Original Article

Clinical profile and predictors for outcome in children presenting with Guillain–Barré syndrome

Sonali Singh[1], Nitin Gupta[2], Arpita M. Gupta[3], Anurag S. Chandel[4], Sneha Waghela[5], Pallavi Saple[5]

[1]Department of Paediatrics, All India Institute of Medical Sciences, New Delhi, [2]Department of Infectious Diseases, Kasturba Medical College, Manipal, Karnataka, [3]Department of Paediatrics, Tata Memorial Hospital, Mumbai, Maharashtra, [4]Department of Paediatrics, Mahatma Gandhi Institute of Medical Sciences, Wardha, Maharashtra, [5]Department of Paediatrics, Grant Government Medical College, Mumbai, Maharashtra, India

Abstract

Introduction: Acute Flaccid Paralysis (AFP) is a group of diverse clinical conditions with Guillain–Barré syndrome (GBS) as one of the most common cause. The aim of this study was to study the clinical features and predictors for the requirement of ventilation in children with GBS. **Materials and Methods:** This is a prospective observational study done at a tertiary care hospital where all consecutive children less than 15 years who presented with AFP were enrolled. Demographic characteristics, symptomatology, and physical findings of those patients who were diagnosed with GBS were recorded using a pre-defined questionnaire. Univariate analysis was done to identify clinical variables associated with a higher requirement of ventilation. **Results:** Of a total of 53 children with AFP enrolled in the study, a total of 30 patients were diagnosed with GBS. A total of 12 (40%) patients required ventilation, while five of these patients eventually died. The following variants of GBS were identified: AIDP (13/30), AMAN (12/30), and ASMAN (2/30). Lower limbs were affected in 97% of the patients, whereas upper limbs were affected in 83% of the patients. Deep tendon reflexes of the upper limb and lower limb were preserved in 56% and 7% of the patients, respectively. Presence of antecedent URTI was associated with a lower requirement of ventilation. Presence of bulbar palsy, lower upper limb power on presentation, and absence of deep tendon reflex in upper limbs were associated with a higher requirement of ventilation. **Conclusion:** GBS is an important cause of AFP in India with no significant difference between the variants in terms of frequency and prognosis. Simple physical findings can be used by primary care physicians to predict the requirement of higher levels of care.

Keywords: Acute flaccid paralysis, intravenous immunoglobulin, mechanical ventilation

Introduction

Acute Flaccid Paralysis (AFP) is a group of diverse clinical conditions of varied aetiology characterized by acute onset of flaccid weakness.[1] Worldwide introduction of immunization and intensive united efforts of all nations has drastically reduced the incidence of poliomyelitis. Although polio has been eradicated from India (Mar 27, 2014), there has been a surge in non-polio AFP cases.[2] Although India reports a high number of AFP cases, the aetiology is not clearly defined in most cases. Studies conducted in different parts of the world have shown Guillain–Barré syndrome (GBS). Although systematic studies are lacking, children with GBS are common in the practice of primary care physicians in India. Respiratory failure is a common complication of GBS seen in up to 20–30% of the patients.[3] Predicting the

Address for correspondence: Dr. Pallavi Saple, Dean and Professor, Paediatrics, Grant Government Medical College, Nagpada-mumbai Central, Mumbai - 400 008, Maharashtra, India.
E-mail: saplepallavi@gmail.com

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requirement of mechanical ventilation will be extremely helpful for primary care physicians as it enables them to initiate early treatment and refer to higher levels of care. Although such studies have been reported in adults, such studies are lacking in children, especially from India.[4,5] The aim of this study was to, therefore, study the clinical features and predictors for the requirement of ventilation in children with GBS.

Materials and Methods

This is a prospective observational study done at a tertiary care hospital of Mumbai for a period of 18 months after taking approval from the Institute's Ethical Committee. All consecutive children who presented with AFP and were less than 15 years were enrolled in the study after obtaining informed consent from parent/guardian. Demographic characteristics, symptomatology, immunization history, other relevant history, and physical findings (including throat examination) were noted for each case in a predesigned proforma. Detailed CNS examination was done. Tone, power, and deep tendon reflexes (including thumb reflex) were noted for each limb. Thorough cranial nerve examination and ophthalmological examination was done. Laboratory investigations and radiological investigations were done at the clinician's discretion. The patients were categorized into diagnostic outcomes based on standardized definitions/ diagnostic criteria. All patients diagnosed with GBS were further analyzed and followed up till death or discharge.

