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Original Article

Paediatrics Section

Guillain-Barré Syndrome: A Clinical Study of Twenty Children

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ABSTRACT

Background: Guillain-Barre Syndrome (GBS) is an acute monophasic demyelinating neuropathy characterized by progressive motor weakness of limbs with areflexia.

Aim: To study the clinical pattern and outcome of children with Guillain-Barre syndrome.

Materials and Methods: It was a cross-sectional study conducted in a pediatric unit of tertiary care hospital over a period of 18 months. We assessed the clinical manifestations, results of electro-diagnostic tests, functional status, treatment instituted and outcome of 20 children diagnosed with GBS.

Results: Of the 20 (male to female ratio = 2.3:1) children studied, all had motor weakness, 5 (25%) had sensory loss, 4 (20 %) had cranial nerve palsies and 4 (20%) had autonomic disturbances. Respiratory paralysis was found in 7 (35%) children requiring assisted ventilation. Antecedent illness preceding GBS was recorded in 50% children. The GBS subtype distribution as per electrodiagnostic studies was as follows: acute motor axonal neuropathy (AMAN) in 7 (38.9%), acute motor sensory axonal neuropathy (AMSAN) in 4 (22.2%), acute inflammatory demyelinating polyradiculoneuropathy (AIDP) in 4 (22.2%) and both axonal and demyelinating neuropathy in 3 (16.7%). Intravenous immunoglobulins (IVIG) constituted the treatment given in majority of the patients. Plasmapharesis was performed in one child in view of poor response to IVIG. Complete recovery was observed in 14 children and the remaining 3 children experienced only incomplete recovery.

Conclusion: Male preponderance and presence of antecedent illness in a majority of subjects was observed in our study. Regardless of the severity of illness at admission and electrophysiological subtypes, a majority achieved full recovery. Intravenous Immunoglobulin and supportive care form the cornerstone of management in childhood GBS.

Keywords: Post infectious polyneuropathy, Intravenous immunoglobulin, Pediatric

INTRODUCTION

The Guillain-Barre syndrome (GBS) is an immune mediated acute polyradiculoneuritis most frequently preceded by an unspecific infection [1]. It is also known as Landry's paralysis [2]. The reported incidence rates of GBS range from 0.6 to 4.0/100,000 population. It manifests as rapidly evolving areflexic motor paralysis with or without sensory disturbance, the usual pattern being ascending flaccid paralysis. Weakness typically evolves over hours to a few days and is frequently accompanied by tingling dysaesthesias in the extremities [2]. Autonomic involvement is common, the usual manifestations being loss of vasomotor control with wide fluctuations in blood pressure, postural hypotension and cardiac arrhythmias [2]. According to pediatric literature, children usually recover in shorter time than adults with a mortality rate of 3-5%. Severe neurological disability leading to ventilatory insufficiency and autonomic failure are the main causes of death [1,3].

Though etiology of GBS is not clearly known, studies have found about 70% cases to be preceded 1 to 3 weeks before the onset of symptoms by acute infectious processes, mostly viral, which is usually respiratory or gastrointestinal. Nerve conduction velocity is usually performed to confirm the diagnosis. Electro-physiologically GBS is characterized by acute motor axonal neuropathy.

Immunoglobulins and plasmapharesis have made a significant change in the course of the illness [4]. We performed a cross sectional study on the natural history in children with GBS to study their clinical profile using intravenous immunoglobulin (IVIG) in addition to supportive management.

AIM

Our aim was to study the clinical profile and outcome of 20 children with Guillain-Barre syndrome.

MATERIALS AND METHODS

It was a cross-sectional study conducted in a pediatric unit of Kasturba Medical College, Manipal, India, during the period of 18 months from October 2012 to April 2014. The subjects of the study were children < 18 years of age diagnosed with GBS. The diagnosis of GBS was made using the Asbury and Cornblath criteria [Table/Fig-1] [5]. We assessed the clinical manifestations, results of electro-diagnostic tests, functional status, treatment instituted and outcome. A comprehensive neurological examination was conducted including examination of cranial nerves, motor system and sensory system and reflexes.

