lww.com/JCMA/A333). Such seasonal variation was in agreement with previous studies of GBS in Taiwanese patients.[16,17,24]

3.3. Subgroup analysis of GBS subtypes according to clinical features, age groups, and electrophysiological features

According to the clinical features, patients were categorized into three clinical subtypes: typical GBS (n = 139, 75.1%), GBS/MFS overlap (n = 24, 13.0%), and MFS (n = 22, 11.9%) (Table 3; Supplementary Table 2, https://links.lww.com/JCMA/A333). Among the 139 patients with typical GBS, over three-fifths belonged to the classic sensorimotor subtype, and around a quarter had pure motor GBS. Other variants were relatively rare and accounted for <5% of all cases, including five cases of pure sensory manifestations, six of facial diplegia with paresthesia, three of pharyngeal-cervical-brachial variant, and two of acute pandysautonomia. Fourteen of the 22 patients (63.6%) with MFS showed the classic triad of presentation features, and eight patients had a limited form of MFS (ie, six mainly with ophthalmoplegia, one with ataxia, and one having Bickerstaff brainstem encephalitis). Three-quarters of the MFS patients had equivocal or normal NCS findings in comparison to 17.0% of the typical GBS patients ($p < 0.001$). When comparing the disease severity and outcomes among the three major clinical subtypes, patients with MFS had significantly better GBS-DS scores at nadir than typical GBS patients and patients with GBS/MFS overlap ($p < 0.001$ and $p = 0.007$, respectively) (Fig. 1B). Similarly, the GBS-DS score at the last follow-up was significantly lower in MFS patients than in patients with typical GBS ($p < 0.001$). However, the score in these patients was not different from that in patients with GBS/MFS overlap ($p = 0.173$) (Fig. 1B). None of the MFS patients required intubation; however, mechanical ventilation was needed in one-sixth of the patients with typical GBS and GBS/MFS overlap (Table 3).

We further compared the clinical characteristics of study participants across different age groups (Table 4). The distribution of clinical subtypes was similar among patients of different age groups. Compared with adolescents and adult patients with GBS, cranial neuropathy and autonomic dysfunction were rarely present in children under the age of 12 years. Patients aged 65 years and above had a significantly longer hospital stay, and higher GBS-DS score at nadir and the last follow-up than patients of other age groups (Fig. 1C). Age also influenced the treatment chosen by the physicians, with IVIg being preferred in children with GBS (75% of the patients with onset age <12 years) and PP being used more frequently in adults (age 18-65) and elderly patients (age >65 years).

When patients were categorized according to their electrophysiological features, patients with axonal form GBS had significantly longer hospital stay, more frequent autonomic dysfunction, a greater need for mechanical ventilation, and received multiple treatments than patients with demyelinating neuropathies (Table 5). As expected, patients with axonal form GBS had a worse MRC sum score at hospitalization, as well as poorer GBS-DS scores at nadir and the last follow-up, than those with demyelinating neuropathies (Fig. 1D).

3.4. Factors related to greater disability

Multivariable ordinal logistic regression was used to determine factors related to greater disability (ie, higher GBS-DS scores) at the last follow-up. Old age (OR [95% CI] = 1.44 [1.27-1.65]), low MRC sum score (OR [95% CI] = 0.94 [0.91-0.96]), requiring mechanical ventilation (OR [95% CI] = 3.80 [1.48-10.09]), and the presence of autonomic dysfunction (OR [95% CI] = 2.34 [1.13-4.91]) were independently associated with higher GBS-DS scores at the last follow-up (Supplementary Table 6, https://links.lww.com/JCMA/A333). Antecedent gastrointestinal infections, admission to intensive care, and treatment preference were not significantly correlated with the outcome in our study.