After collecting the data, a master chart was prepared using MS-Excel. The data has been analyzed using Stata v12. Data have been depicted in frequencies, mean and percentages. Univariate analysis was done to identify clinical variables associated with poor outcomes in patients with GBS. Chi-square test was used as the test of significance for qualitative variables. A *P* value of less than 0.05 has been considered significant.

Results

A total of 53 children were enrolled in the study. GBS was the commonest etiological diagnosis [Table 1]. A total of 55% of the patients were male, and a total of 81% of the patients were either less than four years (38%) or more than seven years (43%). A total of 74% of the patients presented within seven days of onset of weakness. Of the patients where the history of immunization was known, a total of 78% (36/46) were completely immunized till the date of presentation. Lower limbs were affected in 81% of the patients, whereas upper limbs were affected in 70% of the patients. Deep tendon reflexes of the upper limb and lower limb were preserved in 62% and 30% of the patients, respectively. A total of 34% of the patients required ventilation, half of whom expired. All the patients who did not require ventilation were eventually discharged.

A total of 30 patients were diagnosed with GBS. A total of 12 (40%) patients required ventilation, while five of these patients eventually died. The following variants of GBS were identified:

Table 1: Etiological classification of patients with acute flaccid paralysis

Diagnosis	Frequency	Percentage (%)
Guillain–Barré syndrome	30	56.6
Bell's palsy	5	9.4
Post diphtheritic neuropathy	2	3.8
Cerebrovascular accidents	3	5.7
Acute disseminated encephalomyelitis	1	1.9
Acute cerebellitis	1	1.9
Anterior horn cell neuropathy	1	1.9
Transient ischemic attack	1	1.9
Traumatic neuritis	1	1.9
Hypokalemic paralysis	1	1.9
Scurvy with monoparesis	1	1.9
Bulbar palsy	1	1.9
Status epilepticus	1	1.9
Undiagnosed	4	7.5
Total	53	100.0

AIDP (13/30), AMAN (12/30), and ASMAN (2/30). Three patients did not fit into any of the variants. The median age of the patients was six years. The male to female ratio was 1.3: 1. History of antecedent illness was present in 13 patients [fever- 9, upper respiratory tract infection (URTI)- 5, diarrhoea- 4]. The mean day of illness at presentation was 7.2 days. Of the 11 patients who developed respiratory paralysis, the interval between onset of weakness and respiratory muscle paralysis was found to be less than <3 days in 64% and 3-7 days in 36% of the patients. Of the 15 patients who developed bulbar palsy, 67% of the patients developed within three days from the onset of weakness. Neck weakness and facial palsy was present in 43% and 7% of the patients, respectively.

Lower limbs were affected in 97% of the patients, whereas upper limbs were affected in 83% of the patients. Deep tendon reflexes of the upper limb and lower limb were preserved in 56% and 7% of the patients, respectively. Thumb reflex was present in 100% of the patients. An autonomic imbalance was present in 20% of the patients. Of the 27 patients who were treated, the following treatments were given: IVIG (16), steroids (3) and IVIG plus steroids (8).

Presence of antecedent URTI was associated with a lower requirement of ventilation [Table 2]. Presence of bulbar palsy, lower upper limb power on presentation, and absence of deep tendon reflex in upper limbs were associated with a higher requirement of ventilation [Table 2].

Discussion

Acute flaccid paralysis (AFP) is a clinical syndrome characterized by rapid onset of weakness, including (less frequently) weakness of muscles of respiration and swallowing, progressing to maximum severity within days to weeks. GBS was the commonest cause of AFP in our study, similar to previously published studies.[6-9] GBS is a disease that affects all ages and peaks in 3rd

Table 2: Predictors for requirement of ventilation in patients with GBS

Parameter		Patients who did not require ventilation (n = 18)	Patients who required ventilation (n = 12)	P
Age	<4 years	7	4	0.831
	4-7 years	4	3	
	>7 years	7	5	
Sex	Female	10	3	0.232
	Male	8	9	
Variant of GBS	AIDP	8	5	0.983
	AMAN	7	5	
	AMSAN	1	1	
	Not classified	2	1	
Antecedent illness	Fever	5	4	0.745
	Diarrhoea	3	1	0.125
	URTI	5	0	0.046
Day of presentation	<3 days	5	6	0.460
	3-7 days	8	4	
	>7 days	5	2	
Neck weakness		6	8	0.073
Bulbar palsy		5	11	0.003
Upper limb power	Grade 4 and 5	11	1	0.016
	Grade 3 and below	7	11	
Lower limb power	Grade 4 and 5	3	1	0.511
	Grade 3 and below	15	11	
Absent DTR of UL		2	7	0.044
Absent DTR of LL		16	11	0.804
Treatment	IVIG	13	11	0.192
	Steroid	7	4	0.757

to 4th decade in India. In the pediatric population, it is found to affect those above three years of age. In our study, the median age was six years. Similar findings have been observed in other studies as well.[10,11] Most studies show a male preponderance in GBS, including ours.[10-13]