Electrodiagnostic study was done in all subjects and electrophysiological subtypes of GBS were noted. CSF examination was performed in selected hemodynamically stable children. Stool sample was collected and sent for analysis in all subjects according to AFP (acute flaccid paralysis) surveillance programme. All subjects were monitored for respiratory insufficiency and mechanical ventilation was provided in the presence of any of these factors: (1) clinical evidence of the use of accessory muscles, (2) evidence of fatigue of respiratory muscles, (3) presence of severe bulbar weakness with risk of aspiration,(4) arterial blood gas showing pO_2<70 mm Hg or pCO_2>45mm Hg. Majority of children (16) were treated with IVIG in a dose of 2 g/kg body weight over 2-5 days in addition to conventional supportive and intensive respiratory care. Statistical analysis was done and numerical parametric data were presented as percentages.

RESULTS

Twenty children with GBS were managed in our pediatric unit during the study period, of which 14 (70%) were males. Age of the subjects

ranged from 16 months to 17 years. Slight preponderance was observed in the age group of 6-10 years (11 out of 20, 55%). In our case series, history of antecedent illness was found in 10 subjects (50%) in the preceding two weeks. Of these antecedent illnesses, respiratory tract infection was found in 4 cases (20%), diarrhea in 3 cases (15%) and nonspecific febrile illness in 3 children (15%). Other significant antecedent events reported included immunization with tetanus toxoid in one child and Hemophilus type B in other child received 1month prior to the illness. It was interesting to observe GBS in one child previously treated for nephrotic syndrome with steroids who had achieved remission 4 months back.

At admission, all 20 children presented with limb weakness and sensory symptoms (pain and paresthesia) were noted in 5 cases (25%) at the time of onset of illness. Areflexia was a characteristic feature and more proximal reflexes were elicited during the early phase of the disease. Cranial nerve palsy was observed in 4 (20%) children. Of which 2 had bulbar palsy and 1 child had facial palsy and Miller Fischer variant in one child. Autonomic disturbance was noted in 5 cases (25%) during the hospital stay compared to 2 (10%) on the day of admission. Two of them had transient hypertension and remaining three had tachycardia. Apart from these, bladder symptoms were noted in 6 cases (30%), Respiratory insufficiency was found in 7 (35%) children requiring assisted ventilation. The GBS subtype distribution as per electrodiagnostic studies was as follows: acute motor axonal neuropathy (AMAN) in 7 (38.9%), acute motor sensory axonal neuropathy (AMSAN) in 4 (22.2%), acute inflammatory demyelinating polyradiculoneuropathy (AIDP) in 4 (22.2%) and both axonal and demyelinating neuropathy in 3 (16.7%). NCV (nerve conduction velocity) could not be done in 2 children who got discharged against medical advice. CSF analysis could be performed in five children and the characteristic feature of albumin-cytological dissociation (<10 mononuclear cells) was observed in only two children.

Majority of the children reached maximum disability within 3-5 days of admission. IVIG was administered to 16 subjects. One child who presented in the improving phase of motor disability was managed supportively without IVIG and recovered completely. Three children whose parents were not willing for treatment with IVIG were discharged against medical advice. One child required administration of second dose of IVIG in view of poor response to the first dose. Plasmapharesis (4 settings) was performed in one child in view of poor response to IVIG. Complete recovery was observed in 14 children and the remaining 3 children experienced only incomplete recovery. Three children who were discharged against medical advice could not be followed up.

DISCUSSION

Although the occurrence of GBS in children is relatively rare, it is the most common cause of acute flaccid paralysis in infants and children during the post-polio eradication era. GBS affects all age groups. In our case series we included 20 subjects of <18 years of age (range 16 months to 17 years) and majority of them (55%) were 6-10 years age group. Koul R et al., in their study of 61 children under 15 years of age with GBS, found that most of the children who had GBS were below 4 years of age, and only one case was seen in the 10-15 year age group. The authors discussed that this was believed to be due to exposure to several infections, toxins and increased susceptibility of young myelin to demyelination [4]. We found male preponderance in our study with a male: female ratio of 2.3:1. Dhadke et al., observed a male preponderance in their study with a male female ratio of 1.5 to 1 [2].