4. DISCUSSION

The present study delineates the clinical and epidemiological features of GBS patients in Taiwan by retrospectively analyzing

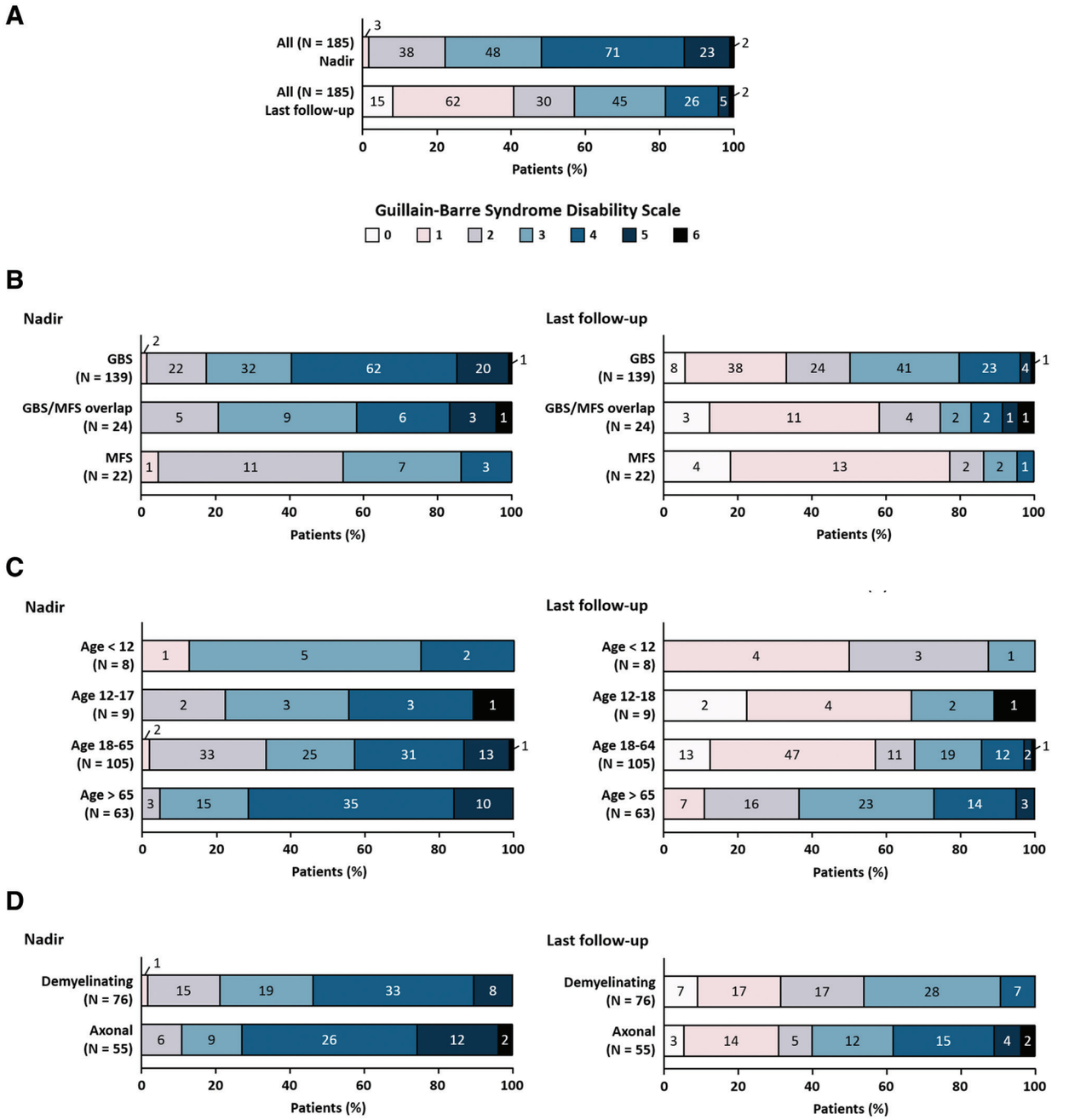

Fig. 1 Distribution of the GBS-DS scores at nadir and the last follow-up in patients with Guillain–Barré syndrome. A, All cases, (B) cases categorized by clinical subtypes, (C) cases categorized by age groups, and (D) cases categorized by electrophysiological subtypes. GBS-DS = Guillain–Barré syndrome disability scale; GBS/MFS overlap = Guillain–Barré/Miller Fisher overlap syndrome.

