Original Article

Journey of Guillain Barre syndrome from the pre-pandemic era to the pandemic era: A 4-year retrospective study

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Abstract

Aims: To study demographic and clinical profiles of Guillain Barre syndrome (GBS) in the pre-pandemic and coronavirus disease 2019 (COVID-19) pandemic era and to compare the GBS incidence, severity, and its outcome in the pre-pandemic and pandemic eras. **Methodology:** This is a 4-year retrospective study done in a tertiary care hospital in Delhi, India, between March 2018 and March 2022. Patients were divided into the pre-pandemic era and pandemic era (2 years before and 2 years after March 2020). **Results:** The number of patients (N) was 25 in the pandemic/vaccine era, while N = 49 in the pre-pandemic era. The mean duration of hospitalization was significantly higher ($P = 0.03$) during the pandemic era (10.68 ± 6.67 days) compared to the pre-pandemic era (7.59 ± 3.55 days). There was no statistical difference in age ($P = 0.56$), gender ($P = 0.70$), GBS variants ($P = 0.40$), clinical spectrum, antecedent infection ($P = 0.91$), Hughes Disability Score on admission and discharge ($P = 0.93$ and $P = 0.52$, respectively), respiratory involvement requiring a ventilator ($P = 0.19$), and mortality ($P = 0.26$) in both the eras. **Conclusion:** Our study showed no association of the incidence of GBS with the ongoing COVID-19 pandemic. The mean hospitalization days were significantly increased during COVID-19 in view of associated respiratory involvement. The commonly held hypothesis of the increase in GBS cases during the pandemic/vaccine era has not been observed in our study.

Keywords: AIDP, COVID-19, GBS, pandemic

Introduction

Guillain Barre syndrome (GBS) is an acute inflammatory auto-immune disease of the peripheral nervous system. About two-thirds of patients who develop GBS report symptoms of an antecedent infection/event in the 6 weeks preceding the onset of the condition. These infections trigger the immune response that causes GBS. Viral infection and vaccination are known antecedent events for GBS with surge in cases during epidemics (more recently being Zika virus epidemic in 2015).[1] This study aims to understand the demographic and clinical profiles of GBS in the pre-pandemic and coronavirus disease 2019 (COVID-19) pandemic eras and to compare the GBS incidence, severity, and its outcome in the pre-pandemic and pandemic eras.

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Received: 18-09-2023 **Revised:** 12-01-2024
Accepted: 16-01-2024 **Published:** 28-06-2024

Access this article online

Quick Response Code:

Website: http://journals.lww.com/JFMPC

DOI: 10.4103/jfmpc.jfmpc_1558_23

Methods and Methodology

The current study is a 4-year retrospective study done at a tertiary care hospital in Delhi, India, between March 2018

How to cite this article: Maini DK, Dixit A, Sharma B, Nanda S, Rehani V, Anand R. Journey of Guillain Barre syndrome from the pre-pandemic era to the pandemic era: A 4-year retrospective study. J Family Med Prim Care 2024;13:2623-7.

and March 2022. India reported its first case in January 2020, whereas in Delhi, the first case was reported on March 2, 2020.[2] So, patients were divided into two groups: pre-pandemic and pandemic (before and after March 2020) [Figure 1]. The data were collected from the medical record room of the hospital after permission from administration.

Inclusion criteria

Diagnosed cases of GBS were included in the study using Brighton criteria.[3]

- Age >18 years.

Exclusion criteria

- Age <18 year
- Any malignancy
- Bedridden patient due to any other disease condition

Disability assessment was done by applying the Hughes Disability Score (HDS).[4]

Permission was taken from hospital administration, and ethical practices were followed during the study.

Data were analyzed and statistically evaluated using SPSS-PC-25 version. A P' value less than 0.05 was considered statistically significant.

Results

Demographic characteristics in the pre-pandemic and pandemic eras

The total number of GBS patients was 49 in the pre-pandemic era and 25 in the pandemic/vaccine era. The mean age of GBS patients was higher in the COVID-19 era (55.12 ± 16.32 years) than the pre pandemic era (52.86 ± 15.64) (P = 0.56). A high female preponderance was seen in the pandemic era (56% in females vs 34.7% in males) (P = 0.07).