In our study, the mortality rate among children with GBS was 16.6%. A study conducted by Wong AH *et al.* at seven hospitals in four different Asian countries found the mortality rate to be 6% (0–13% at different centers).[14] Netto AB *et al.* found the mortality rate to be 10.4% in their study.[15] The mortality rate was slightly higher in our study compared to other studies as ours was a tertiary care referral center receiving complex cases referred from smaller centers.

In our study, the frequency of AMAN, AIDP and ASMAN was 44%, 48%, and 7%, respectively, which is similar to studies published from Japan, Mexico and China.[13,16,17] In the Indian population, AIDP and AMAN have almost equal incidence, though AMAN is more common in the pediatric population.[13,14] Some of the studies have shown that axonal variants were associated with a higher need for ventilation.[4,5,17-20] However, in our study, there was no such statistically significant association. Early studies from India suggested that 1/3rd of the Indian GBS patients gave a positive history of antecedent illness, in contrast to 2/3rd of the western GBS population.[21] In our study, 43% of children had some antecedent symptoms. Similar to previous studies, fever, URTI, and diarrhea were the commonest antecedent symptoms.[22] Similar to a study by Paul *et al.*, history of URTI was associated with lesser requirement of ventilation.[4] Duration of onset to respiratory muscle paralysis (nadir) was found to be <7 days, with 63% presenting within three days. Our finding matched with that of Fokke *et al.* who found that disease reached its nadir in 5–13 days with a mean of 8 days.[23]

Motor weakness was the commonest symptom in our study, similar to previously published studies.[6,12,23] Normal tendon reflexes in arms and legs were found in 56% and 7% patients respectively. A similar finding was reported in a study conducted by Karimzadeh *et al.*[24] We found a significant association between lower upper limb power on the day of admission and requirement of ventilation. Those with power less than/equal to 3 had significantly poor outcome with more requirement of ventilation. In a study by Sharshar *et al.*, inability to lift elbow was a statistically significant predictor of poor outcome with more chances of the requirement of mechanical ventilation.[25] Studies have shown that lower upper limb power predicts poor outcome in the form of increased chances of the requirement of mechanical ventilation.[4] Similar to other studies, the onset of bulbar palsy was a predictor of poor outcome.[4,5,26,27] This is possibly because of the loss of protective reflex of the pharynx.

In summary, GBS is an important cause of AFP in India with AIDP and AMAN being the commonest variants. Contrary to the other published reports, no significant difference was observed between the two variants in terms of frequency and

outcome (requirement of ventilation). Presence of bulbar palsy, lower upper limb power on presentation, and absence of reflexes in the upper limbs predict the need for ventilation. This study is essential in day to day practice of primary care physicians as the assessment of simple physical findings such power and deep tendon reflexes can be used to predict the requirement of higher levels of care.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

