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Research Article

Profile of Children with Guillain Barre Syndrome from tertiary Centre in Eastern Uttar Pradesh: a Prospective Observational Study

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Abstract

Background: Guillian Barre syndrome (GBS) is the most common cause of acute onset flaccid paralysis presenting at the tertiary center in the post-polio eradication era. There is regional variation in the presentation and outcome of GBS worldwide. Objective: We aimed to analyze clinical presentation and short term outcomes of GBS patients admitted to our center.

Methods: All children (1-14 years) of age with a diagnosis of GBS were enrolled in the study. Data were entered in a pre-formed format. Nerve conduction study, Cerebrospinal fluid examination, and other relevant investigations were done. Children received intravenous immunoglobulins (1 gram/kg) over 2 days. Respiratory support was given to children who were required. Functional outcome (Hughes score) were measured at end of 6 months

Results: There were seventy-six patients enrolled in the study over the study period of June 2017 to December 2020. The mean age of the study population was 76.5 ± 45.26 months. There were 49 males. The mean duration of hospital stay was 5.84 ± 2.28 days. Quadriparesis, paraparesis, and cranial nerve involvement were the most common clinical presentation in the study population. AIDP was the most common electrophysiological subtype in this cohort. Mechanical ventilation was required in 4 patients. Fifty-eight patients showed good recovery at the end of 6 months. Ten patients had residual weakness in either upper limb or lower limb at end of the follow-up period of 6 months. The need for mechanical ventilation was associated with poor outcomes at end of 6 months.

Conclusion: The majority of patients showed good functional recovery at end of 6 months follow up. AIDP was the most common electrophysiological subtype in this region, highlighting the regional variation. The need for mechanical ventilation was associated with poor recovery.

Keywords: Guillain; Barre Syndrome; Children; Outcome; India

Introduction

Guillain-Barre Syndrome (GBS) is an immune-mediated polyradiculopathy, presenting with acute onset ascending type paraparesis [1]. Weakness is often associated with hyporeflexia and areflexia [2]. It may be associated with sensory involvement, autonomic dysfunction, and respiratory muscle weakness [2]. The incidence of GBS is 0.6 to 4 per 1 lakh population. The natural course of the disease is characterized by acute onset of weakness, followed by a plateau phase of variable duration and recovery phase of variable degree and duration [2].

There are various subtypes of disease based on Nerve conduction velocity (NCV); (1) AIDP: Acute inflammatory demyelinating polyneuropathy (2) AMAN: Acute motor axonal neuropathy (3) AMSAN: Acute motor and sensory axonal neuropathy (4) MFS: Miller –Fischer Syndrome [3]. Childhood GBS has a more favorable outcome than adults [4,5]. Intravenous immunoglobulin (IVIG) and plasma exchange are the mainstays of therapy [1,6]. There is a scarcity of data regarding the outcome of pediatric GBS patients in the Eastern region of Uttar Pradesh [7-12]. So, this study was planned to assess the clinical presentation, electrophysiological subtypes and short-term outcomes at end of 6 months.

Methods

The study was conducted at the Department of Pediatrics, Institute of medical sciences, Banaras Hindu University from June 2017 to December 2020. The study was approved by the Institute Ethical Committee. Informed consent was taken from the parents or legal guardian in all cases.

Inclusion criteria

The diagnosis of GBS was based on the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) criteria [13]. The electrophysiological subtyping was done by using Haddens's criteria [14].

Exclusion criteria

All cases which mimic acute flaccid paralysis i.e., Traumatic neuritis, poliomyelitis, transverse myelitis in spinal shock, polymyositis, dermatomyositis, spinal muscular atrophy, and myasthenia gravis were excluded from the study.

Detailed history, clinical examination, investigations were entered in predesigned clinical proforma. Autonomic dysfunction was measured for each patient by entering in the datasheet of the following variables: Heart rate, respiratory rate, oxygen saturation, and blood pressure (BP).

