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Guillain-Barre Syndrome: A Clinical Practice Survey in India

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Abstract
Introduction: Guillain-Barre syndrome (GBS), also known as Landry-Guillain-Barre-Strohl syndrome and acute inflammatory demyelinating polyneuropathy (AIDP) is an acute polyradiculoneuropathy disorder having autoimmune pathophysiology. GBS is one of the most common cause of acute or subacute generalized paralysis and diagnosis and treatment is often challenging due to lack of effective therapy measures.
Objective: This cross-sectional survey was conducted in physicians across India to understand the prevalence, presenting features and management practices of GBS in Indian population.
Methods: A total of 55 physicians who treated GBS in their practice participated in the survey. The customized self-administered survey included twenty questions which included information on GBS like prevalence, presenting features, diagnosis, treatment preferences, immunoglobulin therapy and its outcomes, relapse and management of relapse.
Observations: About 34.5% (19/55) physicians reported higher prevalence of GBS in males, 3.6% (02/55) reported common in females, 3.6% (02/55) reported common in children, whereas 58.2% (32/55) reported no specific variation with respect to gender and children.
There was a high seasonal variation reported by 92.7% (51/55) physicians with GBS commonly presented in rainy and winter seasons (94.5%).
Diagnosis of GBS was reported to be done using clinical assessment (87.3%), nerve conduction velocity test (90.9%), lumbar puncture with CSF analysis (70.9%), and electromyography (58.2%).
Intravenous immunoglobulins (IVIg) was the most preferred therapy with about 90.0% (50/55) physicians. The reasons for preference of IVIg were good clinical response or efficacy (94.2%), ease of administration (90.4%) and safety (92.3%) of IVIg over other treatments.
Improvement in GBS symptoms after initiating IVIg therapy was reported to be within 3-15 days by 74.1% (40.54) physicians, whereas 20.4% (11/54) physicians reported improvement in 15-30 days, and only one (1.9%) physician reported improvement after 30 days of starting therapy.
Of the 55, only 29 (52.7%) physicians reported adverse events with IVIg therapy and no events were reported by 26 physicians.
Conclusion: GBS is common in Indian patients and IVIg is the preferred therapy over other options due to better efficacy, ease of administration and better safety profile.

Keywords: Immunoglobulins (Ig)**,** Acute Motor Sensory Axonal Neuropathy (AMSAN), Acute Inflammatory Demyelinating Polyneuropathy (AIDP), generalized paralysis

Introduction
Guillain-Barre syndrome (GBS) is an acute fulminant polyradiculoneuropathy and is the most common cause of acute or subacute generalized paralysis [1]. It is also known as Landry-Guillain-Barre-Strohl syndrome or Acute Inflammatory Demyelinating Polyneuropathy (AIDP). GBS has a higher prevalence in men compared to women [2] with annual incidence of 0.6 to 2.4 cases per 10,000 patients per year globally [3, 4].
Etiology of GBS is not well known and an autoimmune role is believed to be triggered by infection which stimulates the anti-ganglioside antibodies production [1]. Most cases of GBS occur 1-3 weeks after an acute infectious and the organisms could be Campylobacter jejuni (diarrhea), Mycoplasma pneumonia, Haemophilus influenzae, cytomegalovirus, Epstein-Barr virus and influenza [5]. Few vaccines are also known to increase the incidence of GBS.
GBS presents in at least four variations of acute peripheral neuropathy, 1) acute inflammatory demyelinating polyradiculoneuropathy (AIDP) consists of autoimmune neuritis predominantly caused by T cells directed against peptides from the myelin proteins P0, P2, and PMP22; 2) acute motor axonal neuropathy (AMAN); 3) acute motor and sensory axonal neuropathy (AMSAN); and 4) Fisher's syndrome which is associated with antibodies to GQ1b.[6] The AIDP also involves complement activation, whereas the axonal subtypes of GBS (AMAN and AMSAN) are caused by antibodies to gangliosides on the axolemma that target macrophages to invade the axon at the node of Ranvier. Many patients of axonal subtypes of GBS have had a recent *Campylobacter jejuni* infection, and antibodies to GM1, GM1b, GD1a, and GalNac-GD1a oligosaccharides are implicated in the neuropathy [6].
Although there is no specific therapy available for treatment of GBS, intravenous immunoglobulins and plasma exchange are reported to improve outcomes, and 20% of patients are left with persistent and significant disability [6, 7].
The present survey was conducted to understand the prevalence, presenting features, diagnosis, treatment preferences, immunoglobulin therapy and its outcomes, relapse and management of relapse of GBS in clinical practice in India.