1. Fang X, Huda R. Acute flaccid myelitis: Current status and diagnostic challenges. J Clin Neurol 2020;16:376-82.
2. Maan HS, Dhole TN, Chowdhary R. Identification and characterization of nonpolio enterovirus associated with nonpolio-acute flaccid paralysis in polio endemic state of Uttar Pradesh, Northern India. PLoS One 2019;14:e0208902.
3. Nguyen TP, Taylor RS. Guillain Barre syndrome. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2020.
4. Paul BS, Bhatia R, Prasad K, Padma MV, Tripathi M, Singh MB. Clinical predictors of mechanical ventilation in Guillain-Barré syndrome. Neurol India 2012;60:150-3.
5. Luo H, Hong S, Li M, Wang L, Jiang L. Risk factors for mechanical ventilation in children with Guillain-Barré syndrome. Muscle Nerve 2020;62:214-8.
6. Rasul CH, Das PL, Alam S, Ahmed S, Ahmed M. Clinical profile of acute flaccid paralysis. Med J Malaysia 2002;57:61-5.
7. Soltani J, Esmailnasab N, Roshani D, Karimi M, Amjadi MJ. Acute flaccid paralysis and its differential diagnosis in in Kurdistan Province, Western Iran; an 11-year surveillance. Iran J Pediatr 2014;24:131-9.
8. Hussain IHMI, Ali S, Sinniah M, Kurup D, Khoo TB, Thomas TGS, *et al.* Five-year surveillance of acute flaccid paralysis in Malaysia. J Paediatr Child Health 2004;40:127-30.
9. D'Souza R, Kennett M, Antony J, Longbottom H, Elliott E. Acute flaccid paralysis surveillance in Australia progress report 1995-1998. Commun Dis Intell 1999;23:128-31.
10. Parveen A, Khan SA, Talat S, Hussain SNF. Comparison of the clinical outcomes of Guillain Barre Syndrome based on electrophysiological subtypes in Pakistani children. Cureus 2020;12:e8052.
11. Kannan MA, Ch RK, Jabeen SA, Mridula KR, Rao P, Borgohain R. Clinical, electrophysiological subtypes and antiganglioside antibodies in childhood Guillain-Barré syndrome. Neurol India 2011;59:727-32.
12. Tekgul H, Serdaroglu G, Tutuncuoglu S. Outcome of axonal and demyelinating forms of Guillain-Barré syndrome in children. Pediatr Neurol 2003;28:295-9.
13. Nachamkin I, Arzarte Barbosa P, Barbosa PA, Ung H, Ung H, Lobato C, *et al.* Patterns of Guillain-Barre syndrome in children: Results from a Mexican population. Neurology 2007;69:1665-71.
14. Wong AHY, Umapathi T, Shahrizaila N, Chan YC, Kokubun N, Fong MK, *et al.* The value of comparing mortality of Guillain-Barré syndrome across different regions. J Neurol Sci 2014;344:60-2.
15. Netto AB, Taly AB, Kulkarni GB, Uma Maheshwara Rao GS, Rao S. Prognosis of patients with Guillain-Barré syndrome requiring mechanical ventilation. Neurol India 2011;59:707-11.
16. Griffin JW, Li CY, Ho TW, Xue P, Macko C, Gao CY, *et al.* Guillain-Barré syndrome in northern China. The spectrum of neuropathological changes in clinically defined cases. Brain J Neurol 1995;118:577-95.
17. Nagasawa K, Kuwabara S, Misawa S, Fujii K, Tanabe Y, Yuki N, *et al.* Electrophysiological subtypes and prognosis of childhood Guillain-Barré syndrome in Japan. Muscle Nerve 2006;33:766-70.
18. Kalita J, Misra UK, Goyal G, Das M. Guillain-Barré syndrome: Subtypes and predictors of outcome from India. J Peripher Nerv Syst JPNS 2014;19:36-43.
19. Hiraga A, Mori M, Ogawara K, Hattori T, Kuwabara S. Differences in patterns of progression in demyelinating and axonal Guillain-Barré syndromes. Neurology 2003;61:471-4.
20. Kalita J, Kumar M, Misra UK. Prospective comparison of acute motor axonal neuropathy and acute inflammatory demyelinating polyradiculoneuropathy in 140 children with Guillain-Barré syndrome in India. Muscle Nerve 2018;57:761-5.
21. Gupta SK, Taly AB, Suresh TG, Rao S, Nagaraja D. Acute idiopathic axonal neuropathy (AIAN): A clinical and electrophysiological observation. Acta Neurol Scand 1994;89:220-4.
22. Ng YS, Lo YL, Lim PAC. Characteristics and acute rehabilitation of Guillain-Barré syndrome in Singapore. Ann Acad Med Singapore 2004;33:314-9.
23. Fokke C, van den Berg B, Drenthen J, Walgaard C, van Doorn PA, Jacobs BC. Diagnosis of Guillain-Barré syndrome and validation of Brighton criteria. Brain J Neurol 2014;137:33-43.
24. Karimzadeh P, Bakhshandeh Bali MK, Nasehi MM, Taheri Otaghsara SM, Ghofrani M. Atypical findings of guillain-barré syndrome in children. Iran J Child Neurol 2012;6:17-22.
25. Sharshar T, Chevret S, Bourdain F, Raphaël J-C, French Cooperative Group on Plasma Exchange in Guillain-Barré Syndrome. Early predictors of mechanical ventilation in Guillain-Barré syndrome. Crit Care Med 2003;31:278-83.
26. Green C, Baker T, Subramaniam A. Predictors of respiratory failure in patients with Guillain-Barré syndrome: A systematic review and meta-analysis. Med J Aust 2018;208:181-8.
27. Ning P, Yang B, Yang X, Zhao Q, Huang H, Shen Q, *et al.* A nomogram to predict mechanical ventilation in Guillain-Barré syndrome patients. Acta Neurol Scand 2020. doi: 10.1111/ane.13294.