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Original Research Article

Study of clinical profile and outcome in children aged 1-12 years presenting with Guillain Barre syndrome

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ABSTRACT

Background: Guillain-Barré syndrome (GBS) is a group of clinical syndromes involving acute polyneuropathy secondary to an immune-mediated process. The aim of the research is to study clinical profile and outcome in children aged 1-12 years presenting with GBS.
Methods: It is a prospective plus retrospective observational study (5-year retrospective + 18 months prospective). All cases of GBS admitted from January 2020-july 2021 were enrolled for the study and retrospective cases were taken from case record from January 2015 onwards in a tertiary care centre.
Results: Total 45 children were enrolled. The male: female ratio was 1.64:1. Mean age at presentation was 6.3 years, in a range of 1.5 -11.5 years of age. History of antecedent illness prior to the occurrence of GBS was present in 93.3% patients with upper respiratory tract infection being most common seen in 53.3% patients. Following variants of GBS were seen on NCV study performed in 34 patients, the most common was AIDP in 46.7% patients, followed by AMAN in 22.2% subjects and AMSAN in 6.7% patients. All children presented with lower limb weakness which progressed to involve upper limbs. Other associated features like bulbar cranial nerve involvement, respiratory muscle weakness, sensory symptoms and autonomic disturbance (arrythmia, hypotension, tachycardia, bradycardia) was observed in 30,12,7,16 patients respectively. Out of the total 45 patients, 12 patients required mechanical ventilation.
Conclusions: Male predominance seen in GBS. AIDP the most common subtype of GBS. Respiratory distress and autonomic instability were associated with greater severity of Hughes disability score. Factors associated with poor outcome were sensory symptoms, autonomic instability, respiratory distress and bulbar cranial nerve involvement.

Keywords: GBS, AIDP, Hughes disability score, Outcome

INTRODUCTION

Acute flaccid paralysis (AFP) is a group of clinical conditions characterized by acute onset of flaccid weakness.[1] Introduction of immunization has significantly decreased the incidence of poliomyelitis. There has been a surge in non-polio AFP cases, after eradication of polio from India (March 27, 2014).[2]

The first clinical description of GBS was by Landry's publication in 1859 of an ascending paralysis.[3] Later, Asbury defined the clinical, biological, and electrophysiological criteria in 1990.[4] GBS refers to a group of clinical syndromes with acute polyneuropathy secondary to an immune-mediated process, which usually presents with progressive weakness that can involve autonomic, bulbar, and respiratory system, and reduced or diminished deep tendon reflexes.[5]

Incidence of this disease is about 1.3 per lac per year world-wide.[5] Bulbar involvement is seen in 50% cases and autonomic disturbances are seen in about 20%.[6]

Despite the treatments, 20% of cases succumb to complications or remain severely disabled.[7] Respiratory failure that requires mechanical ventilation is seen in around 30% cases of GBS.[8]

Because of the paucity of data from paediatric population in developing countries, we aim to study the clinical profile and outcome of Guillain-Barre syndrome in children.

METHODS

It was a prospective plus retrospective observational study (5-year retrospective+18 months prospective) conducted at department of paediatrics, Lokmanya tilak municipal general hospital and medical college, Mumbai. The study was initiated after institutional ethics committee approval. Sample size of 45 was calculated using the SAS 9.2 package.

All cases of GBS admitted from January 2020-July 2021 were enrolled for study and retrospective cases were taken from case records from January 2015 onwards. Inclusion criteria was all the cases who presented with features of GBS based on Asbury's criteria which include ascending areflexic quadriparesis with or without cranial nerve dysfunction, evolving within a period of four weeks. Exclusion criteria were as follows-If parents refuse to give written informed consent for the study, marked and persistent asymmetry of symptoms and signs, early and prominent bladder and bowel involvement, presence of sharp sensory level, features of other diseases like myasthenia gravis, botulism, poliomyelitis, porphyria and diphtheria, drug or toxin induced acute neuropathy.

Diagnosis of GBS was made clinically in patients showing progressive weakness of more than one limb and areflexia/hyporeflexia, according to criteria suggested by Asbury and Cornblath.[9] Detailed neurologic examination findings in a standardized manner, CSF findings, electrophysiological findings, and spine MRI findings were documented. Patients were assigned functional status according to the Hughes Disability Score both at the time of admission and discharge.[10] Patients were followed up till discharge. The SSEP package was used for statistical analysis. The association of two categorical variables was evaluated by chi-square tests.

