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ORIGINAL ARTICLE

Guillain–Barré Syndrome: Profile of 120 Patients with respect to Response to Various Modalities of Treatment

[1]Vishal A Chafale, [2]Alak Pandit, [3]Satish A Lahoti, [4]Tajendranath Kundu, [5]Goutam Ganguly

ABSTRACT

Introduction: Guillain–Barré Syndrome (GBS) is an inflammatory polyradiculoneuropathy with varied clinical manifestation and often dismal prognosis if not promptly treated. Recommended treatment modalities [intravenous immunoglobulin (IVIG) and plasma exchange (PE)] are costly and the role of steroids is controversial.

Materials and methods: In this study, we reviewed the clinical and laboratory findings of consecutive patients with GBS (n = 120) and explored factors associated with outcome. We also compared response to different modalities of treatment including steroids.

Results: There was no significant difference between the treatment outcomes of IVIG and PE and we found a nonsignificant trend toward improvement with intravenous (IV) steroid. We observed 4.17% mortality and most common cause of death was respiratory failure.

Conclusion: Increasing age, delay in starting treatment, early peak disability, autonomic dysfunction, bulbar weakness, and reduced compound muscle action potential (CMAP) were associated with a poorer outcome. Group of patients treated with IVIG and plasmapheresis showed more improvement than the IV methylprednisolone group.

Keywords: Clinical profile, Guillain–Barré syndrome, Intravenous steroid, Prognosis, Treatment.

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INTRODUCTION

Guillain–Barré syndrome is an acute inflammatory polyneuropathy with an incidence of 0.6 to 1.5/100,000, diagnosis being based on a set of defined clinical and laboratory criteria.[1,2] Multifocal segmental demyelination is the main underlying pathology of the disease.[3]

[1,3]Postdoctoral Student, [2]Associate Professor, [4,5]Professor

[1-5]Department of Neurology, Bangur Institute of Neurosciences Kolkata, West Bengal, India

Corresponding Author: Alak Pandit, Associate Professor Department of Neurology, Bangur Institute of Neurosciences Kolkata, West Bengal, India, e-mail: dralakpandit@gmail.com

Based on clinical features, etiology, pathologic and electrophysiologic studies, GBS may be subclassified into several forms like acute inflammatory demyelinating polyradiculoneuropathy (AIDP), acute motor-sensory axonal neuropathy (AMSAN), acute motor axonal neuropathy (AMAN), Miller Fisher syndrome (MFS), and some other rare variants.[1,4] The GBS has an unpredictable course, with a mortality of 5 to 10%.[1] As compared with the West, reports from India seem to indicate increased mortality, and overall, a more fulminant form of the disease.[5,6]

Intravenous immunoglobulin and PE are effective treatments in GBS.[1] Several conflicting reports have been published regarding role of steroids in GBS. One study revealed the beneficial effect of a combination of IVIG with methylprednisolone, while another recently published study refuted any beneficial effect of addition of methylprednisolone to IVIG.[7-10]

This study aimed to evaluate the clinical and electrophysiological profile of GBS in a tertiary care center of eastern India, to explore factors associated with outcome and to see the response to various modalities of treatment available at present.

MATERIALS AND METHODS

This prospective study was conducted between January 2013 and December 2014 at a tertiary care hospital in eastern India. The study comprised of consecutive 120 cases of GBS (satisfying the Asbury and Cornblath criteria)[2] admitted in the Neuromedicine Ward, Bangur Institute of Neurosciences, Institute of Post Graduate Medical Education & Research, Kolkata, and were followed up for 6 months. This study was approved by the institutional ethics committee. Patients presenting like GBS but with underlying secondary causes like hypokalemia, porphyria, etc., any central nervous system (CNS) infection, and known case of demyelinating disease were excluded from study. The clinical parameters assessed were age, gender, antecedent infection/vaccination, time to peak disability, GBS disability score, pattern of involvement, e.g., cranial nerves, respiratory dysfunction, and autonomic dysfunction. Severity at admission was assessed by the Medical Research Council sum score,[11] valuing the strength from 0 to 5 in 6 muscles (biceps, deltoid, extensors of wrist, iliopsoas, quadriceps, and tibialis anterior)

in both upper and lower limbs on both sides so that the score ranged from 60 (normal) to 0 (quadriplegic) and by the GBS disability score (0 to 6) advocated by Hughes et al.[8] Improvement was measured in terms of decrease in GB disability Score (GDS) by more than 1. Definition of good outcome and poor outcome: Good outcome: GDS 0 to 2 at 6-month follow-up; poor outcome: GDS 3 to 6 at 6-month follow-up.

