Original Article

Impact of COVID-19 on Guillain-Barre Syndrome in India: A Multicenter Ambispective Cohort Study

Yareeda Sireesha[#], Ritu Shree[1#], Madhu Nagappa[2], Anuja Patil[3], Monika Singla[4], MV Padma Srivastava[5], RK Dhamija[6], Neetha Balaram[7], Abhishek Pathak[8], Dileep Ramachandran[9], Sujit Kumar[10], Inder Puri[11], Sudhir Sharma[12], Samhita Panda[13], Soaham Desai[14], Priyanka Samal[15], Aditya Choudhary[16], Pamidimukkala Vijaya[17], Teresa Ferreira[18], S.S. Nair[19], H.P. Sinha[20], S.K. Bhoi[21], Joseph Sebastian[22], Sanjay Sharma[23], Aneesh Basheer[24], Manish Bhartiya[25], N.L. Mathukumalli, Shaikh Afshan Jabeen, Vivek Lal[1], Manish Modi[1], Praveen Sharma P[2], Subash Kaul[3], Gagandeep Singh[4], Ayush Agarwal[5], Divyani Garg[6], James Jose[7], Priya Dev[8], Thomas Iype[9], Maya Gopalakrishnan[13], Ashish Upadhyay[5], Rohit Bhatia[5], Awadh K. Pandit[5], Rajesh K. Singh[5], Manish Salunkhe[5], P.M. Yogeesh[5], Alisha Reyaz[5], Nishant Nadda[12], Menkha Jha[21], Bismay Kumar[8], PK Kushwaha[20], Harshadkumar Chovatiya[14], Bhavani Madduluri, P Ramesh, Abeer Goel[1], Rahul Yadav[14], Venugopalan Y Vishnu[5], on behalf of the GBS consortium

Nizam's Institute of Medical Sciences, Hyderabad, Telangana, [1]Post Graduate Institute of Medical Education and Research, Chandigarh, [2]National Institute of Mental Health and Neuro Sciences, Bangalore, Karnataka, [3]Krishna Institute of Medical Sciences Hospital, Secunderabad, Telangana, [4]Dayanand Medical College, Ludhiana, Punjab, [5]All India Institute of Medical Sciences, [6]Lady Hardinge Medical College, New Delhi, [7]Government Medical College Kozhikode, [9]Government Medical College, Thiruvananthapuram, [19]Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, [22]Caritas Hospital, Kottayam, Kerala, [8]Institute of Medical Sciences, Banaras Hindu University, Varanasi, [10]Apollo Hospitals, Sheshadripuram, Bangalore, [11]PBM Hospital, Sardar Patel Medical College, Bikaner, [13]All India Institute of Medical Sciences, Jodhpur, Rajasthan, [12]Indira Gandhi Medical College and Hospital, Shimla, Himachal Pradesh, [14]Shree Krishna Hospital and Pramukhswami Medical College, Bhaikaka University, Karamsad, Anand, Gujarat, [15]Kalinga Hospital Limited, Bhubaneswar, [21]All India Institute of Medical Sciences, Bhubaneswar, Odisha, [16]Apollo Gleneagles Hospitals, Kolkata, West Bengal, [17]Lalitha Super Specialities Hospital Private Limited, Guntur, Andhra Pradesh, [18]Goa Medical College, Goa, [20]NH MMI Narayana Superspeciality Hospital, Raipur, Chattisgarh, [23]Ramakrishna Care Medical Sciences Private Limited, Raipur, [24]Pondicherry Institute of Medical Sciences, Pondicherry, [25]Army Hospital, Guwahati, Assam, India

[#]Contributed equally.