Majority of multicentric retrospective studies on GBS have revealed significant presence of antecedent illness preceding the onset of illness. Majority of available pediatric literature have mentioned that two third of the cases will develop the neurological signs and symptoms within one to two weeks from the antecedent illness. Dhadke et al., found respiratory infection as the most common preceding illness in their study of 40 subjects, followed by gastro-intestinal infection [2]. Immunization also has been mentioned as one of the rarer triggering factors [6]. In our study, antecedent events preceding GBS included respiratory illness in the majority with diarrhea and nonspecific febrile illness in the remaining subjects. Immunization with tetanus toxoid and Hemophilus influenza type B vaccine was present.

Baseline clinical characteristics of the subjects have been compared with similar GBS studies as depicted in [Table/Fig-2]. All subjects in our study presented with limb weakness with sensory symptoms in majority of children at the onset of illness. Rossi et al., reported that in 75% of the patients the first neurological symptoms were parasthesias in the toes. Dhadke et al., observed 13 of 40 patients in their study with sensory symptoms in the form of tingling, numbness, paraesthesia or pain [2]. Loeffel et al., reported a fifty per cent incidence of cranial nerve palsies in GBS, facial nerve being the commonest [7]. Dhadke et al., found cranial nerve involvement in 62.5% of their patients in which the facial nerve was most commonly involved [2]. Four children had cranial nerve involvement in our study, of which 2 had bulbar palsy and 1 child had facial palsy and Miller Fischer variant in one child. Koul R et al., found three out of 61 children with Miller Fischer syndrome [4]. Seven children out of 61 in the study done by Koul R et al., had hypertension [4]. Though only 2 children had autonomic

I. Features required for diagnosis
(A) Progressive motor weakness of more than one limb
(B) Loss of tendon jerks
II. Features strongly supportive of the diagnosis
(A) Clinical features
1. Progression over four weeks
2. Relative symmetry of weakness
3. Mild sensory symptoms or signs
4. Cranial nerve involvement
5. Recovery, usually beginning two to four weeks after progression stops
6. Autonomic dysfunction
7. Absence of fever at the onset of neuritic symptoms
(B) CSF* features
1. CSF protein raised after the first week of symptoms
2. Counts of 10 or fewer mononuclear leucocytes x 10^6/1
(C) Electrodiagnostic features
Reduction of conduction velocity, conduction block or abnormal temporal dispersion, increased distal latency or abnormal F wave in more than one nerve
III. Features casting doubt on the diagnosis
(A) Marked, persistent asymmetry of weakness
(B) Persistent bladder or bowel dysfunction
(C) Bladder or bowel dysfunction at onset
(D) More than 50 mononuclear leucocytes x 10^6/1 in CSF
(E) Presence of polymorphonuclear leucocytes in CSF
(F) Sharp sensory level
IV. Features that rule out the diagnosis
(A) Indication of any metabolic, infectious, or toxic disease associated with Polyneuropathy
(B) Occurrence of a purely sensory syndrome

[Table/Fig-1]: Diagnostic criteria for Guillain-Barre syndrome after Asbury and Cornblath [5]
*CSF=cerebrospinal fluid

disturbances at admission, 3 more children were noticed to have tachycardia during the hospital stay.

Asbury and Cornblath have described motor weakness to be maximum within 12-14 days and usually the progress of weakness ceases by 4th to 6th week of the onset of illness [5]. Regarding the natural history and the progression of disease, Pi-Lien H et al., demonstrated that the clinical course of childhood GBS had a shorter recovery time compared to the adult patient group [3]. However majority of our subjects reached maximum disability between three to eight days. 11 out of 61 children with GBS in the study by Koul R et al., required ventilation [4]. Paul et al., suggested the identification of GBS patients who are likely at high risk of developing respiratory failure in the course of the illness based on simultaneous onset of weakness in upper and lower limbs, upper limb power grade<3/5 and bulbar involvement. At the same time, preserved upper limb reflexes at nadir of illness signify a lesser likelihood for ventilator support. These factors may necessitate immediate respiratory support and warn of impending respiratory crisis [8]. In our study five children reached severe neurological disability and required ventilatory assistance.