Electrophysiological examinations were performed within 3 weeks of the onset of illness in all patients and included motor and sensory nerve conduction study (NCS), and study of F wave and Hoffmann's reflexes (H reflexes).

We used IVIG and PE in patients with GBS disability score ≥3. Intravenous methylprednisolone (1 gm IV once daily for 5 days) was used with consent in patients not affording these costlier modalities and other patients were subjected to conservative management. We compared response to different modalities of treatment.

Data Analysis

Quantitative data were entered into GraphPad InStat software, version 3.2 and then exported to Statistical Package for the Social Sciences software, version 19.0, for analysis. Data were analyzed and tabulated using frequency distribution tables. A p-value was considered significant if <0.05.

RESULTS

Total 120 patients of GBS were recruited in study and were followed up over 6 months.

Demographic and clinical data are summarized in Table 1.

Table 1: Demographic and clinical data of GBS patients

		Number (n = 120)	*Percentage*
Age (years)	<15	15	12.5
	16–35	60	50
	36–55	32	26.7
	>55	12	10.8
Gender	Male	76	63.3
	Female	44	36.7
Limb weakness	Distal=proximal	66	55
	Distal>proximal	24	20
	Proximal>distal	25	20.83
Cranial nerves (CNs)	Facial palsy	40	33.33
	Unilateral	9	7.5
	Bilateral	31	25.83
	Bulbar palsy	28	23.33
	Ophthalmoplegia	8	6.66
	Other: 5th CN	2	1.66
	11th CN	2	1.66
	2nd CN	4	3.33
Ataxia		5	4.17
Sensory symptoms	Pain	48	40
	Sensory loss	23	19.16
DTRs	Absent	85	70.83
	Variable	24	20
	Present	10	8.3
	Exaggerated	1	0.83
Plantars	Flexor	89	74.17
	Not responsive	31	25.83
	Extensor	1	0.83
Respiratory distress		23	19.16
Mechanical ventilation		10	8.33
Autonomic involvement		30	25
Other rare features	Meningeal signs	2	1.66
	Ptosis	2	1.66
	Optic neuritis	4	3.33
Urinary retention		2	1.66
GBS disability score	Minor signs or symptoms	4	3.33
	Walk without support	18	15
	Walk with support	44	36.7
	Bedridden or chair bound	48	40
	Ventilated	6	5
Mortality		5	4.17

Seasonal Distribution

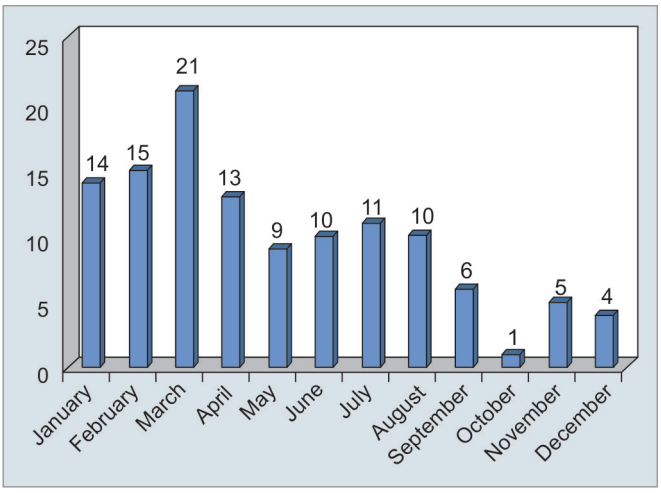
Seasonal distribution is shown in Graph 1.

Thus, cases occurred throughout the year with maximum number of cases (>50%) between January and April; 47.5% patients had some form of antecedent event, most common being fever without localization followed by diarrhea and upper respiratory tract infections (URTIs). The mean time for onset of weakness since the start of the antecedent event was 11.46 ± 8.011 days.