Abstract

Introduction/Aims: Studies conducted during the coronavirus disease 2019 (COVID-19) pandemic have reported varied data regarding the incidence of Guillain–Barre syndrome (GBS). The present study investigated demographic and clinical features, management, and outcomes of patients with GBS during a specified period of the COVID-19 pandemic, and compared these features to those of GBS in the previous year. **Methods:** A multicenter, ambispective cohort study including 26 centers across India was conducted. Data from a pre-COVID-19 period (March 1 to August 31, 2019) were collected retrospectively and collected ambispectively for a specified COVID-19 period (March 1 to August 31, 2020). The study was registered with the Clinical Trial Registry India (CTRI/2020/11/029143). **Results:** Data from 555 patients were included for analysis: pre-COVID-19 ($n = 334$) and COVID-19 ($n = 221$). Males were more commonly affected during both periods (male:female, 2:1). Gastroenteritis was the most frequent antecedent event in 2019 (17.4%), whereas fever was the most common event in 2020 (10.7%). Paraparesis (21.3% versus [vs.] 9.3%, $P = 0.001$) and sensory involvement (51.1% vs. 41.3%; $P = 0.023$) were more common during COVID-19 in 2020, whereas back pain (26.3% vs. 18.4%; $P = 0.032$) and bowel symptoms (20.7% vs. 13.7%; $P = 0.024$) were more frequent in the pre-COVID period. There was no difference in clinical outcomes between the two groups in terms of GBS disability score at discharge and 3 months after discharge. Independent predictors of disability in the pre-COVID period included areflexia/hyporeflexia, the requirementfor intubation, and time to bulbar weakness; in the COVID-19 period, independent predictors included time from onset to admission, intubation, and intubation requirement. The mortality rate was 2.3% during the entire study period (13/555 cases). **Discussion:** Results of this study revealed an overall reduction in the frequency of GBS during the pandemic. The lockdown likely reduced the risk for antecedent infections due to social distancing and improved hygiene, which may have resulted in the reduction of the frequency of GBS.

Keywords: Areflexia, COVID-19, GBS, Guillain–Barré

Introduction

Guillain–Barre syndrome (GBS) has been reported during the coronavirus disease 2019 (COVID-19) pandemic[1]; however, unlike the Zika virus pandemic,[2] epidemiological studies have not demonstrated a definite association between GBS and COVID-19.[3] Moreover, some regions have exhibited a reduction in the incidence of GBS during the COVID-19 pandemic.[3,4] Some experts have argued that a small increase in GBS incidence due to COVID-19 may be disguised behind a larger decline from other causes.[3,4]Because of COVID-19, the Government of India declared a nationwide lockdown from March 25, 2020, restricting a population of 1.38 billion to home, with access only to emergency hospital services.[5,6] During the

Address for correspondence: Dr. Venugopalan Y Vishnu, Department of Neurology, MRC International Fellow in Neuromuscular Genomic Medicine, Room No. 704, CN Centre, Seventh Floor, All India Institute of Medical Sciences, New Delhi, India.
E-mail: vishnuvy16@yahoo.com

Submitted: 13-Jun-2022 **Revised:** 01-Jul-2022 **Accepted:** 10-Jul-2022
Published: 03-Dec-2022

DOI: 10.4103/aian.aian_523_22

lockdown, hospital admissions secondary to all diseases, with the exception of COVID-19, declined throughout India.[7,8]

The present study aimed to study the ramifications of the COVID-19 pandemic on the frequency of admissions for GBS compared with a similar pre-COVID period in 2019. We also aimed to characterize the clinical spectrum, outcomes, and predictors of GBS during the two study periods.

Methods

Study design

The present investigation was a multicenter, national, ambispective, observational cohort study. The Department of Neurology, All India Institute of Medical Sciences (AIIMS), New Delhi, created a GBS consortium consisting of 26 centers across India. Retrospective data were collected from a pre-COVID period (March 1 to August 31, 2019) and ambispective data were collected from a COVID-19 pandemic period (March 1 to August 31, 2020). Ethics clearance was obtained from the Institutional Ethics Committees of each participating center. The study was registered prospectively with the Clinical Trial Registry India (CTRI/2020/11/029143).

Study participants

All GBS patients >12 years of age fulfilling the diagnostic criteria for GBS or one of its variants (as per the National Institute of Neurological Disorders and Stroke [NINDS] criteria) were recruited[9] and admitted within 4 weeks of symptom onset. Informed written consent was obtained from all participants in the prospective period. Patients with suspected subacute inflammatory demyelinating polyneuropathy,[10]toxic neuropathies, and vasculitic neuropathies were excluded.

Data collection

Data were collected using a pre-designed, standardized method, and included demographic information; antecedent events; neurological symptoms; and signs of GBS at study entry, at discharge, and 3 months after discharge; treatment received; and associated morbidity and mortality. Disability was scored using the modified Rankin Scale (mRS)[11] and GBS disability score (Hughes score).[12] Autonomic function testing was performed, gauged by history, examination, nerve conduction study, autonomic function tests (all participating centers used one or more of these), and the presence of autonomic dysfunction was noted.[3] Nerve conduction studies and cerebrospinal fluid (CSF) findings were recorded, along with other investigations. In accordance with a study by Hadden *et al*.[13] the site investigators categorized electrophysiological subtypes as follows: demyelinating, axonal, inexcitable, equivocal, and normal. Anonymized data from all centers were pooled for analysis.