The significance of association of certain factors like the treatment adopted and poor prognosticators with the outcome variables like death, ventilator need, tracheostomy and bedridden state were measured by stepwise logistic regression analysis. Statistical significance was considered when the $p<0.05$.

RESULTS

Out of total 45 children enrolled in study, 28 (62.2%) were males and 17 (37.8%) were females. The male: female ratio was 1.64:1. Maximum prevalence of GBS was seen in age group 3-6 years (40%), mean age at presentation 6.3 years, (range 1.5-11.5 years). Maximum number of patients seen in monsoon season (46.6%).

History of antecedent illness prior to the occurrence of GBS was present in 42 (93.3%) patients, with upper respiratory tract infection (URTI) being most common seen in 24 (53.3%) patients, febrile illness in 10 (22.2%) patients and acute gastroenteritis was identified in 8 (17.8%) children. Peak disability within 7 days of onset of symptoms in 30 (66.7%) patients, while 13 (28.9%) patients had within 8-14 day. Mean duration at onset to peak disability was 6.47 days (Table 1).

All patients presented with weakness of bilateral lower limb progressing gradually to involve the bilateral upper limbs as well. Cranial nerve involvement was present in 30 (66.7%) patients. Respiratory muscle weakness was observed in 12 (26.7%) patients requiring mechanical ventilation and sensory symptoms were present in 7 (15.6%) patients. Autonomic disturbance was observed in 16 (35.5%) patients (Table 1).

Table 1: Demographic and clinical profile, (n=45).

Clinical variables	N (%)
Age (Years)	
<3	7 (15.6)
3-6	18 (40)
6-9	13 (28.9)
9-12	7 (15.6)
Sex	
Male	28 (62.2)
Female	17 (37.8)
Season	
Spring (February to March)	4 (8.9)
Summer (April to June)	7 (15.5)
Monsoon (July-September)	21(46.6)
Autumn (October-November)	7 (15.5)
Winter (December-January)	6 (13.3)
Antecedent illness	
Respiratory	24 (53.3)
Gastrointestinal	8 (17.8)
Other febrile illnesses	10 (22.2)
None	3 (6.7)
Symptoms	
Limb weakness	45(100)
Sensory change/pain	7 (15.6)
Respiratory muscle involvement (required mechanical ventilation)	12 (26.7)
Bulbar cranial nerve involvement	15 (33.3)
Facial nerve involvement	12 (26.7)
Oculomotor nerve involvement	3 (6.7)
Autonomic dysfunction	16 (35.5)

Following variants of GBS were seen on NCV (34 out of 45 patients), the most common was acute inflammatory demyelinating polyneuropathy (AIDP) seen in 21 (61.7%) patients, followed by acute motor axonal

neuropathy (AMAN) seen in 10 (29.4%) subjects and acute motor sensory axonal neuropathy (AMSAN) in 3 (8.8%) patients. MRI spine of 12 (66.6%) out of 18 patients showed thickening and mild enhancement of nerve roots of cauda equina suggestive of GBS. CSF examination of 10 (76.9%) out of 13 patients showed albumin-cytological dissociation (Table 2).

Maximum disability on presentation was noted as per Hughes disability score. Majority of patients (51.1%) were able to walk 5 m with assistance corresponding to Hughes disability score of 3. While 22.2% individuals were confined to bed with a Hughes disability score of 4. Also, 24.4% patients required assisted ventilation with a Hughes disability score of 5. Total 40 (88.9%) patients were treated with IVIG with total dose of 2 gm/kg while 5 (11.1%) patients were managed symptomatically due to minimal weakness on presentation or they were already in recovering phase. On discharge, considerable improvement in disability score observed, 62.2% individuals could ambulate without support corresponding to Hughes disability score of 2 on discharge. Total 20% individuals needed some assistance while ambulating with Hughes disability score of 4. However, 11.1% individuals confined to bed (Table 2).

Of 12 patients with respiratory distress, 11 were associated with Hughes disability score of 5. Similarly, 6 out of 8 patients with autonomic instability were found to have Hughes disability score of 5. Therefore, autonomic disturbance (p=0.003) and respiratory muscle involvement (p=0.001) were found to have significant statistical association with greater severity of the disease (Hughes disability score) (Table 3).

Table 2: Laboratory features and Hughes disability score.

