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Guillain-Barré Syndrome: Clinical Profile of 100 Patients Admitted at Tertiary Care Centre in South India

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ABSTRACT
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. In this study, we reviewed the clinical and laboratory findings of consecutive patients with GBS (n=100) and explored factors associated with outcome. We also compared response to different modalities of treatment including steroids. Treatment with IVIG and plasma pharesis had better outcome than placebo. However there was no significant difference between the treatment outcomes of IVIG and PE and we found a non-significant trend toward improvement with intravenous (IV) steroid. We observed 3% mortality and most common cause of death was respiratory failure. Increased age, early peak disability, autonomic dysfunction, bulbar weakness, and reduced compound muscle action potential (CMAP) delay in starting treatment, were associated with a poorer outcome. Group of patients treated with IVIG and plasma pheresis showed more improvement than the IV methylprednisolone group.

INTRODUCTION

Guillain-Barre 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]. Based on clinical features, etiology, pathologic and electro physiological studies, GBS may be sub classified 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[4]. The GBS has an unpredictable course with a mortality of 5-10%. 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. 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 electro physiological profile of GBS in a tertiary care centre of Southern India, to explore factors associated with outcome and to see the response to various modalities of treatment available at present.

MATERIALS AND METHODS

Study Settings and Period: This prospective study was conducted between January 2017 and December 2019 at a tertiary care hospital in Southern India. The study comprised of consecutive 100 cases of GBS (satisfying the Asbury and Cornblath criteria) admitted in the General Medicine Ward, S. Nijalingappa Medical College and HSK Hospital, Bagalkot, Karnataka, India.

Inclusion and Exclusion Criteria: They were followed up for 6 months. This study was approved by the Institutional Human Ethics Committee (IHEC). 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.

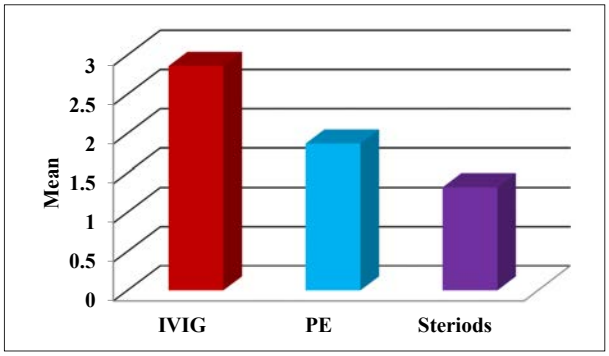
Procedure: The clinical parameters assessed were age, gender, antecedent infection/vaccination, time to peak disability, GBS disability score, pattern of involvement, e.g., cranial nerves, respiratory dysfunction and autonomic dysfunction. Severity at admission was assessed by the Medical Research Council sum score[11], valuing the strength from 0-5 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 (0-6) advocated by Hughes *et.al.,* Improvement was measured in terms of decrease in GB disability Score (GDS) by >1. Definition of good outcome and poor outcome: Good outcome: GDS 0 to 2 at 6-month follow-up., poor outcome: GDS 3-6 at 6-month follow-up. Electro physiological 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 $\geq$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.

Statistical Analysis: Quantitative data were entered into GraphPad InStat software, version 3.2 and then exported to Statistical Package for the Social Sciences (SPSS 19.0) 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 AND DISCUSSIONS

Total 100 patients of GBS were recruited in study and were followed up over 6 months. Demographic and clinical data are summarized in (Table-1).

Seasonal Distribution: Thus, cases occurred throughout the year with maximum number of cases (>60%) between January and April. 55.5% patients had some form of antecedent event, most common being fever without localization followed by diarrhoea and Upper Respiratory Tract Infections (URTIs). The mean time for onset of weakness since the start of the antecedent event was 12.86±9.8 days. According to the GBS disability score, 25 (37.31%) retained the ability to walk (grades 0-2), unlike the remaining 42 (62.68%)