Statistical analysis

Continuous variables are expressed as mean (±standard deviation), median (interquartile range[IQR]), and frequency (%). The Mann–Whitney *U*-test, Wilcoxon Rank Sum test, and Kruskal–Wallis test were used to compare continuous and non-parametric data, and the χ^2 test or Fisher's exact test was used to compare proportions. Shapiro–Wilk test was used to test the normality of the data. Univariate and stepwise multi variable logistic regression analyses were performed to observe the independent effect of factors on mRS at discharge and GBS disability score at discharge and 3 months after discharge. Variables were selected for the regression model if they statistically correlated with the outcome on univariate analysis or were clinically known to be associated with the outcome. Stepwise logistic regression was performed with a probability of removal at 0.1 and a probability of inclusion at 0.05.Differences with a two-tailed $P \leq 0.05$ were considered to be statistically significant. Bonferroni correction was performed, wherever applicable. Stata version 14 (StataCorp, College Station, TX, USA) was used for all analyses.

Results

A total of 555 patients with GBS were identified: $n = 334$ in 2019 (i.e., pre-COVID period) and $n = 221$ in 2020 (i.e., COVID-19 pandemic period).

Demographic and clinical characteristics

The median age was 38 years (interquartile range [IQR] 24–52 years) and 36 years (25–54 years) in 2019 and 2020, respectively. Males were more commonly affected (male: female, 2.1:1 [2019] and 2:1 [2020]). Detailed demographic and clinical characteristics of the two groups are summarized in Table 1. Only five patients acquired COVID-19 preceding GBS. Clinical characteristics were similar in both groups although there were minor differences. Paraparesis and sensory involvement were noted to be more frequent in 2020 than in 2019. Reported back pain and bowel symptoms were less frequent during the COVID-19 period. No other significant differences were noted between the two groups, including symptom onset to admission, bulbar involvement, or intubation. The median duration of baseline features viz. symptom onset to presentation, bulbar weakness, intubation, and treatment did not vary between the two groups [Supplementary Table 1]. There was no difference in electrophysiology pattern [Supplementary Table 2], GBS antibody status, or CSF parameters, except for significantly higher CSF protein values in 2019.

Outcomes

There were significant differences in the percentage of patients receiving treatment for GBS in 2020 versus 2019. However, there was no difference in clinical outcomes between the two groups in terms of GBS disability score at discharge and at 3 months after discharge, and mRS at discharge, including ventilator dependence and complications [Table 2]. Independent predictors of disability, analyzed using multivariate logistic regression, included areflexia/hyporeflexia, the requirement for intubation, time to bulbar weakness in the pre-COVID period, and time from onset to admission, intubation, and requirement for intubation in the COVID-19 period [Supplementary Tables 3 and 4].

Table 1: Clinical characteristics of patients

Clinical characteristics	2019 (n=334)	2020 (221)	P
Comorbidities			
DM	64 (19.2%)	28 (12.7%)	0.044
HTN	39 (11.7%)	29 (13.1%)	0.611
Smoking	5 (1.5%)	11 (4.9%)	0.016
Alcohol	4 (1.2%)	8 (3.6%)	0.055
Others	47 (14.1%)	36 (16.3%)	0.473
None	210 (62.8%)	127 (57.7%)	
Antecedent events			
Gastroenteritis	58 (17.4%)	21 (9.8%)	0.009
URI	32 (9.6%)	17 (7.9%)	0.443
Fever	31 (9.3%)	23 (10.7%)	0.661
UTI	2 (0.6%)	0	0.520
Vaccination	1 (0.3%)	0	0.999
Chickenpox	1 (0.3%)	1 (0.5%)	0.999
Others	6 (1.8%)	7 (3.2%)	0.300
None	204 (61.1%)	143 (66.5%)	
Weakness			
Quadriparesis	288 (86.2%)	169 (76.5%)	0.039
Paraparesis	31 (9.3%)	47 (21.3%)	0.403
UL weakness	1 (0.3%)	0	0.999
Single limb weakness	1 (0.3%)	2 (0.9%)	0.566
No limb weakness	13 (3.9%)	3 (1.4%)	0.118
Sensory signs and/or symptoms	138 (41.3%)	112 (51.1%)	0.023
Autonomic dysfunction	293 (87.7%)	190 (86.4%)	0.614
Bladder symptoms	77 (22.8%)	34 (15.5%)	0.086
Bowel symptoms	69 (20.7%)	29 (13.2%)	0.024
Ataxia	54 (16.2%)	40 (18.2%)	0.547
Reflexes			
Areflexia	215 (64.4%)	120 (55.8%)	0.090
Hyporeflexia	104 (31.1%)	79 (36.7%)	
Normal	15 (4.5%)	16 (7.5%)	
Back pain	88 (26.3%)	40 (18.4%)	0.032
Cranial nerve involvement	142 (42.5%)	83 (37.6%)	0.244
Facial weakness	98 (29.5%)	73 (33.5%)	0.325
Bulbar involvement	85 (25.7%)	46 (21%)	
Oculomotor involvement	23 (6.9%)	14 (6.4%)	
Ventilatory assistance	50 (14.9%)	28 (12.7%)	0.445