Investigations	N (%)
Albumino-cytologic dissociation in CSF, (n=13)	10 (76.9)
Contrast enhancement in spine MRI, (n=18)	12 (66.6)
Subtypes on NCV study (n=34)	
AIDP	21 (61.7)
AMAN	10 (29.4)
AMSAN	3 (8.8)
GBS disability score on admission	
2 (able to walk without support)	1 (2.2)
3 (able to walk with support)	23 (51.1)
4 (confined to bed or chair)	10 (22.2)
5 (require assisted ventilation)	11 (24.4)
GBS disability score on discharge	
1 (capable of running)	3 (6.7)
2 (able to work without support)	28 (62.2)
3 (able to walk with support)	9 (20)
4 (confined to bed/chair)	5 (11.1)

The presence of respiratory distress was seen in 12 patients, with 11 having a bad prognostic outcome (p=0.001). Sensory involvement was found in 5 participants, of which 3 patients had poor prognosis at discharge (p=0.001). In our study 10 patients had bulbar cranial nerve involvement, of which 5 patients had poor prognosis (p=0.004). Autonomic instability in form of tachycardia/bradycardia (p=0.009), hypotension (p<0.001) and arrythmia (p=0.002) were also associated with poor outcome in GBS patients (Table 4).

Table 3: Factors associated with severity of GBS (Hughes disability score).

Variables		Hughes disability score (severity), n (%)				P value
		2	3	4	5	
Respiratory distress	Yes		1 (8.3)		11 (91.7)	<0.001
	No	1 (3)	22 (66.7)	10 (30.3)		
Autonomic involvement	Yes		2 (25)		6 (75)	0.003
	No	1 (2.7)	21 (56.8)	10 (27)	5 (13.5)	

Table 4: Factors associated with poor outcome.

Variables		Good outcome, n (%)	Poor outcome, n (%)	P value
Respiratory distress	Yes	7 (58.3)	5 (41.7)	<0.001
	No	33 (100)	0 (0)	
Tachycardia/bradycardia	Yes	5 (62.5)	3 (37.5)	0.009
	No	35 (94.6)	2 (5.4)	
Hypotension	Yes	2 (40)	3 (60)	<0.001
	No	38 (95)	2 (5)	
Arrhythmia	Yes	1 (33.3)	2 (66.7)	0.002
	No	39 (92.9)	3 (7.1)	
Sensory symptoms	Yes	2 (40)	3 (60)	<0.001
	No	38 (95)	2 (5)	
Bulbar cranial nerve involvement	Yes	10 (66.7)	5 (33.3)	0.004
	No	30 (100)	0 (0)	

DISCUSSION

In our study, the median age was 6.3 years. Similar findings have been observed in other studies.[11,13] Mean age in Rangan et al study and Nasiri et al were 5.4 years and 5.7 years respectively.[16,17] Most studies show a male preponderance in GBS, including ours and a study done by Nasiri et al.[11-14,17] Majority of cases were seen in monsoon season in our study. Similar findings were noted by Meshram et al in their study.[18]

Similar to other previous studies, in our study 93.3% of children had some antecedent symptoms with URTI (53.3%) being the most common.[11,12,15] Similar findings were noted in studies by Pijl et al and Kalita et al.[19,20] However, in study by Rangan et al diarrhoea was the most prevalent antecedent illness.[16] It was observed in our study, 66.7% patients presented with peak disability within 7 days of onset of illness. This is similar to study done by Singh et al where it was observed that mean duration to peak disability was 7.2 days.[13]

In our cohort, all of the patients presented with symmetrical lower limb weakness that gradually progressed to involve bilateral upper limb as well. The findings were comparable to those of Tiwari et al and Singh et al who found that motor weakness in all four limbs as their presenting symptom respectively in 87% and 97% patients.[13,21] In our study 15.6% of patients had sensory involvement in the form of pain and tingling sensation in the bilateral lower limbs. These findings were comparable to those of study by Tiwari et al who found that 13% of patients had sensory involvement.[21]

In our study, respiratory muscle failure who required mechanical ventilation, was seen in 26.7% patients. Similar findings were noted by Sri-udomkajorn et al and Meshram et al with respiratory muscle involvement in 27 % and 23.07% patients in their study respectively.[18,22] At the time of admission, 33.3% of patients had bulbar nerves involvement. While 26.7% of patients had facial nerve involvement and 6.7% had Oculomotor nerve involvement. In their study, Meshram et al found that 33.3% of people had facial nerve palsy, with 46.67% having bulbar nerve involvement.[18] In our study, autonomic disturbance was seen in 35.5% patients. In study done by Incecik et al autonomic disturbance was found in 45.7% patients, whereas autonomic instability was found in 20% and 8.7% patients in studies done by Rangan et al and Nasiri et al respectively.[16,17,23]