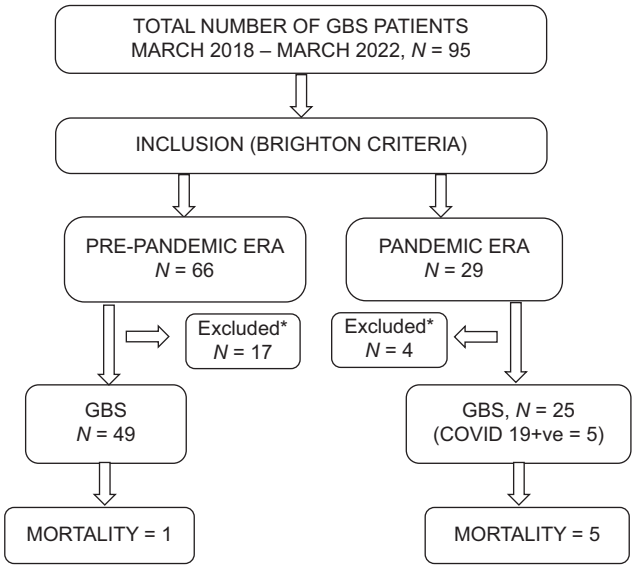

Figure 1: Consort diagram depicting data acquisition

Antecedent infections were higher (64%) in the pre-pandemic era than pandemic (34.7%) (P = 0.91). Out of the total number of GBS patients in the pandemic era, 20% patients had COVID-19 as para infection. One patient reported as post-vaccine-related GBS [Table 1].

Clinical spectrum in the pre-pandemic era and pandemic era

The mean duration of hospitalization in GBS patients is statistically significant during the pandemic era compared to the pre-pandemic era (10.68 ± 6.67 days vs 7.59 ± 3.55 days) (P value = 0.03). There is no phenotypic variation noticed in the sensory, motor, and cranial nerve involvement in both the eras [Figure 1], although respiratory involvement requiring ventilatory support is doubled in the pandemic era (24% vs 12%), which did not achieve statistical significance (P = 0.19) [Table 2]. Acute inflammatory demyelinating neuropathy (AIDP) is the most common variant encountered in both the eras [83% in the pre-pandemic era and 68% in pandemic (P = 0.40)] [Table 3].

Hughes Disability Score during the pre-pandemic era and pandemic era

The mean HDS at admission in the pre-pandemic era was 3.33 ± 0.68, and that in the pandemic era was 3.36 ± 0.99. The increased disability and dependence of patients with GBS in pandemic persisted with higher HDS on discharge with increased mortality (12% vs 2%). However, it is statistically insignificant with P > 0.05 [Table 4].

Discussion

GBS is characterized by progressive muscle weakness, areflexia, sensory impairment, cranial nerve (usually facial and ocular), and

Table 1: Demographic characteristics in the pre-pandemic and pandemic eras

	Group		*P*
	Pre-pandemic Era (*n*=49)	Pandemic era (*n*=25)	
Age group			
Up to 25 years	2 (4.1%)	1 (4.0%)	0.96
26-40 years	10 (20.4%)	5 (20.0%)	
41-55 years	13 (26.5%)	7 (28.0%)	
56-70 years	17 (34.7%)	7 (28.0%)	
>70 years	7 (14.3%)	5 (20.0%)	
Mean age in years	52.86±15.64	55.12±16.32	0.56
Gender			
Male	32 (65.3%)	11 (44.0%)	0.07
Female	17 (34.7%)	14 (56.0%)	
Antecedent event			
No	32 (65.3%)	16 (64.0%)	0.91
Yes	17 (64.7%)	9 (36.0%)	