Nerve conduction study (NCS) was performed using surface electrodes and a stimulator NCS. Motor nerve conduction was performed in median, ulnar, posterior tibial, common peroneal nerve unilaterally. Sensory stimulation was recorded from the median nerve (orthodromic) and the sural nerve (antidromic). F wave was recorded from the median and posterior tibial nerve.

Treatment

All enrolled patients received standard care with IVIg at a dose of 1 gram/kg/day for two days along with necessary supportive care. Those having respiratory failure were shifted to ICU and mechanical ventilation was done. Criteria for shifting to ICU were hemodynamic instability, respiratory failure, and altered sensorium, and loss of consciousness.

Outcome

Primary outcome measures like a recovery at 6 months, death and relapse were recorded. Secondary outcome measures like adverse effects to IVIg, duration of respiratory support, duration of hospital stay were also recorded.All patients were followed at 1, 3, and 6 months period from the date of discharge. Muscle strength was assessed by the medical research council (MRC) scale. Residual neurological deficit (Functional state) was assessed at end of 6 months with Hughes's disability grading [15].

Statistical analysis

Descriptive statistics (mean, median, mode, percentage, standard deviation, interquartile range) were used to describe study parameters. Means were compared with unpaired student t-test (for parametric data) and Wilcoxon rank-sum test (Non-parametric data). Proportions were compared with the chi-square test (parametric data) and Fisher -exact test (Non-parametric data).

Results

In our study, we recruited 82 patients admitted with a diagnosis of GBS from the department of Pediatrics, Banaras Hindu University. Six were excluded from the study as they did not receive IVIg. The mean age of patients in the Study group (n-76) was 76.50 ± 45.26 months. Thirty-nine (51.3%) children in the study group

were below 60 months. Among the 76 enrolled children, there were 49 boys. Fever, cough, loose stools were among predominant preceding complaints in the study group (Table 1). Four children received mechanical ventilation in the study population. The mean duration of hospital stay was 5.84 ± 2.28 days. Quadriparesis, paraparesis, and cranial nerve involvement were the most common clinical presentation in the study population (Table 1).

S/N	Parameter	Value
1	Age (months)	76.50 ± 45.26
2	Total duration of illness(days)	5.75 ± 2.98
3	Duration of hospital stay(days)	5.84 ± 2.28
4	Duration of mechanical ventilation(days)	5.20 ± 2.16
5	CSF cell count (cells/mm^3)	5.75 ± 4.78
6	CSF cell count (Range)	0-18 (min-max)
7	CSF protein (mg /dl)	109.50 ± 47.34
8	CSF protein (Range)	11-325 (min-max)
9	Gender (boys)	49
10	Age (< 60 months)	39
11	Mechanical Ventilation Received	4
12	Fever	43
13	Cough	28
14	Loose stool	19
15	Vomiting	2
16	Quadriparesis	55
17	Paraparesis only	21
18	Cranial involvement	16
19	Autonomic involvement	1
20	Diaphragmatic weakness	4

Table 1: Clinical characteristics of study participants (n-76).
Note: Continuous variables are expressed as mean (sd) and categorical variables are expressed as number.

At the time of the presentation, all the patients had significant lower limb weakness (MRC ≤ 3/5). We observed a steady improvement in power during our study. At discharge, 10.3% of patients had adequate power, at 1 month (39.7%), at 3 months (67.6%). Residual weakness was observed in only 14.7% of patients at the end of this study (Table 2). The most common cranial nerve palsy was bulbar palsy (n-14) followed by facial nerve palsy (n-2). Diaphragmatic and respiratory failure was seen in 4 children.

Lumbar puncture was done in all the enrolled children. Cerebrospinal fluid was examined for cells, protein, and glucose. We found that the majority of 69.7% had normal cell count whereas 30.3% of children had increased cell count (5.75 ± 4.78 cells/mm3). CSF protein was raised in 59 (77.6%) in the study group (mean protein value: 109.50 ± 47.34).