DM: diabetes mellitus, HTN: hypertension, URI: upper respiratory tract infection, UTI: urinary tract infection, UL: upper limb. P value is for the overall group

COVID-19-positive patients in 2020

There were only five (2.3%) patients (male to female ratio, 4:1) with the proven antecedent (real-time polymerase chain reaction positive for severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2] within 4 weeks of GBS onset, n = 4) or concurrent (SARS-CoV-2 positive at the time of GBS onset, n = 1) COVID-19. All patients presented with quadriparesis with areflexia, three exhibited autonomic dysfunction, intubation was required in two patients, and the duration of ventilator support was <1 week. Electrophysiology results were suggestive of axonal and demyelinating patterns in two patients, respectively, whereas it was not performed in one patient. Hyponatremia was noted in only 1 (20%) patient, which was attributed to the syndrome of inappropriate antidiuretic hormone secretion. Intravenous immunoglobulin (IVIG) was administered to four patients, whereas one patient received steroids. One patient died during the hospital stay; the remaining patients had an mRS score ranging from 3 to 5 at discharge.

Discussion

We found a substantial reduction in the number of GBS cases during the government-imposed lockdown for COVID-19. Similarly, an epidemiological study from the United Kingdom (UK) reported a reduction in the incidence of GBS when March–May 2020 was compared with the same months in 2016–2019.[3] Increased hygiene, social distancing, and confinement to home were presumed to have decreased fecal and air-borne transmission of communicable diseases, thereby leading to a lower incidence of GBS. Based on these results, we cannot deny the possible association between COVID-19 and GBS.

Studies have reported a decrease in the incidence of infectious diseases during lockdowns.[14,15] The total number of cases of influenza in Japan was significantly decreased when compared between September 30, 2019, and March 15, 2020, with the time frames from 2014–2019.[14] Similar results were noted when the impact of quarantine on the occurrence of other acute respiratory diseases (influenza A, influenza B, human metapneumovirus) was studied in Brazil during the COVID-19 pandemic.[15] Even the number of cases of tuberculosis has reportedly declined, probably due to a decrease in droplet aerosol transmission.[16,17] These studies suggest that containment measures did, in fact, decrease the spread of other infectious diseases; as such, these results can be used to minimize the spread of other infections in the future. When community hygiene was adopted during the outbreak of severe respiratory distress syndrome in 2003 in Hong Kong, there was also a marked reduction in other respiratory infections.[18]

There are studies, however, that contradict our observations. In Italy, Filosto *et al*.[19] reported a significant increase in the number of GBS cases from March to April 2020 compared to the same months in 2019. The relative incidence in 2020, compared to 2019, was 2.6.[19] Italy witnessed a large number of COVID-19 cases, and a substantial proportion of the population was infected during the study period and was positive for COVID-19 (88%), providing a plausible explanation.[19] However, there is a possibility that specific unknown epidemiological or genetic factors have led to an increased incidence of GBS selective to their region.

Differences in clinical features during the COVID-19 period compared to the pre-pandemic period could be explained by the heterogeneity of the disease. However, the severity and outcomes did not differ despite differences in clinical characteristics. The explanation is likely to be multifactorial, including the COVID-19 pandemic, patient factors, such as reluctance to undergo invasive procedures such as