all patients admitted to a tertiary care center in the past decade. We categorized the cases into clearly defined clinical subtypes based on the standardized guidelines.[4] There are three main findings. First, there was one patient having COVID-19 infection and five individuals receiving COVID-19 vaccination before the development of GBS. However, we did not observe a surge in GBS occurrence during the pandemic as compared with that in the preceding years. GBS patients with antecedent COVID-19 infection/vaccination achieved good recovery with GBS-DS in the range of 0 to 3. Second, the characteristics of GBS patients in Taiwan were similar to the characteristics of GBS patients in East Asian countries, but distinct from GBS cases in Caucasians. One-fourth of the GBS cases in Taiwan belonged to MFS and GBS/MFS overlap, and one-third of all cases had axonal form neuropathy on NCS. The frequencies of MFS subtypes and axonal GBS were much higher than those observed in Caucasians,[12,15] yet similar to those observed in GBS patients in China and Japan.[12–14,25] Third, the mortality rate was only 1% in Taiwanese GBS patients, and 14% of them required mechanical ventilation at disease nadir. Old age, low MRC sum score,

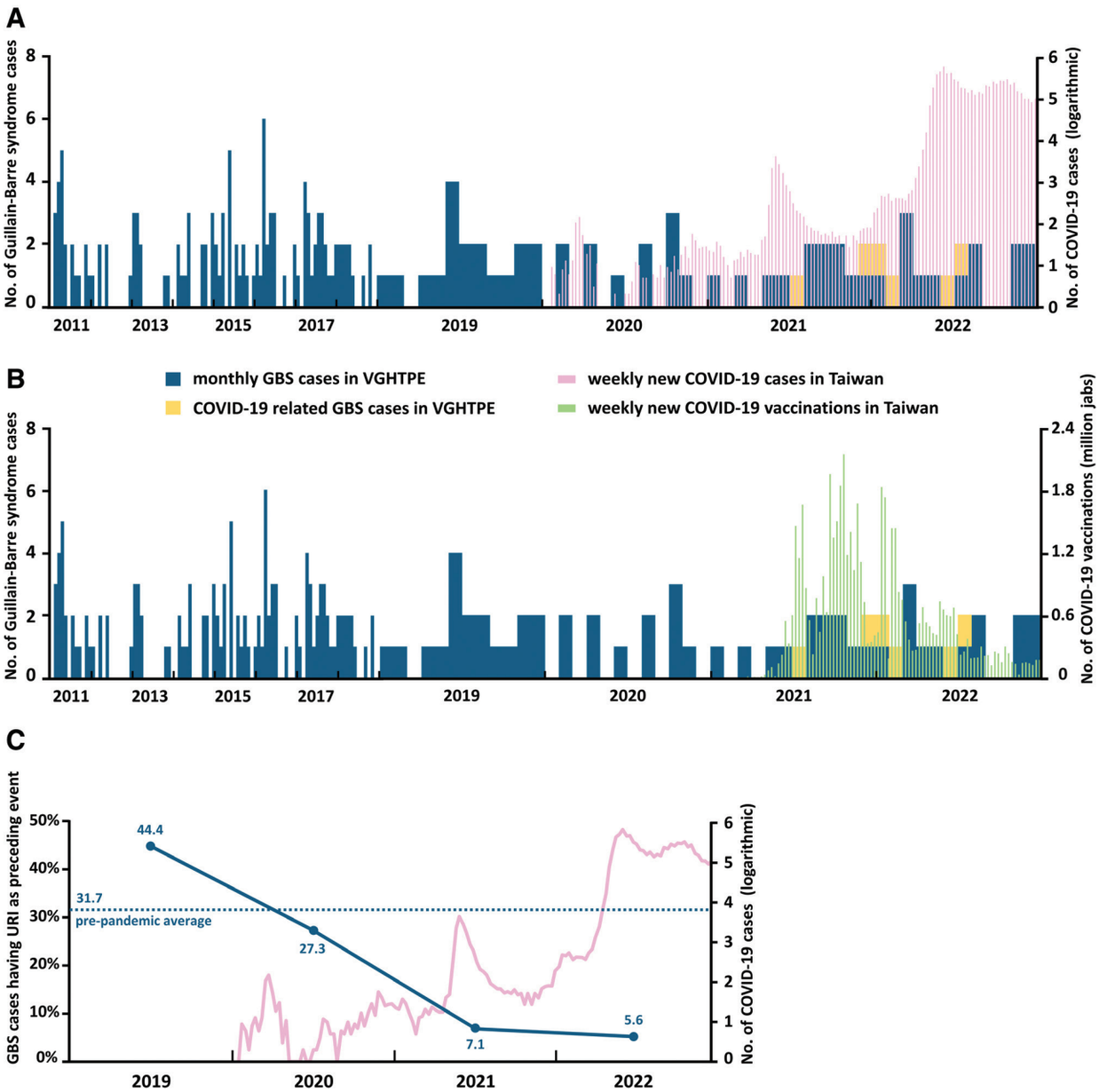

Fig. 2 The relationship between GBS cases and COVID-19 infection/vaccination. A, Newly diagnosed GBS cases, as well as COVID-19–related cases, in VGHTPE are shown in parallel with newly confirmed COVID-19 cases in Taiwan before and during the COVID-19 era. B, Newly diagnosed GBS cases, as well as COVID-19–related cases, in VGHTPE are shown in parallel with newly administered doses of COVID-19 vaccine in Taiwan before and during the COVID-19 era. C, The frequency of GBS cases involving upper respiratory tract infections as antecedent events before and during the COVID-19 pandemic. COVD-19 = coronavirus disease 2019; GBS = Guillain–Barré syndrome; VGHTPE = Taipei Veterans General Hospital.

autonomic dysfunction, and the need for mechanical ventilation were found to have prognostic significance, but antecedent gastrointestinal infections, intensive care admission, and treatment choices did not affect their clinical outcomes.