Nerve conduction studies were done in 34 participants in our study. In our study, the frequency of AIDP, AMAN and ASMAN was 61.7%, 29.4%, and 8.8%, respectively, which is similar to studies published from France, Korea and Karnataka.[11-13,15] Similar findings were present in studies done by Nasiri et al and Kalita et al where AIDP was more prevalent than AMAN among GBS patients.[17,25] Whereas in study done by Rangan et al AMAN was more prevalent than AIDP.[16] MRI spine was done in 18 patients mostly in second week of illness, out of which 12 (66.6%) patients had thickening and mild enhancement of nerve roots of cauda equina on post gadolinium contrast suggestive of GBS. Similarly in a study done by Rangan et al 9 out of 12 patients had findings suggestive of GBS on MRI spine.[16] Cerebrospinal fluid analysis was done in 13 patients out of which 10 (76.9%) patients had significant albumin-cytological dissociation. Similar albumin-cytological dissociation was present in 77% patients in study done by Roodbol et al.[24] CSF analysis was done in a small proportion of patients hence results obtained in this study may not be generalised.

On admission, 73.3% of patients had a Hughes disability score of 3/4, followed by 24.4% of patients who had disability score of 5 on presentation. This finding was comparable to that of Kapoor et al who found that majority of patients had a Hughes disability score of 3/4 in 64% of cases.[25] Greater disability score at presentation is associated with increased morbidity and recovery time.

In our study it was observed that post treatment there was considerable improvement in disability score on discharge as compared to the disability score on admission. About 62.2% patients could ambulate without support (GBS disability score 2) on discharge. However, 20% patients needed some assistance for ambulation (GBS disability score 3) and.11.1% were confined to bed (GBS disability score 4). There was no death observed. Considerable recovery on discharge was observed in all of patients in our study probably as majority of patients were of AIDP variant received treatment and AIDP is known to have a faster recovery as compared to other variants. In a study done by Kanan et al it was observed that a significant improvement was present in all their study subjects.[26] Also in study done by Korinthenberg, 96% of children had significant improvement at the end of observation period.[27]

In our study patients who had respiratory distress and required mechanical ventilation had higher disability scores. (p=0.001). Similar finding were documented in a study by Kalita et al.[20] Significant association was observed between autonomic instability and Hughes Disability score at admission in our study (p=0.003). Similarly, in a study done by Di Mario et al it was observed that autonomic instability on presentation was associated with increased severity.[28]

Cranial nerve involvement was present in 30 (66.7%) patients similar to study by Estrade et al and Tiara et al.[11,14] Respiratory muscle weakness was noted in 12 (26.7%) patients. Study done by Singh et al and Sreekantham et al also observed similar findings in 34% and 19.6% respectively.[13,15] Sensory symptoms were present in 74% and 50% of patients in study conducted in France and Korea compared to 7 (15.6%) patients in our study. Autonomic disturbance was observed in 16 (35.5%) patients as observed in previous studies.[11-15]

Respiratory failure and autonomic instability were associated with a poor prognosis in our study. Occurrence of arrhythmia was related with poor prognosis in research done by Zhang et al, Estrade et al and Kim et al.[11,12,29] It also observed that presence of bulbar cranial nerve involvement is associated with poor prognosis. According to studies done by Kim et al, Singh et al and Tiara et al cranial nerve involvement was linked to poor prognosis.[12-14]

In our study, sensory symptoms, autonomic instability (arrythmia, hypotension, tachycardia, bradycardia) respiratory distress, and bulbar cranial nerve involvement were associated with poor outcome.

Limitations

This study is single centre-based research. Further studies with larger population and wide geographic distribution are required.

CONCLUSION

Upper respiratory tract was the most common preceding illness in GBS. AIDP was the most prevalent subtype. Respiratory distress and autonomic instability were associated with greater severity of Hughes disability score. Factors associated with poor outcome were, sensory symptoms, autonomic instability (arrythmia, hypotension, tachycardia, bradycardia) respiratory distress, and bulbar cranial nerve involvement.

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