Table 2: Management data for 2019 and 2020

Management	2019 (334 Cases)	2020 (221 Cases)	*P*
Treatment received			
IVIG	198 (60.8%)	118 (54.1%)	0.003*
PLEX	66 (20.3%)	35 (16.1%)	
Corticosteroids	24 (7.5%)	14 (6.4%)	
IVIG + PLEX	6 (1.8%)	4 (1.8%)	
IVIG + Corticosteroids	9 (2.7%)	7 (3.2%)	
PLEX + steroids	5 (1.5%)	4 (1.8%)	
IVIG + PLEX + Corticosteroids	1 (0.2%)	4 (1.9%)	
None	17 (5.2%)	32 (14.7%)	
Median days on ventilator (IQR)	0 (0-10)	0 (0-7)	0.713
Median GBS disability at discharge (IQR)	3 (2-4)	3 (2-3)	0.138
Clinical diagnosis at discharge			
Sensorimotor	132 (51.3%)	76 (41.5%)	0.283
Pure motor	111 (43.2%)	103 (56.3%)	0.012
MFS	8 (3.1%)	2 (1.1%)	
MFS GBS overlap	6 (2.4%)	2 (1.1%)	
Median mRS at discharge (IQR)	3 (2-4)	3 (2-4)	0.2783
Complications			
VAP	22 (7.8%)	13 (6.1%)	0.173*
Sepsis	7 (2.5%)	9 (4.2%)	
UTI	6 (7.8%)	6 (2.8%)	
DVT	7 (2.5%)	2 (0.9%)	
AF	1 (0.3%)	0	
Death	6 (2.1%)	7 (3.3%)	
Others	4 (1.4%)	6 (2.8%)	
None	214 (86.1%)	170 (80.2%)	
Recurrent GBS			
Monophasic	317 (96.1%)	212 (96.3%)	0.783*
Fluctuations <8 weeks	7 (2.1%)	0	
Fluctuations >8 weeks	2 (0.6%)	0	
Recurrent	4 (1.2%)	8 (3.7%)	
Median GBS disability score at 3 months (IQR)	1 (1-2)	1 (0-2)	0.890
In-hospital mortality	6	7	0.321
Ventilator dependency	17 (4.8%)	6 (2.9%)	0.718

IVIG: intravenous immunoglobulin, PLEX: plasmapheresis, IQR: interquartile range, MFS: Miller–Fischer syndrome, DVT: deep vein thrombosis, AF: atrial fibrillation. **P*-value is for the overall group

plasmapheresis, and hospital factors such as the concentration of workforce toward COVID-19 management. We did not find any significant difference between the two groups in terms of treatment modality. Outcomes (i.e., mRS and GBS disability scores at discharge and 3 months after discharge) did not differ between the two groups. Our results were similar to those reported in Western countries for all these parameters.[3,20] A cohort study from the UK reported no significant difference in the clinical presentation of GBS during the COVID-19 pandemic, except for the increased need for intubation attributed to the greater pulmonary involvement of COVID-19.[3]

We found significantly higher CSF protein values in 2019, which may be due to differences in the timing of lumbar puncture. The axonal pattern on electrophysiology was most common in both groups. Only five patients were positive for COVID-19, and they exhibited axonal (n = 2) and demyelinating (n = 2) patterns on electrophysiology. A systematic review by Uncini *et al*.[21] reported a demyelinating variant in 80.5% of all GBS cases associated with COVID-19. However, individual case reports have described nearly equal distributions of axonal or demyelinating patterns.[22]

Plasmapheresis was associated with higher GBS disability scores at discharge and 3 months after discharge. The poorer outcomes may reflect its use in more advanced diseases. Several other factors could have confounded this result because decisions regarding plasmapheresis or IVIG depend on individual centers or neurologist preferences, the presence of dysautonomia, sepsis or cardiac issues and, most importantly, financial constraints (i.e., plasma exchange is less expensive than IVIG in our settings). Moreover, the confidence interval (CI) was wide affecting the precision of this finding.

Some patients received corticosteroids alone or in combination with IVIG or plasmapheresis. Although there is no definite

evidence supporting their efficacy in GBS, they have been used in clinical practice, especially when patients cannot afford IVIG or plasmapheresis. A Cochrane review addressing corticosteroids in GBS concluded that there was no significant difference in disability after 4 weeks of use. However, two large trials (467 patients) reported a slight improvement in disability after 4 weeks with the use of intravenous corticosteroids.[23]

In our study, the mortality rate was only 2.3% (13/555), which is lower than the overall mortality rate in the International GBS Outcome Study (IGOS) (44/659 [7%])[24] and that reported by Hughes *et al*.[25] (approximately 5%). Both lower mortality and less ventilatory assistance may be due to the greater treatment response in our population.