In this single-center study, we did not observe an apparent increase in GBS occurrence during the COVID-19 pandemic. In fact, the population-based research conducted in the UK, Sweden, and South Korea even revealed a decrease in GBS incidence during the pandemic,[9–11] in contrast to a 2.6-fold increase in GBS incidence in an Italian study.[8] This contrast suggested that the relationship between GBS and COVID-19 infection was far from causal. In addition, the reduced incidence of GBS may be related to the initiation of preventive measures for COVID-19, such as social distancing and wearing of face masks, which could have led to a decline in the transmission of other respiratory infectious diseases.[10,26] Therefore, we could not exclude the possibility that the transmission of conventional preceding infectious agents (eg, campylobacter and cytomegalovirus) was reduced by social distancing and improved health care. Moreover, the decreased transmission would counteract an increase in COVID-19–related GBS. Aligned with this perspective, we found that significantly fewer patients had upper respiratory tract infections as preceding events during the COVID-19 pandemic than in the prepandemic period,

Table 3

Comparison of the clinical features of GBS patients categorized by different clinical subtypes

Clinical subtypes	All (n = 185)	Diagnostic certainty[a], n				ICU ad	MV	GBS-DS, median (IQR)		
	n (%)	1	2	3	4	n (%)	n (%)	Nadir	Discharge	Last
Typical GBS	139 (75.1)	72	41	4	22	33 (23.7)	21 (15.1)	4 (3-4)	3 (2-4)	2 (1-3)
Classic sensorimotor	86 (46.5)	57	25	0	4	19 (22.1)	12 (14.0)	4 (3-4)	3 (2-3)	2 (1-3)
Pure motor	37 (20.0)	15	12	4	6	13 (35.1)	8 (21.6)	4 (4-4)	3 (2-4)	3 (1-4)
Pure sensory	5 (2.7)	0	0	0	5	0 (0)	0 (0)	2 (1-2)	1 (1-1)	1 (1-1)
BFP	6 (3.2)	0	1	0	5	0 (0)	0 (0)	2.5 (2-3)	2 (1-3)	1.5 (1-2.8)
PCB	3 (1.6)	0	2	0	1	1 (33.3)	1 (33.3)	2 (2-3.5)	2 (1.5-3)	1 (1-2.5)
Acute pandysautonomia	2 (1.1)	0	1	0	1	0 (0)	0 (0)	4 (4-4)	3.5 (3.3-3.8)	4 (4-4)
GBS/MFS overlap	24 (13.0)	6	13	2	3	7 (29.2)	4 (16.7)	3 (3-4)	2 (1-3)	1 (1-2.3)
GBS/MFS overlap, complete form[b]	12 (6.5)	3	8	0	1	3 (25.0)	1 (8.3)	3 (3-4)	2 (1-3)	1 (0.8-2)
GBS/MFS overlap, incomplete form[c]	12 (6.5)	3	5	2	2	4 (33.3)	3 (25.0)	3.5 (2.8-4.3)	2.5 (1.8-3.3)	1.5 (1-3.3)
MFS	22 (11.9)	9	5	1	7	2 (9.1)	0 (0)	2 (2-3)	2 (1-2)	1 (1-1)
MFS, classic triad	14 (7.6)	8	5	1	0	1 (7.1)	0 (0)	2.5 (2-3)	2 (2-2)	1 (1-1.8)
AO	6 (3.2)	0	0	0	6	0 (0)	0 (0)	2 (2-2)	1 (1-1.8)	1 (0.3-1)
AAN	1 (0.5)	0	0	0	1	0 (0)	0 (0)	3	1	1
Bickerstaff brainstem encephalitis	1 (0.5)	1	0	0	0	1 (100)	0 (0)	4	4	4
Statistics (GBS vs GBS/MFS overlap vs MFS)						$p = 0.225$	$p = 0.107$	$p < 0.001$	$p < 0.001$	$p < 0.001$

