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CLINICAL PROFILE AND OUTCOMES OF GUILLAIN-BARRÉ SYNDROME AT A TERTIARY CARE CENTRE IN SOUTHERN INDIA

Neurology

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ABSTRACT

Introduction: Guillain-Barré syndrome (GBS) is a demyelinating polyneuropathy characterized by progressive symmetric motor weakness with reduced or absent deep tendon reflexes. Clinical features, CSF analysis and electro-diagnostic studies aids in diagnosis.

Methods: This study included patients with GBS admitted to a tertiary care center in South India for 3 years from June 2013. Data pertaining to history, examination and laboratory reports were obtained from medical records and captured into a pre-formatted data sheet and was analysed using SPSS v20.0.

Results: Among the 48 patients (31 males, 17 females) included in this study, 31% had no antecedent illness, while 30% had history of a non-specific febrile illness prior to onset of symptoms. The mean duration between the antecedent event and onset of weakness was 6.75 days. Areflexia and quadriparesis were the most common clinical features. The incidence of cranial nerve involvement was highly variable, facial nerve being the commonest. Ten patients progressed to develop respiratory paresis and needed mechanical ventilation. Acute inflammatory demyelinating polyneuropathy (AIDP) was the commonest variant (57%), followed by acute motor axonal neuropathy (AMAN, 21%) and acute sensorimotor axonal neuropathy (AMSAN, 19%). There was no statistically significant association between age, gender, type of GBS, mode of treatment and final outcome, though IvIg and plasmapheresis decreased the mean duration of hospital stay by approximately 10 days compared to those managed conservatively alone.

Conclusion: Areflexia and quadriparesis were the commonest presenting features. IVIg and plasmapheresis hasten recovery but did not alter the outcome.

KEYWORDS

Guillain-Barré syndrome, Clinical profile, AIDP, AMAN, AMSAN, Miller-Fisher Variant, Adults, IvIg, Plasmapharesis.

INTRODUCTION AND NEED FOR STUDY

Guillain-Barré syndrome (GBS) also known as Acute Inflammatory Demyelinating Polyneuropathy (AIDP) is characterized by progressive symmetric muscle weakness with reduced or absent deep tendon reflexes. GBS occurs world over with an incidence of 1 to 2 cases per 1,00,000 population per year.[1] The progressive ascending flaccid paralysis reaches a nadir between 7 - 28 days.[2]

Though a probable autoimmune mechanism has been widely accepted, etiology of GBS is uncertain. Antibodies against GQ1b, GM1, GD1a, GalNac-GD1a, GD1b, GT1a and GD1b are seen among the various variants of GBS, but these due to non-availability are not used routinely for diagnosis. Nerve conduction studies showing features of demyelination and Cerebrospinal fluid (CSF) analysis showing albuminocytologic dissociation aids in diagnosis.[3]

The recommended standard of care in GBS is Intravenous immunoglobulin (IvIg), though the response to IvIg and plasmapheresis are favourable.[4] Quality nursing and intensive care including ventilator support are of paramount importance as a third of the patients develop respiratory paralysis.[5] There are few studies describing the clinical profile of GBS in South Indian population. Hence the need for this study.

AIMS AND OBJECTIVES

1. To study the Clinical profile of adult patients with GBS.
2. To compare the outcome among patients managed with IvIg and plasmapheresis.

MATERIALS AND METHODS

STUDY DESIGN AND STUDY POPULATION

This retrospective study on patients with GBS (diagnosed using a combination of clinical criteria, NCS and CSF analysis) admitted in the wards and intensive care units of a tertiary care hospital in Southern India for a period of 3 years from June 2013.

INCLUSION CRITERIA

1. Patients with GBS admitted to this hospital
2. Patients who have not received IvIg or plasmapheresis prior to admission.

EXCLUSION CRITERIA

1. Patients below the age of 18 years.
2. Patients diagnosed with GBS at an outside hospital and who have been referred after onset of respiratory muscle weakness for assisted ventilation.
3. Patients treated with IvIg or plasmapheresis at an earlier hospital and then referred for further management.