AIDP was the most predominant subtype (70/76) patients followed by AMAN (4/76) and AMSAN (2/76). There was no reported MFS case in our study. MRI spine was done in 10% of children enrolled due to financial constraints. Spinal nerve roots thickening and contrast enhancement was seen in all children (100%). The mechanical ventilation requirement was in four children. Two of them had relapsed at 3 months of follow up. There were 3 boys and 1 girl. The mean duration of mechanical ventilation was 5.50 ± 2.38 days. Three of them had residual weakness of grade 4 (Hughes grade) at 6 months of follow up (Table 3). Two cases of relapse presented to us with Hughes's disability score of 4. Both had a preceding viral infection. Both were managed with a second course of IVIg and plasmapheresis. Both responded well and had a Hughes score of 3 at end of 3 months from the second admission. Both required mechanical ventilation support for 14 days and were discharged on tracheostomy tube after 21 days and 25 days of hospital admission respectively.

Power (upper limb)	At Admission	At Discharge	At 1 month	At 3 months	At 6 months
≤ 3/5	45	27	14	3	2
>3/5	23	41	54	65	66
Power (lower limb)	At Admission	At Discharge	At 1 month	At 3 months	At 6 months
≤ 3/5	68	61	41	22	10
>3/5	0	7	27	46	58

Table 2: Depicting Power in upper limb and lower limb using MRC (Medical Research Council) SCALE.

Patient	Age	Gender	Presentation at admission	Cranial nerve involvement	Relapse	Duration of mechanical ventilation in days in first admission	Hughes grade at 6 months
1	60 months	Male	Quadriparesis	yes	yes	9	4
2	168 months	Male	Quadriparesis	yes	no	5	0
3	24 months	Male	Paraparesis	no	yes	4	4
4	42 months	Female	Paraparesis	yes	no	4	4

Table 3: Clinical and outcome characteristics of four patients requiring mechanical ventilation (n-4).

IVIg was given to all the 76 children enrolled in the study. Adverse effects were documented in 5(6.57%) children. Among these, 4 children had a fever, whereas chills and rigors were seen in 2 and 3 children respectively. We have tabulated important parameters between two groups at 6 months of follow up (Group 1 - Residual weakness versus Group 2- No-residual weakness) (Table 4). There were ten cases (7 boys and 3 girls) that had residual weakness of Hughes category 4. Nine of ten were presented with quadriparesis. One had autonomic dysfunction. Three had cranial nerve involvement. Two had relapsed at 3 months. The only need for mechanical ventilation was found to be significant between the two groups.

Parameter		Group 1 (n-10)	Group 2 (n-58)
Age	Mean (sd)	76.8 (42.4) months	71.36 (41.78)
	Median (Range)	66 (12-168) months	60 (11-168)
	Mode	60 months	24
Gender (m/f)		7/3	38/20
Weakness of limbs		Quadriparesis (9); paraparesis (1)	Quadriparesis s(41); paraparesis (17)
Autonomic dysfunction		1	0
Cranial nerve involvement		4	12
Mechanical ventilation requirement *		3	1
Relapse		2	0
Death		0	0

Table 4: Parameters of GBS patients (Residual weakness –Group 1 versus No-residual weakness- Group 2) at end of 6 month follow up.

Note: * Denotes RR (CI): RR: 6.85 (2.79-16.85); P < 0.05;

Abbreviations: RR - Relative risk; CI - Confidence interval; GBS- Guillian barre Syndrome; m-male; f-Female

Discussion

Guillain-Barre syndrome is one of the most common diagnoses of lower motor neuron flaccid paralysis presenting to the tertiary care center. Various reports are citing the different clinical presentations of GBS in adults and children. There is a scarcity of data from pediatric GBS from India. So, we reviewed recently reported original articles of Indian pediatric GBS patients for better comparison with our study (Table 5). Younger age presentation and male preponderance coincide with earlier reports in the literature [16,17]. Majority of cases of our study cohort (39/76) are below 60 months. This age predilection has been found in other Indian studies [7,8,12,18]. This can be explained by the occurrence of more upper respiratory tract infections and gastroenteritis episodes in this age group. This puts them further into the risk of having post-infectious, immune-mediated polyradiculopathy. Upper respiratory tract infections and diarrhea were the preceding illness as reported in earlier literature [19].