Graph. 1: Mean improvement in GDS at 6 months

Table-1: Demographic and clinical data of GBS patients

Demographic and clinical data	Observation	Number	Percentage (%)
Age (years)	<15	13	13.00
	16-35	55	55.00
	36-55	22	22.00
	>55	10	10.00
Gender	Male	61	61.00
	Female	39	39.00
Limb weakness	Distal=proximal	57	57.00
	Distal>proximal	21	21.00
	Proximal>Distal	22	22.00
Cranial nerves	Facial palsy	32	32.00
	Unilateral	12	12.00
	Bilateral	20	20.00
	Bulbar palsy	31	31.00
	Opthalmoplegia	11	11.00
	Others	2	2.00
Sensory symptoms	Ataxia	4	4.00
	Pain	45	45.00
	Sensory loss	22	22.00
DTRs	Absent	72	72.00
	Variable	22	22.00
	Present	5	5.00
	Exaggerated	1	1.00
Plantars	Flexor	75	75.00
	Not responsive	24	24.00
	Extensor	1	1.00
Respiratory distress	-	21	21.00
Mechanical ventilation	-	9	9.00
Autonomic involvement	-	22	22.00
Urinary retention	-	2	2.00
GBS disability score	Minor signs or symptoms	4	4.00
	Walk without support	16	16.00
	Walk with support	44	44.00
	Bedridden or chair bound	38	38.00
	Ventilated	6	6.00
Mortality	-	4	4.00

Table-2: Electophysiology findings

Electophysiology findings	Observation	Number	Percentage (%)
F wave	Abnormality	70	70.00
	Normal	29	29.00
	Impresistent	4	4.00
	Chrono dispersion	11	11.00
	Absent	62	62.00
H reflex	-	74	74.00
Motor NCS	DL	30	30.00
	CV	22	22.00
	CB	20	20.00
	CMAP	43	43.00
	With normal DL	33	33.00
	With prolonged DL	11	11.00
Sensory NCS	Prolonged DL	13	13.00
	Reduced/absent SNAP	16	16.00
	Reduced/absent sural SNAP	4	4.00

Table-3: Factors associated with poor outcome

		6 months follow up		
Factors	Observation	Nondisabling (Good outcome)	Disabling (Poor outcome)	p value
Severity at admission	Nondisabling	18	0	0.021
	Disabling	69	21	
Rapid progression	>1 week	51	5	0.006
	<1 week	43	15	
Age (Years)	<15	15	0	0.024
	16-35	49	9	
	36-55	24	7	
	>55	6	6	
Cranial nerve involvement	Absent	62	6	0.002
	Present	32	15	
Bulbar palsy	Absent	76	11	0.025
	Present	18	10	
Respiratory distress	Absent	82	10	0.01
	Present	12	11	
Autonomic involvement	Absent	77	8	0.01
	Present	16	14	
CMAP	Normal	57	10	0.002
	Reduced with normal DL	28	3	
	Reduced with prolonged DL	9	8	

We observed 4% mortality and overview of deceased patients (Table-4).

Table-4: Overview of deceased patients

n	Age	Gender	Time from Onset of death admission	GDS at admission	Subtype	Phase of disease	Treatment	Ventilation	Cause of death
3	75	Male	7	5	AIDP	Progressive	IVIG	Required	RF
10	58	Male	17	5	AMSAN	Progressive	IVIG	Required	ADF
13	58	Male	9	5	AIDP	Progressive	IVIG	Required	RF
60	43	Male	23	4	AIDP	Plateau	IVIG	Required	RF and VAP

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. Electro physiology 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.

Treatment Outcome: Some kind of treatment was offered to (73%) patients: 36(36%) received IVIG, 16 (16%) received PE, 21(21%) IV methylprednisolone; 27(27%) 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 2.86±1.27, 1.87±0.91 and 1.32±0.78 respectively (Graph-1). At 6-month follow-up, we found the following factors associated with poor outcome (Table 3).

The mean age of presentation in this study was 35.36±14.32 years and most of the patients affected were in the age group of 15-35 years (50%). Study from India by Kalita[12] had similar age of presentation while most of the patients were older than 55 years in the study by Suarez *et.al.,* we did not get linear increase in incidence with age nor bimodal presentation as described in previous studies[13-18]. The youngest patient affected was 34, 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[18] found no seasonal preponderance, while study from Spain by Suarez *et.al.,* 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 diarrhoea 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[18] cranial nerve involvement is not uncommon in GBS and incidence varies from 45-75% of cases in different series. 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[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. 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[12] and Jin[18] However, some authors from China have earlier reported higher proportion of AMAN variant (up-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.

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 non-significant trend toward improvement with IV steroid. There was neither deterioration nor with steroid nor was there any relapse over the 6-month follow-up. Hughes et al8 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

Advancing 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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