Data Collection

Data was collected by accessing information from the in-patient and out-patient records from the medical records department. Data collected included standard demographic details, history regarding the current illness, history of preceding illness (if any), timeline of progression, details of hematological and biochemical investigations including CSF analysis, nerve conduction velocities, treatment (IvIg or plasmapharesis, ventilator support) , duration of hospital stay and outcome.

RESULTS

Forty-eight patients were included in this study (31 males and 17 females). Most patients belonged to the age group of 41 - 60 years. (26 out of 48, 54.16%).

Sixty-eight percent of patients had a preceding febrile illness. A non-specific febrile illness was the commonest, seen in 29.2 % of patients. Upper respiratory tract infection and acute gastroenteritis were seen in 16.7% and 18.8% respectively. The mean duration between the illness to the onset of GBS was 6.75 days. There was one account each of GBS developing 4 days after ingestion of endosulphan and 12 days after an intra-uterine death.

Areflexia with quadriparesis were the common clinical manifestations seen in 87.5% of patients. Cranial nerve involvement was seen in 9 patients. Four patients had bilateral 7th cranial nerve involvement. Paralysis of the 3rd nerve (ophthalmoplegia) was seen in 3 patients, 1 patient had unilateral facial nerve paralysis and 1 had involvement of both glossopharyngeal and vagus nerve. Paraesthesias of limbs was seen i% of patients, but, only 6.3% had demonstrable clinical signs of sensory loss. Bladder involvement was seen in one patient.

Ten patients progressed to develop respiratory paralysis and needed ventilator support. Two patients progressed to respiratory paresis within a week of onset of illness, 6 patients between 1-2 weeks and 2 patients more than 2 weeks (Table 1).

TABLE - 1. Duration between onset of symptoms to progression to respiratory paralysis

Duration between onset of symptoms to respiratory paralysis	Frequency
< 1 week	2 (20%)
1 – 2 weeks	6 (60%)
> 2 weeks	2 (20%)

Lumbar puncture for CSF analysis was done in all patients within a week after admission (most of the patients (83.3%) underwent LP-CSF analysis on days 2 and 3 post admission). Albumino-cytologic dissociation was seen in 10 patients (20.8%) with the mean CSF protein being 86.6mg/dl (Range : 68mg/dl-178mg/dl).

NCS done in the first week of admission showed slower nerve conduction velocities in all patients. Based on clinical findings and NCS, patients were diagnosed as Acute inflammatory demyelinating polyneuropathy (AIDP), Acute Motor Axonal Neuropathy (AMAN), Acute Motor Sensory Axonal Neuropathy (AMSAN), Miller Fisher Variant of GBS. Other findings which were seen were absent H reflex, F wave persistency, absent F wave and prolonged F wave. Fifteen patients with AIDP had sparing of sural nerve on NCS.

TABLE - 2. Albumino-cytologic dissociation as seen in the various subtypes of GBS

	Albumino-Cytologic Dissociation		
Type of GBS	**Absent**	**Present**	
AIDP	22 (45.8%)	5 (10.41%)	χ^2=1.471
AMAN	8 (16.67%)	2 (4.2%)	
AMSAN	6 (12.5%)	3 (6.25%)	p=0.689
Miller-Fisher Variant	2 (4.2%)	0	

There was no significant difference between the type of GBS and the presence of albumin-cytologic dissociation. (Table -2.) Patients with AIDP had higher mean CSF protein levels (146.7mg/dl) compared to AMAN and AMSAN (74mg/dl and 71mg/dl respectively).

TABLE - 3. Association between Mode of treatment and final outcome.