Electrophysiological study showed AIDP (n-70) was the most common variant reported in this cohort followed by AMAN (n-4) and AMSAN (n-2). There are conflicting reports of subtype in literature. Most Indian studies and others have reported AMAN as a major subtype [7,12]. Kalita., *et al*. and Sarkar., *et al*. have reported AIDP as predominant subtype in their study cohort of 142 and 139 pediatric patients respectively [9,20]. The predominance of AIDP in

Authors	Period of study	N	Age group	Mean age (years ± SD) at presentation	Loss of ambulation (n)	Cranial nerve involvement (n)	Pts requiring ventilator (n)	Dysautonomia	Nerve conduction study	Percentage of children with Residual weakness at end of study
Yadav., *et al*; 2019	December 2013-March 2015	36	2-18 years	5.1 ±2.1 < 2 years: 15 2-10 years: 17 > 10 years: 2	33	24	6	3	AMAN -25. AIDP-9. In excitable -2	1 Patient non-ambulatory at 3 months follow up of 32 patients
Gupta., *et al*; 2019;	January 2014-March 2015	57	6-12 years	68±40 months Median age of presentation: 52 months (IQR: 32-164.5	Upper limb weakness -35 Lower limb weakness- 53 Facial weakness -21 Neck weakness-13 Bulbar weakness- 20 Intercostal weakness -19 Diaphragm weakness -18 Truncal weakness -32	6	19	22	AMAN-19; AIDP-20; AMSAN-1; Inexcitable-12; Unclassified-5	AMAN had poor recovery than AIDP subtype (12 versus 19 in follow up) Death: 3
Kalita., *et al*; 2018 (Ref 9)	2006-2016	142	< 21 years	11.7 ±5.4	71	73	28	21	AMAN-33; AIDP-95; AMSAN-6; Equivocal-2; normal-2, Inexcitable-2	Complete recovery -66 Partial recovery-24 Wheelchair bound 34 Lost to follow up-13 Death -3

Kumar., *et al*; 2015 (Ref 10)	October 2012 to April 2014	20	< 18 years	Range: 16 month-17 years	Limb weakness: 20	4	7	5	AMAN: 7. AIDP: 4 AMSAN: 4 Unclassified/mixed: 3 Not done: 2	Complete recovery (n-17): 14 Incomplete recovery (n-17): 3
Sankhayan., *et al*; 2014 (Ref 18)	2009-2011	65	1mon-18 years	Median age: 60 months (range: 2-13 years)	Not mentioned	Not mentioned	6	Not mentioned	AMAN-27; AIDP-15; AMSAN-3; In excitable -12; Unclassified: 8	Death: 2
Sarkar., *et al*; 2011; Retrospective study (Ref 20)	July 2000 to June 2010	139	2-12 years	< 1 year: 8 1-15 years: 118 >15 years: 13 <5 years: 22	Limb weakness (at admission): 107 Limb weakness (at peak deficit): 139	4	15	At admission: 19 At peak deficit: 49	AIDP-124	Majority made full recovery
Kannan., *et al*; 2011; (Ref 11)	August 2006 and July 2007	43	1-18 years	Median age: 8 years Range: 11months-18 years	Motor weakness: 42	33	4	6	AIDP-21 AMAN-19 Unclassified: 3	Majority showed complete recovery in both AMAN and AIDP group
Kalra., *et al*; 2009 (Ref 12)	December 2003 to September 2006	52	< 16 years	Median age -5 years; Age Range -12 months-15 years	Quadriparesis (n-40): 33	10	10	9	AMAN-18 AIDP-5 Inexcitable -10 Only done in 33 patients	One year follow up (n-40): 35 recovered fully. More than one year follow up (n-40): 38 recovered fully Median duration of follow up: 25 months (Range: 12-48 months) Lost to follow up: 6 Death -6