Our study had several limitations. First, data extraction for the 2019 period and a significant proportion of 2020 (as per approval of the Institute Ethics Committee) was performed retrospectively from the medical record sections of hospitals. As such, we may have missed some cases or some parameter data. Moreover, we did not collect data regarding total hospital admissions. Second, the data represent only a small proportion of the Indian population and do not include data from primary and/or secondary health care systems. Third, the lockdown restricted access to travel, which may have contributed to the decreased number of patients. Finally, we did not test COVID-19 antibodies in patients presenting to us with GBS in 2020 and, therefore, may have missed milder cases of COVID-19-triggered GBS.

In conclusion, India witnessed an overall decrease in the frequency of GBS, with no phenotypic variations, during the COVID-19 pandemic. The lockdown measures likely decreased the risk for antecedent infections and probably reflected a beneficial decrease in GBS frequency during the pandemic period.

Ethics approval

Institutional ethics approval was taken from the All India Institute of Medical Sciences (IEC-808/07.08.2020, RP-21/2020) and all participating centers as well.

Abbreviations

AF, atrial fibrillation; COVID-19, coronavirus disease 2019; CSF, cerebrospinal fluid; CTRI, Clinical Trial Registry India; DM, diabetes mellitus; DVT, deep vein thrombosis; GBS, Guillain–Barre syndrome; HTN, hypertension; IGOS, International GBS Outcome Study; IQR, interquartile range; IVIG, intravenous immunoglobulin; MFS, Miller–Fischer syndrome; MRI, magnetic resonance imaging; mRS, modified Rankin Scale; NINDS, National Institute of Neurological Disorders and Stroke; PLEX, plasmapheresis; SARS-CoV-2, severe acute respiratory syndrome Coronavirus 2; UK, United Kingdom; UL, upper limb; URI, upper respiratory tract infection; UTI, urinary tract infection; VAP, ventilator-associated pneumonia

Acknowledgement

V.Y.V. is supported by a Medical Research Council (UK) strategic award to establish an International Centre for Genomic Medicine in Neuromuscular Diseases (MR/S005021/1).

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Galassi G, Marchioni A. Facing acute neuromuscular diseases during COVID-19 pandemic: Focus on Guillain-Barré syndrome. ActaNeurolBelg 2020;120:1067-75.
2. Brito Ferreira ML, Militão de Albuquerque MF, de Brito CA, de Oliveira França RF, Porto Moreira ÁJ, de Morais Machado MÍ, *et al*. Neurological disease in adults with Zika and Chikungunya virus infection in Northeast Brazil: A prospective observational study. Lancet Neurol 2020;19:826-39.
3. Keddie S, Pakpoor J, Mousele C, Pipis M, Machado PM, Foster M, *et al*. Epidemiological and cohort study finds no association between COVID-19 and Guillain-Barré syndrome. Brain 2021;144:682-93.
4. Umapathi T, Er B, Koh JS, Goh YH, Chua L. Guillain-Barré syndrome decreases in Singapore during the COVID-19 pandemic. J PeripherNervSyst 2021;26:235-6.
5. COVID-19: Lockdown across India, in line with WHO guidance, UN News. March 22 2020.
6. Singh KD, Vindu, Kumar, Hari, Gettleman, Jeffrey. "India, Day 1: World's Largest Coronavirus Lockdown Begins": The New York Times. ISSN 0362-4331; 25 March 2020.
7. Bewal N, Minhas S, Krishna Prasad G, Yadav A, Sreedhar C, Bhasin D, *et al*. Impact of COVID 19 lockdown on emergency admissions at a large Zonalhospital. Med J DY PatilVidyapeeth 2020;13:603-7.
8. Saini MK, Kumar H, Saini K, Behera A, Pannu AK, Soundappan K, *et al*. Impact of lockdown on medical emergency visits during the COVID-19 pandemic in India. Postgrad Med J 2021;postgradmedj-2021-140850. doi: 10.1136/postgradmedj-2021-140850. Online ahead of print.
9. Asbury AK, Cornblath DR. Assessment of current diagnostic criteria for Guillain–Barré syndrome. Ann Neurol 1990;27(Suppl):S21-4.
10. Oh SJ, Kurokawa K, de Almeida DF, Ryan HF Jr., Claussen GC. Subacute inflammatory demyelinating polyneuropathy. Neurology 2003;61:1507-12.
11. vanSwieten JC, Koudstaal PJ, Visser MC, Schouten HJ, van Gijn J. Interobserver agreement for the assessment of handicap in stroke patients. Stroke 1988;19:604-7.
12. Hughes RA, Newsom-Davis JM, Perkin GD, Pierce JM. Controlled trial prednisolone in acute polyneuropathy. Lancet 1978;2:750-3.
13. Hadden RD, Cornblath DR, Hughes RA, Zielasek J, Hartung HP, Toyka KV, *et al*. Electrophysiological classification of Guillain-Barré syndrome: Clinical associations and outcome. Plasma Exchange/SandoglobulinGuillain-Barrésyndrome trial group. Ann Neurol 1998;44:780-8.
14. Sakamoto H, Ishikane M, Ueda P. Seasonal influenza activity during the SARS-CoV-2 outbreak in Japan. JAMA 2020;323:1969-71.
15. de Souza Luna LK, Perosa DA, Conte DD, Carvalho JM, Alves VR, Cruz JS, *et al*. Different patterns of influenza A and B detected during early stages of COVID-19 in a university hospital in São Paulo, Brazil. J Infect 2020;81:e104-5.
16. Lai CC, Yu WL. The COVID-19 pandemic and tuberculosis in Taiwan. J Infect 2020;81:e159-61.
17. Komiya K, Yamasue M, Takahashi O, Hiramatsu K, Kadota JI, Kato S. The COVID-19 pandemic and the true incidence of tuberculosis in Japan. J Infect 2020;81:e24-5.
18. Lo JY, Tsang TH, Leung YH, Yeung EY, Wu T, Lim WW. Respiratory infections during SARS outbreak, Hong Kong, 2003. Emerg Infect Dis 2005;11:1738-41.
19. Filosto M, CottiPiccinelli S, Gazzina S, Foresti C, Frigeni B, Servalli MC, *et al*. Guillain-Barré syndrome and COVID-19: An observational multicentre study from two Italian hotspot regions. J NeurolNeurosurg Psychiatry 2021;92:751-6.
20. Berlit P, Bösel J, Gahn G, Isenmann S, Meuth SG, Nolte CH, *et al*. "Neurological manifestations of COVID-19"-guideline of the German