	Outcome			
Mode of treatment	**Recovered**	**Residual paralysis**	**Death**	
IvIg	12 (25%)	3 (6.25%)	2 (4.2%)	χ^2=1.952
Plasmapharesis	8 (16.67%)	5 (10.42%)	2 (4.2%)	p=0.745
Supportive	8 (16.67%)	6 (12.5%)	2 (4.2%)	

Patients were managed either by IvIg or plasmapheresis. Patients not willing for either were given quality intensive care, ventilatory support and nursing care. Six (12.5%) patients succumbed to the illness during the course of hospital stay. (Table - 3) Twenty-eight patients showed a complete recovery (58.33%). There was no association between, age and gender with the final outcome (p values of 0.201 and 0.532 respectively). No significant difference was noted between mode of treatment and final outcome (Table 3)

Five out of 6 patients who required mechanical ventilation, died due to development of ventilator associated complications due to need for prolonged ventilation (p = 0.001).

Twenty-seven (56.3%) were diagnosed to have Acute inflammatory demyelinating polyneuropathy (AIDP). The rest i.e 21 (43.7%) were diagnosed as having one of the variants of GBS such as AMAN (20.8%), AMSAN-18.8% and Miller-Fischer variant (4.2%).

TABLE – 4. Mean duration of hospital stay of the various variants of GBS

Type Of GBS	Mean Duration of hospital stay
Acute inflammatory demyelinating polyneuropathy	16.259
AMAN	18
AMSAN	21
Miller-Fisher Variant	13.5

No difference was observed between the various types of GBS and their antecedent/preceding illness and CSF findings of albuminocytologic dissociation. The mean duration of hospital stay among the various variants of GBS is as shown above in Table – 4.

DISCUSSION

GBS affects all age groups. Kaplan et al suggested that GBS has a bimodal distribution i.e between 15-35 years and between 50-75 years.[6] A Swedish study described GBS to have two peaks, one between 20-24 years and the next between 70-75 years.[7] A north Indian study,most patients were in the age group 30-40.[10] This study had most patients (54.2%) in the age group 40-60 years with a range of 20 to 96 years. This difference is likely due to various genetic, ethnic, cultural, social differences between the different study populations.

An Italian study by Ropper AH found a higher incidence of GBS in males with a male: female ratio of 1.88.[11] In the study done by Dhadke SV et al the ratio was 1.5:1.[10] In this study 1the ratio was 1.823: 1. GBS is precipitated by a viral (flu-like illness) or bacterial (Campylobacter jejuni) infection for which males have a higher risk of exposure due to a greater level of social activity compared to females.

GBS occurs 1 to 2 weeks following a respiratory infection or a diarrheal disease. Jacobs BC et al and Hadden RDM et al found a significant history of preceding illness in half of patient with GBS.[8,12] Following the infection, two-third developed neurological signs and symptoms within one-two weeks. Thirty-three percent patients had a respiratory illness, 25% had acute enteritis (usually campylobacter jejuni) and 25% had influenza-like illness in the study by Hadden RDM et al. Other rarer infections seen were Cytomegalovirus, Ebstein - Barre Virus, Varicella and HIV infections.[8] In this study, history of an antecedent illness was seen in 68.7% of patients. Most of the patients had a non-specific short febrile illness (29.2%). Respiratory and diarrheal disease was seen in 16.9% and18.8% patients respectively. The mean duration between the illness and the onset of GBS was approximately a week as seen in previous studies. In 21% of cases, the antecedent illness occurred less than 5 days before onset of weakness. The widely accepted mechanism being an altered immune response that destroys nerve tissue of the host, by recognizing cell surface molecules on nervous tissue similar to the ones present on the antigen(molecular mimicry).[13]

Loeffel Rossi et al found 75% of the patients to have acroparesthesia and more than 50% of patients to have cranial nerve involvement. Facial nerve was the commonest affected among them.[9] The present study found acroparesthesias only in 43.75% of patients. Cranial nerve involvement was seen in 18.8% of patients with facial nerve being the commonest affected. This difference shows that GBS has varying manifestations as progressive weakness with varied sensory and cranial nerve involvement.