Present study	June 2015 to June 2017	76	1-14 years	Mean Age: 76.5±45.266 months Median: 60 (36-96) months Range: 11-168 months	Quadriparesis: 55 Paraparesis: 21	16	4	1	AIDP-70 AMAN-4 AMSAN-2	Poor functional recovery: 10 Complete recovery at 6 months follows up: 58 (85.2%)

Table 5: Summary of characteristics of Indian Paediatric GBS studies (N-8).

the eastern part of India is further strengthened by this study. The likely factors playing role in such different subtypes are indigenous risk factors, heterogeneity in antecedents but, it is still unclear.

The rate of mechanical ventilator requirements in Indian pediatric studies ranges from as low as 9.2% to 35% [7-12,18,20]. Only four patients required mechanical ventilation in this study cohort. The probable reason could be our study cohort had the majority of the AIDP subtype. The study by Gupta., *et al*. and Nachamkin., *et al*. had shown a ventilator requirement is more common in the AMAN subtype [8,21].

The frequency of dysautonomia in India studies ranges from 3% to 38.59% [7-12,20]. Autonomic involvement in form of blood pressure instability, sinus tachycardia, abnormal sweating was seen in only 1 patient. This could be due to methods of evaluation. We used only the bedside clinical examination without any particular testing. This patient had a poor functional disability score (Hughes score-4) at 6 months follow up. A study by Barzegar., *et al*. had shown disability score > 3, autonomic involvement, cranial nerve involvement, and absent CMAP were predictors of poor outcome in his study cohort of 324 pediatric patients [22].

Functional recovery at 6 months (Hughes score 0, 1) was found in 58 patients (n-66), while ten patients had a functional residual weakness (Hughes score 4) at end of 6 months of follow up. Korinthenberg., *et al*. had found good functional recovery in 96% of patients at the end of 1 year in his study of 95 children [16]. A recent study by Barzegar., *et al*. has also found good functional recovery in 96% of children at end of 1 year [22]. The figure of 85.2% is lower than the above two studies. This could be because of the smaller duration of follow up (6 months). The requirement of mechanical ventilation was associated with poor outcomes at 6 months of follow up. This finding is in congruence with previous findings of Kalra., *et al*. in Indian patients [12]. Although all ten patients with poor functional recovery were from the AIDP subtype. Konushan., *et al*. have found no relation to prognosis based on subtypes of electrophysiological studies in his cohort of 236 children [17]. In another study by Chareyre., *et al*. axonal forms of GBS have a poor outcome in the French pediatric case series [23,24]. So, there are conflicting results regarding prognostic factors in pediatric GBS patients.

Conclusion

The strength of this paper is a large group of patients was being followed for 180 days (6 months) for assessing the outcome of the disease. GBS disability score (Hughes score) was used to score the outcome in pediatric patients. Electrophysiological study was done in all patients to classify the type of GBS. The main drawback of study eight patients who were lost to follow up in 6-month prospective data recording. We could not assess the etiological agent in the preceding infection. We did not measure anti-ganglioside antibodies due to nonavailability.

Despite these limitations, the present study has brought the following conclusions. Guillain Barre syndrome is the most common cause of acute flaccid paralysis in the era of polio eradication. Quadriparesis was the most common clinical presentation. AIDP was the most common electrophysiological finding in NCV. The majority of our patients showed good functional recovery at end of 6

months. The requirement of mechanical ventilation was associated with poor outcomes at end of 6 months. We need to have a multicentre study for a better understanding of factors governing the poor outcome.

Bibliography

1. Korinthenberg R and Schulte Monting J. "Natural history and treatment effects in Guillain-Barre syndrome: a multicentre study". *Archives of Disease in Childhood* 74 (1996): 281-287.

2. Hahn AF. "Guillain-Barré syndrome". *Lancet* 352.9128 (1998): 635-641.

3. Hughes RA and Rees JH. "Clinical and epidemiological features of Guillain-Barré syndrome". *The Journal of Infectious Diseases* 176 (1997): S92-S98.