AAN = acute ataxic neuropathy; AO = acute ophthalmoparesis; BFP = bifacial weakness with paresthesia; GBS = Guillain–Barré syndrome; GBS-DS = Guillain–Barré syndrome disability scale; GBS/MFS overlap = Guillain–Barré/Miller Fisher overlap syndrome; ICU ad = intensive care unit admission; IQR = interquartile range; MFS = Miller Fisher syndrome; MV = mechanical ventilation; PCB = pharyngeal-cervical-brachial.

[a]Level of diagnostic certainty of GBS and MFS proposed by the Brighton Collaboration.

[b]Classic sensorimotor with classic triad of MFS (n = 7), pure motor with classic triad of MFS (n = 4), PCB variant with classic triad of MFS (n = 1).

[c]Classic sensorimotor with AO (n = 3), pure motor with AO (n = 2), classic sensorimotor with AAN (n = 5), pure motor with acute ptosis (n = 1), classic sensorimotor with AAN with acute ptosis (n = 1).

Table 4

Comparison of the clinical features of GBS patients categorized by four age groups

n (%) or median (IQR)	Age < 12 y	Age 12-17 y	Age 18-65 y	Age > 65 y	*p*
	(n = 8)	(n = 9)	(n = 105)	(n = 63)	
Sex, male	5 (62.5)	5 (55.6)	62 (59.0)	40 (63.5)	0.945
Clinical subtypes					0.402
Typical GBS	7 (87.5)	8 (88.8)	72 (68.6)	52 (82.5)	
GBS/MFS overlap	1 (12.5)	1 (11.1)	16 (15.2)	6 (9.5)	
Miller Fisher syndrome	0 (0)	0 (0)	17 (16.2)	5 (7.9)	
MRC sum score	47 (42-50)	44 (35-48)	47 (37-58)	45 (33-49)	0.266
Cranial neuropathy, any	2 (25.0)	5 (55.6)	64 (61.0)	28 (44.4)	0.071
Autonomic dysfunction	0 (0)	3 (33.3)	22 (21.0)	9 (14.3)	0.238
Length of hospital stay, d	10 (7-13)	17 (7-18)	15 (10-28)	25 (17-39)	<0.001
ICU admissions	1 (12.5)	3 (33.3)	23 (21.9)	15 (23.8)	0.776
Required mechanical ventilation	0 (0)	1 (11.1)	14 (13.3)	10 (15.9)	0.859
Died	0 (0)	1 (11.1)	1 (1.0)	0 (0)	0.176
GBS-DS at nadir	3 (3-3.3)	3 (3-4)	3 (2-4)	4 (3-4)	0.002
GBS-DS at discharge	2 (1-3)	2 (2-3)	2 (1-3)	3 (3-4)	<0.001
GBS-DS at the last follow-up	1.5 (1-2)	1 (1-3)	1 (1-3)	3 (2-4)	<0.001
No treatment	2 (25.0)	2 (22.2)	28 (26.7)	18 (28.6)	0.987
Two or more treatments	0 (0)	1 (11.1)	7 (6.7)	4 (6.3)	0.860
Received intravenous immunoglobulin	6 (75.0)	5 (55.6)	32 (30.5)	22 (34.9)	0.042
Received plasmapheresis	0 (0)	2 (22.2)	48 (45.7)	27 (42.9)	0.039

GBS = Guillain–Barré syndrome; GBS-DS = Guillain–Barré syndrome disability scale; GBS/MFS overlap = Guillain–Barré/Miller Fisher overlap syndrome; ICU = intensive care unit; IQR = interquartile range; MRC = Medical Research Council.

because social distancing measures had been strictly implemented in Taiwan.