According to the GBS disability score, 25 (37.31%) retained the ability to walk (grades 0–2), unlike the remaining 42 (62.68%) which showed a severe affection (grades 3–6). Mean time between symptom onset and admission was 8.992 ± 7.584 days which was significantly lower in the severe cases (mean 5.17 days) compared with the mild ones (mean 8.87 days). Mean time for onset to maximum weakness was 9.193 ± 6.834 days. Average duration of hospital stay was 10.792 ± 6.629 days.

Mean duration for NCS after onset of weakness was 8.991 ± 7.58 days. Electrophysiology findings are summarized in Table 2. Two patients had normal NCS at admission, but repeat NCS after a week showed F wave abnormality and absence of H reflex. Nerves were inexcitable in two patients. Elecrophysiology findings are summarized in Table 2.

The distribution of the different subtypes of GBS was: AIDP in 41 (63.3%), AMAN in 26.7%, AMSAN



Graph 1: Seasonal distribution of cases of GBS

Table 2: Electrophysiology findings

	Frequency (n = 120)	*Percentage*
F wave abnormality	82	68.33
Normal	38	31.66
Impersistent	3	2.5
Chrono dispersion	10	8.33
Absent	69	57.5
H reflex	86	71.66
Motor NCS		
DL	33	27.5
CV	24	20
CB	21	17.5
CMAP	49	40.83
With normal DL	37	30.83
With prolonged DL	12	10
Sensory NCS	30	25
Prolonged DL	11	11.67
Reduced/absent SNAP	19	15
Reduced/absent sural SNAP	4	3.33

in 4.2%, and MFS in 4.2%; 1 patient presented with dysautonomia variant, while another one had sensory variant of GBS.

Treatment Outcome

Some kind of treatment was offered to 77 (64.1%) patients: 29 (24.16%) received IVIG, 30 (25%) received PE, 17 (14.17%) IV methylprednisolone; 43 (35.83%) of cases never received treatment due to the mild symptoms or long evolution of the disease. In one patient, both treatments (methylprednisolone followed by PE) were dispensed sequentially and this case was excluded from statistical analysis. Baseline characteristics of patients in all three groups (IVIG, PE, and steroids) were comparable and all patients were followed up for 6 months. All groups showed improvement (decrease in GDS by more than 1). Mean improvement in GDS at 6 months in IVIG, PE, and steroids groups was 2.45 ± 1.27, 1.79 ± 0.87, and 1.06 ± 0.899 respectively (Graph 2).

Table 3: Factors associated with poor outcome

	6-month follow-up		
	Nondisabling (Good outcome)	*Disabling (Poor outcome)*	*p-value*
Severity at admission			0.021
Nondisabling	21	0	
Disabling	73	21	
Rapid progression			0.006
>1 week	52	4	
<1 week	42	17	
Age (years)			0.024
<15	15	0	
16–35	49	9	
36–55	24	7	
>55	6	6	
Cranial nerve involvement			0.002
Absent	62	6	
Present	32	15	
Bulbar palsy			0.025
Absent	76	11	
Present	18	10	
Respiratory distress			0.01
Absent	82	10	
Present	12	11	
Autonomic involvement			0.01
Absent	77	8	
Present	16	14	
CMAP			
Normal	57	10	0.002
Reduced with normal DL	28	3	
Reduced with prolonged DL	9	8	

Good outcome (nondisabling): GBS disability score: 0–2; Poor outcome (disabling): GBS disability score : 3–6

Factors associated with Poor Outcome

At 6-month follow-up, we found the following factors associated with poor outcome (Table 3).

Mortality

We observed 4.1% mortality. Overview of Deceased patients is given in Table 4.