society of neurology. Neurol Res Pract 2020;2:51.
21. Uncini A, Vallat JM, Jacobs BC. Guillain-Barré syndrome in SARS-CoV-2 infection: An instant systematic review of the first six months of pandemic. J NeurolNeurosurg Psychiatry 2020;91:1105-10.
22. Caress JB, Castoro RJ, Simmons Z, Scelsa SN, Lewis RA, Ahlawat A, *et al*. COVID-19-associated Guillain-Barré syndrome: The early pandemic experience. Muscle Nerve 2020;62:485-91.
23. Hughes RAC, Brassington R, Gunn AA, van Doorn PA. Corticosteroids for Guillain-Barré syndrome. Cochrane Database Syst Rev 2016;10:CD001446.
24. Doets AY, Verboon C, van den Berg B, Harbo T, Cornblath DR, Willison HJ, *et al*. Regional variation of Guillain-Barré syndrome. Brain 2018;141:2866-77.
25. Hughes RA, Swan AV, Raphaël JC, Annane D, van Koningsveld R, van Doorn PA. Immunotherapy for Guillain-Barré syndrome: A systematic review. Brain 2007;130:2245-57.

Supplementary Table 1: Median duration of baseline features

Median durations (days) with IQR	2019 (334 cases)	2020 (221 cases)	*P*
Symptom onset to admission in days	6 (4-10)	6 (4-10)	0.715
Symptom onset to bulbar weakness	3 (1-6)	3 (1-5)	0.629
Symptom onset to intubation	3 (0-5.75)	3.5 (0-7)	0.216
Symptom onset to treatment	7 (4-11)	6 (4-10)	0.881

Supplementary Table 2: Electrophysiology and laboratory features in the 2 cohorts