In the present study, there were five cases reporting COVID-19 vaccination as potential GBS triggers. Four were mRNA-based (Moderna) vaccines and one was adenovirus-vectored (Oxford–AstraZeneca). Many analyses have revealed an increased risk of GBS after receiving adenovirus-vectored vaccines within 6 weeks,[27–29] and one study in Italy suggests that the Moderna vaccine is associated with an excess GBS risk.[30] Overall, GBS is an extremely infrequent occurrence after COVID-19 vaccine administration.[28] Based on data from the Taiwan Food and Drug Administration in December 2022, 0.06 cases per 100,000 doses and a total of 37 cases (19 adenovirus-vectored, 16 mRNA-based, 2 protein subunit) involved GBS as an adverse event following vaccinations. Our study, contrary to a review study,[31] suggested a generally good prognosis in COVID-19 vaccine–related GBS cases; all but one patient could walk unaided at the last follow-up. Two out of five patients in our study had bifacial

Table 5

Comparison of the clinical features of GBS patients categorized by electrophysiological subtypes

n (%) or median (IQR)	Demyelinating	Axonal	*p*
	(n = 76)	(n = 55)	
Age at onset, y	63 (41-74)	54 (41-73)	0.325
Sex, male	54 (71.1)	28 (50.9)	0.019
Antecedent gastrointestinal infections	7 (9.2)	11 (20.0)	0.077
Clinical subtypes			0.787
Typical GBS	66 (86.8)	46 (83.6)	
GBS/MFS overlap	8 (10.5)	6 (10.9)	
Miller Fisher syndrome	2 (2.6)	3 (5.5)	
MRC sum score	47 (38-51)	38 (26-47)	0.003
Cranial neuropathy	41 (54.0)	22 (40.0)	0.115
Autonomic dysfunction	9 (11.8)	15 (27.3)	0.024
Length of hospital stay, d	20 (12-30)	25 (17-57)	0.018
ICU admissions	15 (19.7)	18 (32.7)	0.091
Required mechanical ventilation	8 (10.5)	14 (25.5)	0.024
Died	0 (0)	2 (3.6)	0.174
GBS-DS at nadir	4 (3-4)	4 (3-4.5)	0.007
GBS-DS at discharge	3 (2-3)	3 (3-4)	0.009
GBS-DS at the last follow-up	2 (1-3)	3 (1-4)	0.013
No treatment	23 (30.3)	10 (18.2)	0.116
Two or more treatments	2 (2.6)	7 (12.7)	0.035
Received intravenous immunoglobulin	26 (34.2)	16 (29.1)	0.535
Received plasmapheresis	28 (36.8)	34 (61.8)	0.005

Patients with normal or equivocal nerve conduction studies were not included in the analysis.

GBS = Guillain–Barré syndrome; GBS-DS = Guillain–Barré syndrome disability scale; GBS/MFS overlap = Guillain–Barré/Miller Fisher overlap syndrome; ICU = intensive care unit; IQR = interquartile range; MRC = Medical Research Council.

weakness, in accordance with reports indicating that facial diplegia is more common in GBS patients after receiving COVID-19 vaccination.[31,32]

Our study confirmed that Asian GBS patients have two features different from Caucasian GBS patients, namely a higher proportion of MFS and GBS/MFS overlap and more frequent axonal neuropathy on NCS. In our study, MFS and GBS/MFS overlap patients represented 25% of all GBS cases, similar to the frequency of 26% to 34% in Japanese studies,[13,14] a little higher than the frequency of 18% to 19% in past Taiwanese cohorts,[16,33] but considerably higher than that in Western populations (3%-11%).[12,14] For electrophysiology classifications, 30% of GBS cases in the current Taiwanese cohort were axonal form neuropathy, comparable to 33% of axonal GBS reported in the population of Northeastern China and slightly higher than that reported in Japan (13%-23%).[13,25,34] In contrast, axonal GBS only accounted for 3% to 17% of the GBS cases in Northern America and Europe.[12,13,15]