DISCUSSION

The mean age of presentation in this study was 33.13 ± 15.124 years and most of the patients affected were in the age group of 15 to 35 years (50%). Study from India by Kalita et al[12] had similar age of presentation while most of the patients were older than 55 years in the study by Suárez et al.[13] We did not get linear increase in incidence with age nor bimodal presentation as described in previous studies.[14-17] The youngest patient affected was

Table 4: Overview of deceased patients

No.	Age/sex	Time from onset to death	GDS at admission	Subtype	Phase of disease at death	Treatment received	Ventilation	Cause of death
3	75/M	7 days	5	AIDP	Progressive	IVIG	Required	Respiratory failure
10	58/M	17 days	5	AMSAN	Progressive	IVIG	Required	Autonomic dysfunction
13	58/M	9 days	5	AIDP	Progressive	IVIG	Required	Respiratory failure
42	60/M	10 days	4	AIDP	Plateau	PE	No	ICH
60	43/M	23 days	4	AIDP	Plateau	PE	Required	Respiratory failure and VAP

9 months and the oldest was 75 years. We found male preponderance with male-to-female ratio of 1.72:1 and this corresponds with previous studies.[1,12]

The GBS is considered as a sporadic illness, without a seasonal cluster.[1,15] In our study, occurrence was throughout the year, but >50% cases clustered between months of January and April. Study from Southeast Asia by Jin et al[18] found no seasonal preponderance, while study from Spain by Suárez et al[13] found trend to accrue in winter. This difference in seasonal variation of incidence could be due to environmental factors influencing the occurrence of inciting events (e.g., infection) for GBS.

In this study, 47.5% patients had history of antecedent event, most common being fever (without localization), followed by diarrhea and URTI. Two patients had history of surgery while one patient presented with prior history of trauma. The mean duration for development of symptoms following antecedent event was 11.46 ± 8.011 days. The incidence of antecedent event in this study is lower as compared with previous studies.[12-15] Minor illnesses with mild grade fever and minimal symptoms often go unnoticed and thus not reported. However, we have not done serological study to confirm the pathogen associated with such events.

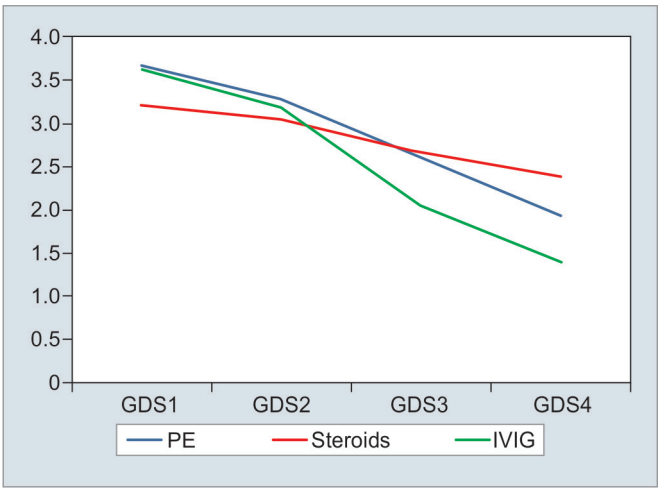
The mean duration of illness prior to hospital admission was 8.99 ± 7.584 days. Patients with severe weakness reported earlier as compared with those with minimal symptoms. As in previous series, weakness (95.83%) and hypo/areflexia (90.83%) were the most frequent symptoms, followed by neuropathic pain (40%) and numbness (19.16%). The GBS is an ascending type of paralysis. In this study, 82.5% patients had onset of weakness in lower limbs, while in 13.33% patients, weakness first started in upper limbs. These findings are in accordance with study by Jin et al.[18]

Cranial nerve involvement is not uncommon in GBS and incidence varies from 45 to 75% of cases in different series.[1] In this study, cranial nerve involvement was present in 57.5% cases and 7th cranial nerve was most commonly involved (33.33%) followed by bulbar palsy (23.33%) and external ophthalmoplegia (6.66%). Facial nerve palsy was bilateral in 77.5% cases while unilateral involvement was noted in 22.5% cases. Other cranial nerves less frequently involved were 5th and 11th cranial nerves, being involved in 2 cases each. Respiratory involvement was seen in 19.16% of cases and 8.33% of cases required ventilator support. Autonomic dysfunction was present in 25% of cases.