Methods

Study Design

This cross-sectional survey was conducted in 55 physicians across India during February 2017 to December 2017 who treated patients of Guillain-Barre syndrome (GBS) in their routine clinical practice.

Survey questionnaire

The survey was self-administered by the physicians based on their own judgement and practice experiences. The survey consisted of twenty questions as given in table 1. The questions included prevalence of GBS in practice, the variations in age, gender and seasons, prevalence of Acute Motor Sensory Axonal Neuropathy (AMSAN), diagnosis and treatment options of GBS, practice trends for use of intravenous immunoglobulins (IVIg) for treatment of GBS, therapy outcomes with IVIg, and common adverse events observed with te use of IVIg therapy.

Table 1: Survey questions

Sr.	Question
1.	How many patients (on average) with Guillain-Barre Syndrome (GBS) do you treat in a month?
2.	Based on experience, please describe your observation regarding GBS?
	Gender
	Age groups
	Seasonal variation
3.	What percentage of your GBS patients have the Acute Motor Sensory Axonal Neuropathy (AMSAN) form of GBS?
4.	During your routine practice, how do you diagnose patients with GBS?
5.	Which current therapy option do you prefer for the treatment of GBS patients?
6.	In the case of GBS patients with the AMSAN type, do you prefer a different therapy option?
7.	What percentage of your GBS patients do you treat with Intravenous Immunoglobulins (IVIg) therapy?
8.	Why do you prefer IVIg as a treatment therapy for GBS patients?
9.	Based on the Hughes GBS disability scale, please tick the initial symptoms on the basis of which you would prescribe IVIg therapy:
10.	What dosage do you routinely prescribe for the IVIg therapy of GBS patients?
11.	How many days of IVIg treatment do you prescribe for GBS patients?
12.	How early GBS patients do shows clinical improvement following the administration of IVIg?
13.	If the patient was on ventilation, how long did it take to wean them away from ventilation following IVIg therapy?
14.	Please rate the clinical recovery of patients after IVIg administration.
15.	Have you noticed any adverse reactions during IVIg therapy?
16.	What is the percentage of relapse in GBS cases who underwent the following treatment earlier?
17.	How do you manage relapse cases of GBS?
18.	Do you believe that the majority of doctors -both Indian and worldwide -prefer IVIg therapy for the management of GBS?
19.	Do you prefer Physiotherapy in GBS patients following IVIg therapy?
20	For which other indications do you prescribe IVIg therapy as treatment?

Statistical Analysis

This being a survey, there was no specific study hypothesis and descriptives are presented for all data responses. Responses to the survey items are presented as numbers with percentages (proportions).

Results

GBS prevalence and presentation

The number of patients presenting with GBS in their practice at the rate of 1-3 per months was reported by 52.7% (29/55) physicians, whereas upto 3 patients per month was reported by 90.9% (50/55) physicians. About 34.5% (19/55) physicians reported higher prevalence of GBS in males, 3.6% (02/55) reported common in females, 3.6% (02/55) reported common in children, whereas 58.2% (32/55) reported no specific variation with respect to gender and children. About 72.7% (40/55) reported GBS to be commonly presented in age group 18-40 years and only 20.0% (11/55) in age group <18 years. There was a high seasonal variation reported by 92.7% (51/55) physicians with GBS commonly presented in rainy and winter seasons (94.5%).