Table 2: Clinical spectrum in pre-pandemic era and pandemic era

	Group		*P*
	Pre-pandemic Era (*n*=49)	Pandemic era (*n*=25)	
Cranial nerve involvement			
Cranial Nerves	2 (4%)	2 (8.0%)	0.21
Bulbar	4 (8.2%)	0	
Facial	4 (8.2%)	2 (8.0%)	
None	39 (79.6%)	21 (84.0%)	
Motor involvement	49 (100.0%)	24 (96.0%)	0.33
Sensory involvement	25 (51.0%)	9 (36.0%)	0.22
Need of mechanical ventilation	6 (12.2%)	6 (24.0%)	0.19
Hospitalization days (mean±SD)	7.59±3.55	10.68±6.67	0.03

Table 3: Type of GBS variant seen during the pre-pandemic era and pandemic era

GBS variant	Group		*P*
	Pre-pandemic Era (*n*=49)	Pandemic Era (*n*=25)	
AIDP	41 (83.7%)	17 (68.0%)	0.40
AMAN	4 (8.2%)	3 (12.0%)	
AMSAN	3 (6.1%)	3 (12.0%)	
MFS	1 (2.0%)	2 (8.0%)	

AIDP, Acute Inflammatory Demyelinating Polyneuropathy; AMAN, Acute motor axonal neuropathy. AMSAN, Acute motor sensory axonal neuropathy; MFS, Miller Fisher Syndrome

Table 4: HDS during pre-pandemic and pandemic eras

HDS	Group		*P*
	Pre-pandemic Era (*n*=49)	Pandemic Era (*n*=25)	
At admission			
1	0	1 (4.0%)	0.39
2	1 (2.0%)	1 (4.0%)	
3	36 (73.5%)	16 (64.0%)	
4	7 (14.3%)	2 (8.0%)	
5	5 (10.2%)	5 (20.0%)	
Mean±SD	3.33±0.68	3.36±0.99	0.93
At discharge			
1	0	1 (4.0%)	0.16
2	0	1 (4.0%)	
3	32 (65.3%)	12 (48.0%)	
4	11 (22.4%)	5 (20.0%)	
5	5 (10.2%)	3 (12.0%)	
6	1 (2.0%)	3 (12.0%)	
Mean±SD	3.49±0.76	3.68±1.24	0.52

autonomic nervous system involvement. The incidence of GBS is between 1.1 to 1.8 per lakh per year, which increases with age.[5] About two-thirds of patients who develop GBS report symptoms of an antecedent infection/event in the 6 weeks preceding the onset of the condition. COVID-19 infection is caused by severe acute respiratory syndrome coronavirus (SARS COV2.). It was first reported in Wuhan province of China in December 2019, from where it spread to other parts of the world and was declared a pandemic by World Health Organization in March 2020.[6] These infections trigger the immune response that may act as an antecedent infection to cause GBS. Rapid accurate diagnosis of GBS helps in early administration of specific immunotherapy to decrease the morbidity and mortality of this treatable disorder.

Ling M. *et al*.[7] in their study revealed that 36.4% symptomatic COVID-19 patients had neurological manifestation with headache being the most common. Taga *et al*. reported peripheral nervous system (PNS) manifestations to be ranging from 1.3% to 9.5%. Among PNS manifestations, anosmia and hypogeusia were most common, followed by Bell's Palsy and GBS.[8] In a systematic review and meta-analysis done by Palaiodimou *et al*., the overall GBS prevalence was 0.15% among COVID-19 population.[9] PNS involvement is via systemic inflammation triggering cytokine storm, following SARS COV 2 attack, causing demyelination of the neurons leading to GBS and other manifestation.[8,10] There are contrasting views on the incidence of GBS and its association with COVID-19. The number of GBS patients reported in our study during the pandemic era is reduced by 50%, with 20% patients having concomitant COVID-19 and GBS reported in other studies as well.[11,12] On the contrary, an Italian study by Filosto *et al*. and Gigli *et al*. reported an increase in number of GBS cases along with clinical severity. "Fear of COVID19 infection" seems to be one of the possible reasons of patients not reporting to hospital with mild to moderate symptoms.[13,14] Bodilsen *et al*.[15] reported government-imposed lockdown with travel restrictions could have resulted in an overall decrease in number of non-COVID patients reporting to hospital. A study by Aguiar de Sousa *et al*.[16] showed inability of the elderly population to go to the hospital in case of medical emergency (stroke) due to social isolation. Physicians must be always alert to the possibility of post-viral and post-vaccine patients complaining of sensory and motor symptoms, particularly in prevalent epidemic settings. We see seasonal surge in dengue, chikungunya, Zika,[1] and even COVID-19.

