Cluster of Fulminant Guillain–Barre Syndrome in Maharashtra from June to October 2023: Multicentric Survey

Dear Editor,

Guillain–Barre syndrome (GBS) is an acute, immune-mediated polyradiculoneuropathy, often triggered by an infection. The disease typically reaches a nadir by 4 weeks, followed by slow recovery.[1,2] Most patients have favorable outcomes, and long-term disability is seen in less than 5%.[1] Many case series of GBS have been reported from India.[3-6] A rise in GBS cases has been observed after certain bacterial or viral outbreaks, for instance, following post Zika virus outbreak in South America, 2016, *Campylobacter jejuni* outbreak in Peru, 2018-19 and during the COVID-19 pandemic, in Western India, 2021.[6 8] [Figure 1a, Table 1]. We describe a rise in fulminant GBS with poor outcomes during the annual monsoon of 2023 in adults (>18 years) from the state of Maharashtra [Figure 1b].

We included adult patients diagnosed as GBS (Brighton's criteria) with a fulminant course, which we defined as limb weakness (Medical Research Council grade 0–1/4) rapidly progressing to respiratory muscle weakness requiring ventilatory support in less than 48 h of symptom onset. Thirty-two such patients were identified from 17 centers across Mumbai, Pune, Aurangabad, and Nagpur from July to October 2023. The median age was 45 years with the interquartile range being 15–88 years, and 80% of them were males [Table 1]. Of the patients, 82% reported antecedent events, with fever being the most common (62%). Seventy-eight percent presented with rapidly ascending quadriparesis, and cranial nerve involvement was observed in more than 90% of cases [Table 1].

Over 50% patients had axonal GBS on electrophysiological studies, consistent with acute motor axonal neuropathy/ acute motor and sensory axonal neuropathy variant. Nine of the 32 patients underwent serological testing, of which five were positive for antineuronal antibodies (GM1, GD1,

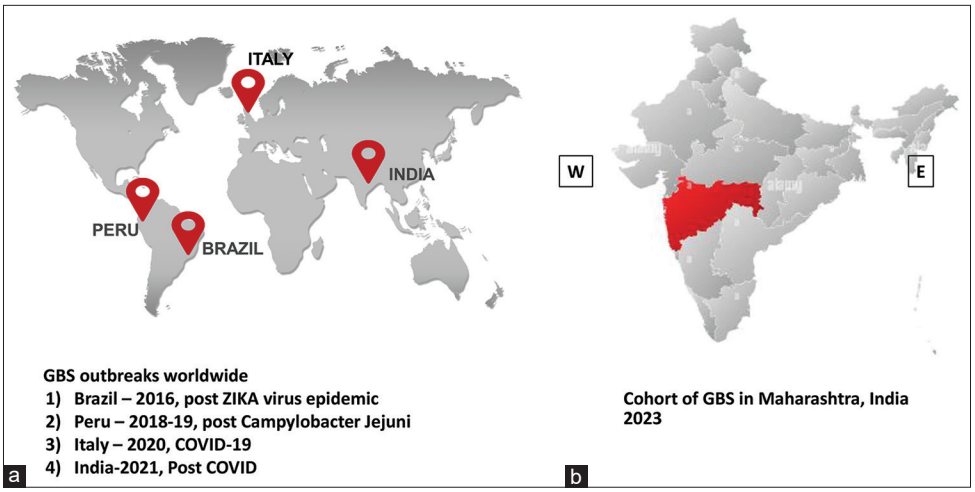

Figure 1: (a) GBS outbreaks worldwide. (b) Cohort of GBS in Maharashtra, India. GBS: Guillain–Barre syndrome

Table 1: Recent GBS outbreaks worldwide

Study published	Study period	Site of study	Number of GBS cases surveyed (n)	Number of GBS cases requiring ventilatory support, Frequency (%)	Number of fulminant GBS cases[a] Frequency (%)	GBS variant
Our study	June–October 2023	Maharashtra, India	173	42 (24%)	32 (18%)	AMAN=21 (66%) AIDP=11 (34%)
Dhamne et al.[6]	March–November 2020	Maharashtra, India	42	20 (47%)	Not known	AIDP=25 (60%) AMAN=17 (40%)
Styczynski, et al.[9]	April–July 2015	Brazil	42	11 (26%)	Not known	AMAN >> AIDP[a]
Filosto, et al.[10]	March–April 2020	Italy	30	25 (83%)	Not known	AIDP > AMAN
Díaz-Soto et al.[11]	2018	Peru	174	Not known	Not known	AMAN

[a]Fulminant GBS – Rapidly progressing quadriparesis requiring mechanical ventilatory support in 48 hours. AIDP: acute inflammatory demyelinating neuropathy, AMAN: acute motor axonal neuropathy, GBS: Guillain–Barre syndrome

GQ1b, NF155). Cerebrospinal fluid (CSF) analysis showed albuminocytological dissociation in 14/23 patients. CSF BioFire was negative in those tested [Table 2].

All 32 patients received one or more immunomodulatory treatment, including immunoglobulin (IVIg), plasmapheresis (PLEX), or intravenous pulse steroids or rituximab. The most common first-line treatment was IVIg (80%), initiated within first 5 days of disease onset [Table 2]. Thirty-one (>90%) patients did not respond well to first-line treatment; of these, 13 patients received IVIg, PLEX, or rituximab as a second-line treatment [Table 3].