AMSAN subtype

AMSAN subtype of GBS was reported to be <10% by 34.5% (19/55) physicians and between 10-25% by 50.9% (28/55) physicians. Thus, 85.4% (47/55) physicians report AMSAN prevalence to be below 25%.

Diagnosis of GBS

Diagnosis of GBS was reported to be done using clinical assessment (87.3%), nerve conduction velocity test (90. 9%), lumbar puncture with CSF analysis (70.9%), and electromyography (58.2%). Thus, all four methods were used by 49.1% (27/55) physicians.

IVIg therapy for GBS

Intravenous immunoglobulins (IVIg) was the most preferred therapy with about 90.0% (50/55) physicians. Second preferred therapy was plasma exchange (49.1%), followed by steroids (23.6%) and other treatments (5.5%). The therapy preference was similar for AMSAN subtype GBS patients for 83.6% (46/55) physicians with majority reporting IVIg (52.9%, 18/34) as the preferred treatment for AMSAN patients.

All patients were treated with IVIg by 22.8% (12/54) physicians, whereas 48.1% physicians treated GBS with IVIg in their 50-75% patients, and 24.1% physicians treated their 25-50% GBS patients with IVIg. The reasons for preference of IVIg were good clinical response or efficacy (94.2%), ease of administration (90.4%) and safety (92.3%) of IVIg over other treatments. The dose of IVIg used for GBS was daily 400 mg/kg. The most common duration of IVIg therapy was about 2-3 weeks (34.8%, 8/23). Some physicians use IVIg till improvement (13.0%, 3/23) and till patient walks (4.3%, 1/23). Some physicians use IVIg based on the severity of the disease (4.3%, 1/23), and one physician reported IVIg use for indefinite period. Majority of physicians (88.7%) believe that

IVIg therapy is preferred worldwide for treatment of GBS.

Basis for IVIg therapy as per Hughes disability scale

The most common symptom for the basis of IVIg therapy was 'able to walk with stick' by 47.3% physicians, followed by 'able to walk with support' (29.1%), 'confined to bed' (27.3%), and 'required assisted ventilation' (18.2%).

Improvement with IVIg therapy

Improvement in GBS symptoms after initiating IVIg therapy was reported to be within 3-15 days by 74.1% (40.54) physicians, whereas 20.4% (11/54) physicians reported improvement in 15-30 days, and only one (1.9%) physician reported improvement after 30 days of starting therapy (figure 1).

The time to weaning from ventilator was reported to be 7-10 days by 79.6% (39/49) physicians, and 2-5 days by 18.4% (9/49) physicians. Only one physician reported the time to ventilator weaning to be less than 2 days (2.0%).

The clinical recovery with IVIg therapy was reported as excellent too well by 96.3% (52/54) physicians (figure 1).

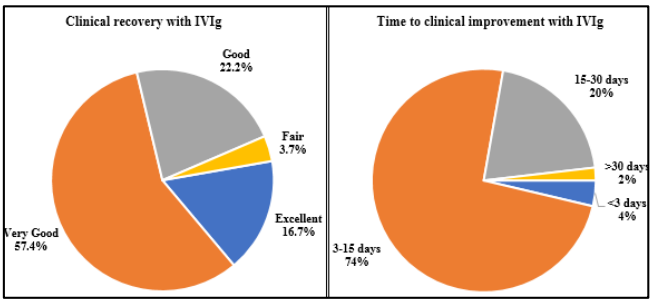

Fig 1: Clinical recovery and time to recovery with IVIG in GBS (%, n=54)

Relapse with IVIg and plasma exchange

Relapse of symptoms in GBS in upto 2% was reported by 56.0% physicians with IVIg therapy as compared to 50.0% physicians with plasma exchange therapy. Relapse was reported to be about 10-15% by 15.2% (7/46) physicians with plasma exchange therapy and only 8.0% physicians with IVIg therapy. The relapse rate was 5-10% reported by 10.9% physicians with plasma exchange and 10.0% physicians with IVIg therapy (figure 2). Thus, greater relapse rates are reported with plasma exchange compared to IVIg therapy.