CSF analysis was performed in 5 children. Typical CSF finding of less than 10 mononuclear leukocytes per cubic millimeter was found in only 2 cases. Three cases showed 11 to 50 mononuclear leukocytes. Asbury and Cornblath have mentioned counts of 10 or fewer mononuclear leukocytes/mm^3 in CSF as being strongly supportive of the diagnosis. Counts of 11 to 50 mononuclear leukocytes have been considered as a variant finding [5].

Nerve conduction velocity (NCV) is considered as a very useful tool for diagnosis as well as prognostication of GBS. Most of the pediatric patients in the study by Pi-Lien H et al., belonged to the AIDP group [3]. According to the findings in the NCV, the patterns of neuropathy in the patients were categorized. Seven children had acute motor axonal neuropathy, 4 had acute motor and sensory axonal neuropathy. Four Acute Inflammatory Demyelinating Polyradiculoneuropathy (AIDP), 3 had both axonal and demyelinating neuropathy and NCV could not be done in 2 children who got discharged against medical advice. Axonal NCV changes compared with signs of acute demyelination or normal values were found in older patients and were indicative of a longer duration until freedom from symptoms [1]. We observed that 7 children who required mechanical ventilation and experienced incomplete recovery had NCV finding of acute motor axonal neuropathy. Pi-Lien H et al., reported 8% of patients with residua at a follow up of one year or more and no fatality [3]. Three of our patients had significant residual weakness at the end of 6 months.

Intravenous immunoglobulins or plasmapharesis with good supportive care is considered as treatment of choice by many studies. IVIG in the dose of 400mg/kg/day for 5 days is recommended [2]. 16 patients received IVIG our study, one child received four cycles of plasmapharesis with poor response and improved subsequently on IVIG.

	Characteristics	Korinthenberg et al., [1]	Dhadke SV et al., [2]	Akbayram S et al., [9]	Our study
1.	Study population (n) Study period Age range Male: Female ratio	175 5 years 11mth-17.7yrs 1.27:1	40 1yr 8mths 13yrs-40yrs 1.5:1	36 6yrs 6mths-180mths 1.25:1	20 1yr 6mths 16mths-17yrs 2.3:1
2.	Preceding events prior to the illness (%)	79	55	69.4	50
3.	Clinical presentation (%) (a) Limb weakness (b) Sensory dysfunction (c) Cranial nerve dysfunction (d) Autonomic dysfunction (e) Respiratory insufficiency requiring assisted ventilation	 69.5 42 35.6 19.5 16	 100 32.5 62.5 None 32.5	 94.4 27.8 12.0 25.0 8.3	 100 25 20 25 35
4.	Albumino-cytological dissociation in CSF analysis (%)	-	65.3 (26 of 40)	51.4	2 out of 5
5.	Electrodiagnostic categorization (%) (a) AIDP (b) AMAN (c) AMSAN (d) Unclassified/mixed	 67 19 - 14	 100 - - -	 69.4 27.8 2.8 -	 22.2 38.9 22.2 16.7
6.	Recipients of IVIG (n)	70	14	34	16
7.	Recipients of plasmapharesis(n)	19	4	-	1
8.	Outcome (%) (a) Complete recovery (b) Incomplete recovery (c) Death	 92 (98 of 106) 8 -	 75 5 20	 80.5 11.2 8.3	 82.4(14 of17) 17.6 -

[Table/Fig-2]: Comparison of demographic and clinical characteristics of subjects with other three studies

CONCLUSION

Male preponderance and presence of antecedent illness in a majority of subjects was observed in our study. Regardless of the severity of illness at admission and electrophysiological subtypes, a majority achieved full recovery. Strong limitation of our study was the low number of subjects. Hence we could not statistically compare the subgroups of GBS. Rarity of GBS and relatively shorter period of study compared to other studies may be attributed to the small sample size. Except for 3 children who got discharged against medical advice, there was no mortality observed during the hospital stay. Intravenous Immunoglobulin and supportive care form the cornerstone of management in childhood GBS. IVIG administered early in the course results in better recovery. Plasmapharesis may be a cost effective modality in those with poor response to IVIG therapy.

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