4. Asbury AK. "New concepts of Guillain-Barre syndrome". *Journal of Child Neurology* 15 (2000): 183-191.

5. Abd-Allah SA., *et al*. "Intravenous immunoglobulin as therapy for pediatric Guillain- Barré syndrome". *Journal of Child Neurology* 12 (1997): 376-380.

6. Kanra G., *et al*. "Intravenous immunoglobulin treatment in children with Guillain-Barré syndrome". *European Journal of Paediatric Neurology* 1 (1997): 7-12

7. Yadav S., *et al*. "Guillain-Barre syndrome in North Indian children: Clinical and serial electrophysiological features". *Neurology India* 67 (2019): 724-727.

8. Gupta PK., *et al*. "How Different is AMAN from AIDP in Childhood GBS? A Prospective Study from North India". *Indian Journal of Pediatrics* 86 (2019): 329-334.

9. Kalita J., *et al*. "Prospective comparison of acute motor axonal neuropathy and acute inflammatory demyelinating polyradiculoneuropathy in 140 children with Guillain-Barré syndrome in India". *Muscle and Nerve* 57 (2018): 761-765.

10. Kumar M., *et al*. "Guillain-barré syndrome: a clinical study of twenty children". *Journal of Clinical and Diagnostic Research* 9 (2015): SC09-SC12.

11. Kannan MA., *et al*. "Clinical, electrophysiological subtypes and antiganglioside antibodies in childhood Guillain-Barré syndrome". *Neurology India* 59 (2011): 727-732.

12. Kalra V., *et al*. "Outcome in childhood Guillain-Barré syndrome". *Indian Journal of Pediatrics* 76 (2009): 795-799.

13. Asbury AK and Cornblath DR. "Assessment of current diagnostic criteria for Guillain-Barré syndrome". *Annals of Neurology* 27 (1990): S21-S24.

14. Hadden RD., *et al*. "Electrophysiological classification of Guillain-Barré syndrome: Clinical associations and outcome. Plasma Exchange/Sandoglobulin Guillain-Barré Syndrome Trial Group". *Annals of Neurology* (1998): 780-788.

15. Hughes RA., *et al*. "Controlled trial prednisolone in acute polyneuropathy". *Lancet* 2 (1987): 750-753.

16. Korinthenberg R., *et al*. "Clinical presentation and course of childhood Guillain-Barré syndrome: a prospective multicentre study". *Neuropediatrics* 38.1 (2007): 10-17.

17. Konuşkan B., *et al*. "Electrophysiological Subtypes and Prognostic Factors of Childhood Guillain-Barré Syndrome". *Archives of Neuropsychiatry* 55 (2018): 199-204.

18. Sankhyan N., *et al*. "Childhood Guillain-Barré syndrome subtypes in northern India". *Journal of Clinical Neuroscience* 21 (2014): 427-430.

19. Yuki N and Hartung HP. "Guillain-Barré syndrome". *The New England Journal of Medicine* 366 (2012): 2294-2304.

20. Sarkar UK., *et al*. "Spectrum of Guillain-Barré syndrome in tertiary care hospital at Kolkata". *Journal of Natural Science, Biology and Medicine* 2 (2011): 211-215.

21. Nachamkin I., *et al*. "Patterns of Guillain-Barre syndrome in children: results from a Mexican population". *Published Correction Appears in Neurology* 72 (2009): 1110.

22. Barzegar M., *et al*. "Predictive factors for achieving independent walking in children with Guillain-Barre syndrome". *Pediatric Research* 82 (2017): 333-339.

23. Chareyre J., *et al*. "Acute axonal neuropathy subtype of Guillain Barré syndrome in a French pediatric series: Adequate follow-up may require repetitive electrophysiological studies". *European Journal of Paediatric Neurology* 21 (2017): 891-897.

24. Varkal MA., *et al*. "Pediatric Guillain-Barré syndrome: Indicators for a severe course". *Annals of Indian Academy of Neurology* 18 (2015): 24-28.