Majority of physicians prefer to treat the relapse of GBS with IVIg therapy (75.0% physicians), whereas few prefer repeat cycle of plasma exchange (25.0% physicians).

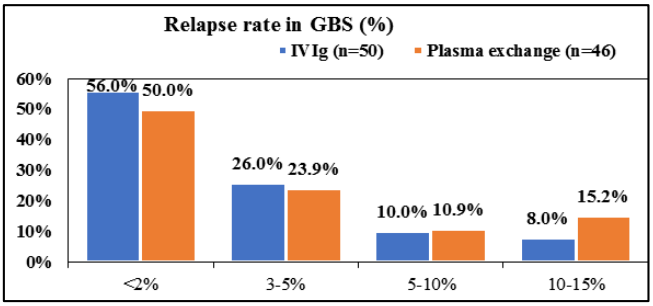

Fig 2: Relapse with IVIg and plasma exchange

The dose of IVIg used for treatment of relapse varies between 100 to 400mg/kg/day with most physicians using a higher dose of 400 mg/kg/day (59.0%) and 17.9% preferring the same dose of IVIg which was used earlier. Most of the physicians (80.6%) use IVIg for a 5-day period for treatment of relapse.

Safety of IVIg therapy

Of the 55, only 29 (52.7%) physicians reported adverse events with IVIg therapy and no events were reported by 26 physicians.

Physiotherapy and IVIg therapy

Majority of physicians (96.4%) prefer to use physiotherapy along with IVIg therapy, with the physiotherapy continued for over 2-3 weeks or till improvement of patient's condition.

Other indications of IVIg therapy

Other indications of IVIg therapy where physicians used were CIDP (47.3%), myasthenia gravis (38.2%), myasthenia gravis crisis (27.3%), autoimmune encephalitis (21.8%), and other neuromuscular disorders (9.1%). IVIg is also used for other conditions like polymyositis, attention deficit hyperactivity disorder (ADHD), idiopathic thrombocytopenic purpura (ITP), motor neuron disorders, myositis, acute inflammatory myopathy, Kawasaki's disease and multiple sclerosis.

Discussion

This survey was conducted to find out the practice trends of physicians in the treatment of GBS. Our survey points to a higher prevalence in males compared to females, which is in agreement with other studies which also report higher prevalence in males [8]. However, one study reported no gender differences in GSB in Indian patients [9]. This study by Sudulanguta *et al* (2015) reports a seasonal occurrence predominantly in winter which is similar to our observations as reported by physicians. Increased incidence of GBS has been reported from Italy and Spain with advancing age [10, 11], whereas our survey finds highest cases of GBS in age group of 18-40 years and less cases above 40 years.

This survey suggests a higher number of GBS cases in winter and rainy season. Findings of Sriganesh K *et al*. (2013), who reported increased occurrence of GBS during the months of June to August (rainy) and December to February (winter) agree with our observations [12]. However, Kaur *et al*. (2013) [13] reported a peak incidence between June–July and Sharma *et al*. (2011) [14] who reported a peak incidence between Sept–October.

Nerve conduction studies are reported to be done by most of the physicians (90.9%) as observed in our survey. These nerve conduction studies have shown to have significant changes in the recordings and these have been found to be useful for diagnosis of GBS [15, 16].

The study by Sudulanguta *et al* (2015) report no differences in complications and outcomes between IVIg and plasma exchange therapies [9]. However, our survey points to better therapy outcomes with IVIg and better safety of IVIg compared to plasma exchange. A Cochrane systemic review provides moderate quality evidence that, in severe disease, IVIg started within two weeks from onset hastens recovery as much as PE [17]. Also, patients receiving IVIg therapy are significantly much more likely to be complete therapy than PE due to less serious adverse events [17].

Conclusions

GBS is common in Indian patients and IVIg is the preferred

therapy over other options due to better efficacy, ease of administration and better safety profile.

Conflict of Interest
The authors declare that they have no conflict of interest

Informed Consent
Not applicable

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