Table 2: Demographic and clinical profile of patients with fulminant GBS

Demographics	Number of patients: N=32
Age (years)	Mean age- 45 years (range- 15–88, SD±20)
Gender	M:F=13:3
Temporal and clinical profile	**Frequency distribution (%)**
❖ Antecedent events	27 (82%)
• Isolated fever	20 (62%)
• Diarrhea	7 (22%)
• Vomiting	3 (9%)
• Cough	9 (28%)
• Animal bite	1 (3%)
• Surgery	1 (3%)
• Recent travel	1 (3%)
❖ Pattern of GBS involvement	
• Ascending	25 (78%)
• Descending	7 (21%)
❖ Cranial nerve involvement	
• Bulbar weakness	31 (97%)
• Bifacial weakness	27 (84%)
• Ophthalmoplegia	10 (31%)
❖ Autonomic dysfunction	22 (68%)
❖ Electrophysiological subtypes[a]	n=32
• AMAN	14 (44%)
• AMSAN	7 (22%)
• AIDP	11 (34%)
❖ CSF analysis	n=23
• <5 cells	18 (78%)
• >5 cells	5 (22%)[b,c]
• Albuminocytological dissociation	14 (61%)
❖ Serum neuronal antibodies	n=9[d]
• Anti-GM1	2
• Anti-GD1	1
• Anti-Gq1b	1
• Paranodopathy (NF155)	1
❖ MRI	n=21[e]
• Contrast-enhancing cauda equina roots	3 (14%)

AIDP: acute inflammatory demyelinating neuropathy, AMAN: acute motor axonal neuropathy, AMSAN: acute motor and sensory axonal neuropathy, CSF: cerebrospinal fluid, GBS: Guillain–Barre syndrome, MRI: magnetic resonance imaging, NCS: nerve conduction studies. n: number of patients. [a]Time of NCS study from disease onset – mean duration 3±2 days. [b]CSF BioFire, n=3 – negative. [c]CSF cultures- negative. [d]n=5 patients tested positive for serum neuronal antibodies. [e]MRI of the brain: six, MRI of the spine: one, MRI of the brain + spine: 14

Despite aggressive treatment, at the time of discharge, over 90% patients had poor outcomes. Seven of the 32 patients (22%) died during the hospital stay, while 70% had significant disability (modified Rankin Scale 3–5) and complications due to immobility; they needed a prolonged hospital stay and also prolonged neurorehabilitation. Complete or near-complete clinical recovery was seen only in three patients (<10%) at the time of discharge, and only 35% patients had recovered to their baseline functional state on a 3-month follow-up [Table 3].

At our 17 participating centers from Maharashtra, 152 patients with GBS were admitted in 2022 and 183 were admitted in 2023. However, cluster of patients with fulminant GBS, who required early and prolonged ventilatory support, was seen only in the monsoon of 2023. It is possible that a regional infection might have triggered the inflammatory neuropathy. Though numerous studies, including recent GBS outbreaks [Table 1, Figure 1a], have documented the clinical profile, treatment, and outcomes of GBS, the data on fulminant GBS is largely limited to isolated case reports only.[7-11] Therefore, close vigilance for fulminant GBS cases or outbreaks and prompt screening of the affected population to identify the infectious or other trigger during such outbreaks would help in understanding the pathophysiology of GBS in these cases, institute measures to stop the outbreak and streamline the treatment protocols. Our case series also highlights the need for regional and global healthcare institutions to set up protocols to scale up the existing medical facilities and expedite epidemiological surveys in case of future outbreaks of fulminant GBS.

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Conflicts of interest

There are no conflicts of interest.

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Table 3: Treatment modality, secondary complications, and outcomes

Treatment modality	No. of patients (%)	Mean duration of starting therapy from onset of disease
❖ First line	n=32	
• IVIg	22 (68%)	2±2 days
• PLEX	10 (32%)	2±3 days
❖ Second line	n=10	
• Second course of IVIg	1 (10%)	Day 15
• IVIg followed by PLEX	5 (50%)	13±8 days
• PLEX followed by IVIg	4 (40%)	15±4 days
❖ Additional immunosuppressants	n=8	
• Steroids	5 (16%)	7±5 days
• Rituximab	3 (9%)	30±11 days
❖ Duration of ventilatory support	n=32	
• <30 days	15	
• >30 days	17	
❖ Secondary complications	n=22	
• Urosepsis	9 (41%)	
• Pneumonia	14 (63%)	
• Bedsores	6 (27%)	
• Nosocomial infections	2 (9%)	
❖ Outcomes on discharge (mRS scale)[a]	n=32	
• Complete recovery (mRS 0)	1 (3%)	
• Mild disability (mRS 1, 2)	2 (6%)	
• Moderate disability (mRS 3, 4)	11 (34%)	
• Severe disability ((mRS 5)	11 (34%)	
• Death (mRS 6)	7 (22%)	
❖ Three-month follow-up (mRS)		
• Complete recovery (mRS 0)	3 (9%)	
• Mild disability (mRS 1, 2)	8 (25%)	
• Moderate disability (mRS 3, 4)	7 (22%)	
• Severe disability (mRS 5)	7 (22%)	
• Death (mRS 6)	0	

IVIg: Immunoglobulin, PLEX: Plasmapheresis, mRS scale: Modified Rankin scale Grades. [a]Grade 0 – No disability, Grade 1 – Able to carry out daily activities, despite some symptoms, Grade 2 -Slight disability to carry out all previous activities, Grade 3-Moderate disability requiring some help, but walks unassisted, Grade 4 – Moderate severe disability, unable to walk unassisted, Grade 5 – Severe disability, bedridden and incontinent, Grade 6 – Dead

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