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

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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.[9] 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.[10] 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.[11] Predicting the
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.\textsuperscript{[6-9]} 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 83% 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 56% 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: 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.\textsuperscript{[6-9]} GBS is a disease that affects all ages and peaks in 3rd

### 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          |
to 4th decade in India. In the pediatric population, it is found to affect those above 3 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.[3,16,17] In the Indian population, AIDP and AMAN have almost equal incidence, though AMAN is more common in the pediatric population.[3,14] Some of the studies have shown that axonal variants were associated with a higher need for ventilation.[15,17,20] 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

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

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