The International Guillain–Barré syndrome Outcome Study has shown that the outcomes in developed Asian countries are slightly superior to those in Western countries, which in part could be attributed to the higher occurrence of MFS cases in Asia.[12] In our cohort, less than one in seven patients needed a mechanical ventilator at nadir, and the mortality rate was 1%. To be noticed, there have been improvements in prognosis in comparison with Taiwanese studies conducted over two decades ago, in which 23% to 27% of patients required mechanical ventilation and 3% to 5% had died.[16,17] Our study also demonstrated that a patient's age influences the preference for GBS treatment. IVIg causes the least adverse effects and there is no need for large vascular access.[5] Therefore, this treatment modality was the predominant treatment choice for children. PP, equally effective as IVIg, was more appealing to older adults in Taiwan. This finding should be interpreted in the context of Taiwan's National Health Insurance policy. Since IVIg is not reimbursed for adult GBS patients without impending respiratory failure, financial considerations may influence treatment choices. Five patients received methylprednisolone pulse therapy—two with pulse therapy alone and three in combination with IVIg or PP, based on their physicians' clinical judgement. However, a diagnosis of chronic inflammatory demyelinating polyneuropathy was highly unlikely, given the monophasic disease course, the absence of relapse, and the lack of chronic immunosuppressive treatment. One patient had a history of ankylosing spondylitis and was treated with sulfasalazine without long-term steroid use, whereas the remaining four had no history of autoimmune diseases.

The current study confirmed that age and MRC sum score are important predictors of outcomes in GBS patients. To our surprise, preceding gastrointestinal infection was not associated with prognosis in the present study. The modified Erasmus GBS Outcome Score (mEGOS) derived from Dutch data recognizes old age, poor muscle strength, and preceding diarrhea as risk factors for being unable to walk within six months of GBS onset.[20] A validation study reasoned that the prognostic effect of antecedent diarrhea is minimal because diarrhea has numerous causes, but the most impactful association linking prodromal diarrhea to unfavorable outcomes is *Campylobacter jejuni* infection, which is often followed by axonal GBS.[35] The current study also identified ventilator dependency and the presence of autonomic dysfunction as significant factors of unfavorable outcomes of GBS. The former is a well-documented risk factor of disability in GBS patients.[5,16,36] The latter is an indication for urgent treatment and predicting respiratory failure,[5,37] but it has rarely been described as a disability predictor in GBS patients. Interestingly, we found that intensive care admissions may not always indicate a poor prognosis, suggesting that substantial improvement can occur in GBS patients after adequate management.

A few limitations of this study must be acknowledged. First, this is an epidemiological study from a single center; therefore, the determination of GBS incidence, particularly during the

COVID-19 pandemic, may be underpowered and may not reflect true population-level incidence rates. Next, a causal relationship between GBS and SARS-CoV-2 cannot be excluded entirely since GBS cases developed from asymptomatic COVID-19 infection were not evaluated in this study. Due to the retrospective approach of the study, the serology tests for antiganglioside antibodies and *Campylobacter jejuni* were not available, and the electrodiagnostic subtyping of GBS patients may be suboptimal since not every patient underwent serial NCS.[15,38] Nevertheless, the clinical significance of GBS lies in the early recognition and management of the disease, in which the clinical features, rather than electrophysiological subtypes, play a greater role.[5]

To conclude, we did not find a surge in GBS occurrence during the COVID-19 pandemic, nor did we observe a significant association between GBS and COVID-19 infection/vaccination. GBS patients in Taiwan are characterized by the relatively high occurrence of MFS and GBS/MFS overlap subtypes and the more frequent axonal form of GBS. These findings highlight the geographical variation in GBS features between East Asian and Western countries. Future domestic studies on GBS are encouraged to tailor treatments to improve the long-term outcomes of GBS patients, especially for those with rare subtypes.

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APPENDIX A. SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://links.lww.com/JCMA/A333.

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