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# A Retrospective Single-center Study of Presentation and Prognosis of Guillain-Barré Syndrome in Pediatric Patients

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## Abstract

**Background:** Guillain-Barré syndrome (GBS) is a post-infectious immune-mediated peripheral neuropathy, progressing bilaterally and often symmetrically and affecting sensory and motor function. Most cases completely recover, but around 20% of cases may lead to complications, incomplete recovery, or even death.
**Objectives:** This study aims to assess the prognosis of GBS in pediatric patients and possible associated conditions regarding recovery or prognosis.
**Methods:** We investigated 71 cases of GBS admitted to Mofid Pediatric Hospital from March 2014 to March 2017. Demographic, clinical, and laboratory data were retrospectively recorded and analyzed. Two follow-up visits were performed after 1 to 3 and 5 to 8 years from onset, according to the GBS Disability Scale, and recovery of motor function was assessed during patients' visits to the clinic.
**Results:** We found 35 male and 36 female subjects with an average age of 6.17 ± 3.82 (range 0.9 up to 15 years old); cases were mostly presented with myalgia and weakness (78.9%) followed by headache, found in 5 patients (7%). Around 84.5% of patients had an upper respiratory infection as their antecedent infection. Fifteen cases of autonomic dysfunction were observed, and 15 patients had cranial nerve involvement. Most cases had the acute inflammatory demyelinating polyradiculoneuropathy (AIDP) form of GBS on electrophysiologic tests. Analysis showed only axonal involvement was significantly correlated with poor prognosis (P-value<0.05), and other variables were not significantly correlated.
**Conclusions:** Compared to the current literature, we found fewer autonomic dysfunctions, cranial neuropathies, and a smaller percentage of AIDPs in our data. Altogether, the axonal form of GBS is reported as a predictor of an unfavorable prognosis in GBS patients.

*Keywords:* Guillain-Barré, Pediatric, Prognosis

## 1. Background

First described in the 19th century by Guillain, Barré, and Strohl, Guillain-Barré syndrome (GBS) is an immune-mediated peripheral neuropathy usually characterized by rapidly progressive bilateral and often symmetrical loss of sensory and motor functions of the limbs, which might also involve respiratory or cranial nerve-innervated muscles (1, 2). GBS is frequently preceded by an infection that often has been caused by *Campylobacter jejuni* or other bacterial or viral agents such as CMV, EBV, *Mycoplasma pneumoniae*, or *Hemophilus influenza* (3-6). While some immunizations were previously thought to be correlated with subsequent GBS, current evidence indicates that, with rare exceptions, associations between GBS and such vaccines have been only temporal. For other vaccines, current data is, as of yet, either inconclusive or reported to have minimal effect on incidence. (5, 7). Evidence suggests that anti-ganglioside antibodies may play some role in GBS, but its underlying etiology and pathophysiology are not well understood (6-8). The overall incidence of GBS across all age groups is estimated between 1.1 and 3.3 per 100,000/year, and in individuals less than 18 years of age, the incidence is estimated to range from 0.5 to 1.5 per 100,000 (3, 9).

GBS can be further divided into several forms based on clinical and electrophysiological studies. These are

acute inflammatory demyelinating polyradiculoneuropathy (AIDP), two axonal forms of GBS including acute motor-sensory axonal neuropathy (AMSAN) and acute motor axonal neuropathy (AMAN), Miller Fisher syndrome (MFS), pharyngeal-brachial and pure paraparesis variants (5, 10, 11).

Treatment options range from just observation to Intravenous Immunoglobulins (IVIG) and possible use of plasmapheresis; whereas some cases recover spontaneously and without sequelae, others may need intensive care such as mechanical ventilation, and complete recovery may never ensue (4). Despite various efforts and treatments, reportedly around 20% of cases, GBS complications lead to severe disability (1, 5).

## 2. Objectives

This study aims to assess the prognosis of GBS in pediatric patients and investigate possible associated conditions that might affect recovery or prognosis.

## 3. Methods

The current study collected all cases of GBS diagnosed by the National Institute of Neurological Disorders and Stroke (NINDS) criteria, including bilateral weakness and areflexia, albuminocytologic dissociation, nerve conduction findings, disease progression over days to four weeks, symmetry, mild sensory abnormalities, cranial nerve involvement and autonomic dysfunction, (12) admitted to Mofid Pediatric Hospital, Tehran, Iran from March 2014 to March 2017. Demographic, clinical, and laboratory data were retrospectively collected from the patient's medical records. These include age, sex, disease presentation, initial physical examination, prodromal symptoms (e.g., prior upper respiratory infection), early vital signs, dysautonomia signs including labile hypertension, orthostatic hypotension, sinus tachycardia or sinus arrest, cranial neuropathy signs and symptoms including dysphagia, ptosis, diplopia or strabismus, respiratory distress, and severity of muscle weakness in limbs. Electrophysiological studies of patients were recorded. Electrophysiological studies in patients with GBS usually reveal a sensorimotor polyradiculoneuropathy or polyneuropathy, illustrated by reduced conduction velocities, reduced sensory and motor evoked amplitudes, abnormal temporal dispersion and/or partial motor conduction blocks (12). Also, laboratory data comprises findings in CSF samples (WBC count, neutrophils count, protein concentration, glucose Concentration) and blood samples (WBC count, neutrophils count, hemoglobin, platelets, erythrocyte sedimentation rate (ESR), C-reactive Protein (CRP), blood sugar (BS), blood urea nitrogen (BUN), creatinine, electrolytes, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP ) levels) were recorded.