GBS is a disease which is more likely to affect males, unlike in our study, which shows female preponderance in the pandemic era, which is also reported by Altaweel YA *et al*.[17] However, larger studies with a higher sample size will be needed to support the finding for gender predilection.

In our study, patients manifesting GBS after antecedent infections in the pandemic era are markedly reduced. Social distancing, good hand hygiene, and wearing masks in the pandemic era reduced prevalence of acute gastroenteritis and respiratory infections during COVID-19 pandemic.[18]

Solitary case post-vaccine-related GBS is observed in our study. Therefore, claims of whether vaccine has an immunogenic effect in triggering GBS cannot be commented.

There is an increase in mean hospitalization days in pandemic era GBS as compared to pre-pandemic GBS. This is due to respiratory and systemic involvement and dependency on a mechanical ventilator related to the severity of the disease.[19] In our study, prolonged hospital stays (>20 days) of a patient with an axonal variant during the pandemic era are the reason for

this significant shift in our cohort. According to Gupta *et al.*,[20] COVID-19-related GBS showed hospitalization with residual paralysis and dysphagia for a prolonged period as compared to non-COVID GBS.

Although statistically insignificant, dependence on ventilatory support doubled in pandemic as compared to pre-pandemic due to concomitant disease occurrence having respiratory involvement by SARS COV-2. There is however no difference in the clinical spectrum of GBS in the pre-pandemic and pandemic/vaccine eras with respect to motor, sensory, or cranial nerve involvement. The demyelinating variant is more common in both the eras as compared to axonal variants, also reported by Caress *et al.*, Sriwastava *et al.*, and Khan *et al.*, who studied the electrophysiological features in COVID-19-related GBS.[19,21,22] In our study, mortality is higher in the pandemic era due to the presence of respiratory involvement requiring ventilatory support in both diseases, thus adding to the severity of disease and poor prognosis. GBS and COVID-19 both can affect the respiratory system independently, leading to respiratory distress and poor prognosis.[22,23] Our study is a single-center, retrospective study having a low sample size. Multi-centric studies involving a greater number of patients with wider geographical distribution in the case-control pattern are required to prove or refute any significant association.

During the pandemic, there was an acute shortage of beds across the country, particularly in Delhi; thus, many COVID-19-negative GBS patients would have not been admitted. Despite the results showing a relative decrease in number of patients during COVID-19 pandemic, antecedent viral illness and vaccination in a patient complaining of sensory symptoms, autonomic dysfunction, and muscle weakness (usually symmetrical) with the absence of fever and bladder/bowel involvement need to be rapidly investigated for possible GBS. The possibility of mimics like hypokalemia, metabolic disorders, electrolyte imbalance, porphyria, functional paralysis, drug abuse, and myelopathy should be ruled out prior to the clinical diagnosis of GBS. Electrodiagnosis plays a significant role in diagnosing GBS in pandemic times with limited intervention required as with lumbar puncture. Samir Abu-Rumeileh *et al.*[24] in systemic review reported GBS as a post COVID 19 infection, with male predominance and AIDP as a common variant. Thus, there was no difference in the clinical spectrum and epidemiology in the post COVID 19 infection GBS with the classical GBS.

However, the dearth in the literature is still inconclusive for correlating of COVID-19 as a trigger in the auto-immune disease of peripheral nervous system GBS.

Conclusion

Our study showed mean hospitalization days of GBS patients in the pandemic era to be significantly increased. There is no significant difference with respect to gender predilection, age group, variants of GBS, clinical spectrum, and outcome of GBS during the pre-pandemic and pandemic/vaccine eras. The hypothesis of the increase in GBS cases during the pandemic/vaccine era has not been observed/validated in our study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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