Investigations	2019 (334 cases)	2020 (221 cases)	*P*
Electrophysiology			
Normal	16 (4.9%)	5 (2.3%)	0.200
Abnormal	308 (93.3%)	210 (95.4%)	
Not done	6 (1.8%)	5 (2.3%)	
Electrophysiological diagnosis			
Demyelinating	134 (40.7%)	88 (40.6%)	0.117
Axonal	156 (47.4%)	115 (53%)	
Inexcitable	5 (1.5%)	2 (0.9%)	
Equivocal	13 (3.9%)	2 (0.9%)	
Normal	15 (4.6%)	5 (2.3%)	
Not done	6 (1.8%)	5 (2.3%)	
Electrophysiological findings			
Sensorimotor	144 (47.7%)	113 (56.2%)	0.331
Pure motor	140 (46.4%)	77 (38.3%)	
Pure sensory	2 (0.6%)	2 (1%)	
Normal	10 (3.3%)	4 (2%)	
Not done	6 (2%)	5 (2.5%)	
Hyponatremia			
Present	51 (17.5%)	24 (14%)	0.326
Missing data	43	50	
Median CSF protein in mg/dl (IQR)	72 (42.5-91)	63.3 (49-110)	0.025
Median CSF cell count/mm^3 (IQR)	2 (0-5.25)	3 (0-5)	0.231
Median CSF glucose in mg/dl (IQR)	71.5 (61.25-93.5)	70 (64.25-85.75)	0.791
MRI Spine			
Normal	52 (28.3%)	25 (20.5%)	0.294
Abnormal	21 (11.4%)	14 (11.5%)	
Not done	111 (60.3%)	83 (68%)	
Missing data	150	99	
Porphyria status			
Negative	115 (37.3%)	25 (13.4%)	-
Not tested	193 (62.7%)	162 (86.6%)	
Missing data	26	34	
GBS antibody status			
Present	13 (4.2%)	10 (4.8%)	
Absent/not tested	297 (95.8%)	200 (95.2%)	0.757
Missing data	24	11	

Supplementary Table 3: Predictors of disability

mRS	Univariate	Multivariate
mRS 0-2 in 2019	Time from onset to intubation ; p-0.0007	Areflexia (OR-0.43; p-0.009; CI: 0.23-0.81)
	Quadriparesis; p-0.049	No Intubation requirement (OR-5.7; p-0.012; CI: 1.46-22.32)
	Areflexia; p-0.000	Normal sodium levels (OR-6.32; p-0.029; CI: 1.20-33.20)
	No limb pain; p-0.002	
	Intubation requirement; p-0.007	
	SIADH; p-0.001	
	Normal sodium levels; p-0.048	
mRS 0-2 in 2020	Age; p-0.0005	Hyporeflexia (OR-0.22; p-0.002; CI: 0.08-0.56)
	Onset to admission time; p-0.0032	No Intubation requirement (OR-11.53; p-0.027; CI: 1.32-100.67)
	Onset to intubation time; p-0.0015	
	Onset to treatment time; p-0.0465	
	CSF cells; p-0.0237	
	Paraparesis; p-0.002	
	Bladder involvement; p-0.015	
	Bowel involvement; p-0.006	
	Bulbar weakness; p-0.001	
	Intubation requirement; p-0.000	
	Axonal subtype; p-0.031	
	Hyporeflexia; p-0.008	
	Plasmapheresis; p-0.015	
mRS 0-2 combined	Hyporeflexia; p-0.000	Hyporeflexia (OR-0.18; p-0.000; CI: 0.09-0.35)
	Limb pain; p-0.009	No Intubation requirement (OR-5.30; p-0.002; CI: 1.82 – 15.42)
	Cranial nerve involvement; p-0.044	
	Bulbar weakness; p-0.000	
	Intubation requirement; p-0.000	
	Axonal pattern; p-0.004	
	Time of onset to intubation; p-0.001	

Supplementary Table 4: GBS disability score at discharge and at 3 months in 2019, 2020 and combined

Predictors	Regression co-efficient	*P*	Confidence interval
GBS disability score at discharge in 2019			
Normal reflexes	-2.12	0.020	-3.90--0.34
Intubation requirement	0.74	0.031	0.07-1.42
Time from onset of weakness to bulbar weakness	0.08	0.044	0.01-0.17
GBS disability score at discharge in 2020			
Time from onset to admission	-0.06	0.019	-0.11 - -0.01
Intubation requirement	0.82	0.007	0.24-1.39
Time from onset to intubation	0.08	0.002	0.03-0.14
GBS disability score at discharge combined			
Normal reflexes	-1.79	0.019	-3.28-0.30
Intubation requirement	1.10	0.000	0.62-1.57
Plasmapheresis	0.51	0.033	0.04-0.98
GBS disability score at 3 months in 2019			
Time from onset to admission	-0.19	0.05	-0.39-0.00
Age	0.06	0.015	0.01-0.11
GBS disability score at 3 months 2020			
Bladder involvement	2.31	0.004	0.86-3.76
GBS disability score at 3 months combined			
Intubation requirement	1.74	0.000	1.12-2.35
Age	0.02	0.023	0.00-0.03
Plasmapheresis	0.79	0.027	0.09-1.42