Reflexes were absent in 70.83% of cases while variable hyporeflexia was noted in 20% of cases. Preserved deep tendon reflexes (DTRs) may be a finding during the first few days of illness; however, preserved or exaggerated DTRs may occur in about 10% cases throughout illness.[4,19] In this study, 8.3% of cases had preserved DTRs throughout disease course, all being AMAN variants. One patient of AMAN variant had exaggerated DTRs. In this case, magnetic resonance imaging (MRI) of brain and cervical spine was normal. Thus, the possibility of the GBS should not be excluded in a patient with normal or brisk reflexes if all other features are supportive of the diagnosis, especially in AMAN variant.[4,19] Possible explanation for hyperreflexia could be dysfunction of inhibitory systems in the spinal interneurons, functional corticospinal tract involvement, and purely axonal lesions sparing sensory afferents.[20-22]

Atypical features of GBS observed in this study were: Optic neuritis (3.33%), meningeal signs (1.66%), ptosis (1.66%), urinary retention (1.66%), exaggerated DTRs (0.83%), and extensor planter response (0.83%). Optic neuritis and extensor planter response may be due to associated CNS involvement in cases of GBS.[23-25] Involvement of upper cervical roots by demyelination may be a cause for meningeal signs.

The AIDP was the most common subtype (63.3%) followed by AMAN (26.7%), AMSAN (4.2%), and MFS (4.2%). One case had dysautonomia variant while another one presented with sensory variant. This distribution of subtypes is in accordance with other Indian studies by Kalita et al[12] and Jin et al.[18] However, some authors from China have earlier reported higher proportion of AMAN variant (up to 65%) and MFS (up to 18%).[1,26] These differences in subtype distribution can be due to environmental and ethnic factors. Moreover, the criteria used for defining demyelinating and axonal damage greatly influence the relative frequency of the various forms in GBS.



Graph 2: Treatment outcome of different treatment groups

Absent H reflex was the commonest NCS abnormality (71.66%) followed by F wave abnormalities (68.33%). Prolonged distal latency, reduced conduction velocity, and conduction block were noted in 27.5, 20, 17.5% of cases respectively. Reduced CMAP was present in 40.83% of cases and in 10% of cases, reduced CMAP was associated with prolonged distal latency. Sensory abnormalities in the form of prolonged distal latency, absent/reduced sensory nerve action potential (SNAP) was present in 25% cases and out of these, 13.33% had sural nerve involvement. In 2 cases, nerves were inexcitable.

At the end of 6-month follow-up, all groups showed improvement (Graph 2). There was no significant difference between the treatment outcomes of IVIG and PE while improvement caused by steroid was not statistically significant as compared with IVIG and PE. We found a nonsignificant trend toward improvement with IV steroid. There was neither deterioration with steroid nor was there any relapse over the 6-month follow-up. Hughes et al[8] showed negative results with oral prednisone and discouraged the use of steroid in the management of acute inflammatory neuropathy since the prognosis is not improved and chances of relapse may be increased. Six trials with 587 participants concluded that corticosteroids are ineffective.[27] In two trials with a combined total of 467 participants, there was a nonsignificant trend toward more benefit from IV corticosteroids.[28] In one trial, however, there was a nonsignificant trend toward more rapid improvement when IV methylprednisolone 500 mg daily for 5 days was added to IVIG.[29] Also there are anecdotal reports of benefit with IV steroids.[1,9] However, in the absence of control group, it is not possible to quantify and compare the effects of steroid in GBS. Also low sample size in steroid group could be a possible reason for statistical insignificance. Thus, a large case–control study is required to address this issue.

Factors associated with poor outcome in this study were advancing age, severity at admission, rapid progression, cranial nerve involvement, bulbar dysfunction, respiratory distress, autonomic involvement, and secondary axonal changes.

We observed 4.17% mortality in this study and most common cause of death was respiratory failure. Factors associated with mortality were older age, more severe weakness at entry, bulbar palsy, and ventilation.

CONCLUSION

Advanciwng age, severity at admission, rapid progression, cranial nerve involvement, bulbar dysfunction, respiratory distress, autonomic involvement, and secondary axonal changes were associated with a poorer outcome. The IVIG and PE were equally effective while there was a nonsignificant trend toward improvement with IV steroid. Early institution of immunomodulatory treatment, adequate monitoring and prompt management of autonomic disturbances, bulbar dysfunction, and respiratory distress can lead to improvement of outcome in GBS.

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