Ascending and symmetric muscular weakness with absent deep tendon reflexes was seen in 90% and 97.5% of patients ins tudies by Hadden RDM et al and Dhadke et al respectively.[7,10] Respiratory muscle weakness with respiratory failure was seen in 20% of patients. The mean duration between onset of weakness and respiratory muscle paralysis was 3 weeks.[7] Asbury and Cornblath have described motor weakness to be maximum within 12-14 days. They found the progression of the weakness to cease by 4th to 6th week of onset of illness.[14] In this study, quadriparesis with areflexia was seen in 87.5% of patients. This is in sync with the results of previous studies. In the study done at Solapur, 37.5% of patients progressed to respiratory failure.[10] Twenty-one percent (10/48) patients included in this study developed respiratory paralysis of which 6 patients developed paresis within 2 weeks after onset of limb weakness (Mean duration -12.84 days).

Hadden RDM et al found albumino-cytological dissociation in 80% of patients.[7] The study done in Solapur, India found albumin-cytological dissociation in 65% of patients.[10] In the present study, Albumin-cytologic dissociation was seen in 20.8% of patients. Albumino-cytologic dissociation is more likely to be seen when CSF analysis is done during the second week of illness.[15] The presence of albumin-cytologic patients in this study was low as CSF analysis was done within 1 week of onset of weakness.

A mean CSF protein level of 86.6mg/dl (Range: 68mg/dl-178mg/dl) was observed among those with albumin-cytologic dissociation in this

study. Mean CSF protein was higher in patients with the demyelinating variant (AIDP) compared to that in patients with axonal neuropathy. (AMAN and AMSAN). This is similar to that observed in previous studies.[11,15]

All patients showed Nerve conduction studies consistent with GBS. Findings seen on NCS were absent H reflex, F wave persistency, absent F wave and prolonged F wave. Fifteen patients (53.57%) with AIDP also had sparing of sural nerve on NCS. Yadegari S et al found sural nerve sparing to be present in 33.3% of patient with AIDP.[17] Sural nerve sparing on NCS was the finding which could consistently differentiate GBS from its mimics as per Derksen et al.[18]

Intravenous immunoglobulin (IvIg) and plasmapheresis along with good nursing and supportive care is considered to be the most effective mode of management.[8] Previous studies have found no difference in outcomes between those treated by IvIg and plasmapheresis.[5,9,10,17,19,20] Plasma exchange showed a significant reduction in the time taken to wean of ventilator by 14 days when done within two weeks from symptom onset.[21,22] A Dutch trial comparing the efficacy of IvIg with plasmapheresis found lesser progression to respiratory paresis among the group treated with IvIg (27%) versus the group treated with plasma exchange (42%).[20] Both modalities showed significant reduction in the duration of hospital stay, but time to recovery was 2 to 3 months in both modalities.[21-23] As 30% patients progress to respiratory paresis, good supportive care is the single most important aspect in management of GBS.[23,24] In this study, there was no significant difference between the mode of treatment and final outcome. Patients who developed respiratory failure and needed ventilator support had mortality rate of 50% which was significant. Thus, development of respiratory failure is a poor prognostic indicator. IvIg and plasmapheresis reduced the mean duration of hospital stay by 10 days as compared to those managed conservatively.

The limitations of this study are small sample size and the design as a retrospective study.

CONCLUSION

GBS can occur at any age group with a higher male preponderance. History of antecedent illness is usually seen in many cases of GBS but could be absent in a large number of patients. Areflexia with quadriparesis is the most common clinical feature. Albumino-cytologic dissociation shown to be a common feature by previous studies is not a very consistent finding if CSF analysis is done during the first of illness. Nerve conduction studies should always be done in suspected cases of GBS. IvIg and plasmapheresis with good nursing care were shown to significantly reduce the duration of hospital stay of patients with GBS.

CONFLICTS OF INTEREST

- Authors have not received any grants from funding agencies.

DISCLOSURE

- Authors have no disclosures to make.

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