Two follow-up visits were performed after 1 to 3 and 5 to 8 years from onset, according to the GBS Disability Scale (2), and recovery of motor function was assessed during patients' visits to the clinic.

GBS Disability Scale is defined as the following: 0- healthy; 1- minor signs or symptoms of neuropathy but capable of manual work; 2- able to walk without the support of a stick but incapable of manual work; 3- able to walk with a stick, appliance, or support; 4- confined to bed or chair-bound; 5- requiring assisted ventilation; and 6- deaths.

Paired and unpaired *t*-tests analyzed quantitative data, and the Chi-square test was used to analyze qualitative data.

## 4. Results

Of 71 GBS cases enrolled in this study, 35 were male (49%), and 36 were female (51%). The average age of patients was 6.17 years, ranging from 0.9 to 15 years old (SD 3.82 years). The most common initial presentation was myalgia and weakness, which presented itself in 56 patients (78.9%), followed by headache and inability to balance found in 5 and 4 patients, respectively (7% and 5.6%) (Table 1).

**Table 1.** Initial Presentations of Patients

| Initial Presentation | No. (%) |
|---|---|
| **Myalgia & weakness** | 56 (78.9) |
| **Headache** | 5 (7) |
| **Inability to balance** | 4 (5.6) |
| **Sensory symptoms** [a] | 3 (4.2) |
| **Cranial nerves** | 2 (2.8) |
| **Dysarthria** | 1 (1.4) |

[a] Sensory symptoms: paresthesia, hypoesthesia, anesthesia.

Moreover, 60 (84.5%) patients had a preceding upper respiratory infection, 14 (19.7%) had nausea and vomiting, and 7 (9.9%) had diarrhea (1 patient had bloody diarrhea) as their prodromal symptoms.

In assessing autonomic dysfunction throughout the disease, five patients had hypertension (7%), 5 had tachycardia (7%), 3 had bradycardia (4.2%), and 2 had hyperthermia (2.8%). Physical exams revealed 15 patients to have cranial nerve neuropathy (21.1%), and 50 cases (70.4%) had decreased deep tendon reflexes (DTR); none of the cases had meningismus signs.

Of those having cranial nerve neuropathy, eight patients had dysphagia (53%), 2 had ptosis (13%), two patients had diplopia (13%), one patient had strabismus (7%), one patient was unable to close their eyes (7%), and one patient had trouble speaking (7%).

Furthermore, 64 patients (90%) underwent electrodiagnostic studies in the first and second weeks of their admission, which in the first week resulted in 29 cases of demyelination disorder (45%), 12 cases of axonal disruption (19%), 1 case of axonal-demyelination disorder (2%), 1 case of Miller Fisher syndrome, and the rest 21 (32%) had no abnormality in their EMG. Follow-up in the second week resulted in 40 cases of demyelination disorder (62%), 12 cases of axonal disruption (19%), 1 case of axonal-demyelination disorder (2%), 1 case of Miller Fisher syndrome (2%) and the remaining 10 cases (15%) did not have an abnormal EMG after two weeks of admission (Table 2).

**Table 2.** Frequency of Electrophysiologic Subtypes of GBS [a]

| Subtype | No. (%) |
|---|---|
| **AIDP** | 40 (62) |
| **AMAN/AMSAN** | 12 (19) |
| **Normal** | 10 (15) |
| **Miller-Fisher syndrome** | 1 (2) |
| **Axonal involvement & demyelination** | 1 (2) |

[a] Results were obtained in the second week of admission.

For treatment, 67 patients (94.9%) received intravenous immunoglobulins (IVIG) for an average of 3.19 days (SD = 1.88 days), and five patients (7%) underwent plasmapheresis.

On average, patients were admitted for 8.7 days (SD = 9.58 days), ranging from 1 day up to 70 days.

Upon discharge, four patients (6%) had a complete recovery, and 67 patients (94%) had an incomplete recovery. Follow-up after 1 to 3 years, according to GBS Disability Scale (2), showed 53 (74.6%) cases of complete recovery in patients, while 18 patients (25.4%) did not recover completely. In those having residual symptoms according to GBS Disability Scale ($1 \leq$), 13 cases (72.2%) had limping, four patients experienced myalgia upon exertion or illness, and one patient (5.5%) had hand tremors. After a follow-up of 5 - 8 years, we could access 43 patients' information. 35(81.3%) patients had complete recovery, 6(14%) had minor symptoms, and 2(4.7%) needed support for walking. All patients' diagnosis was not changed during that time.

Analyses of two groups of complete vs. residual symptoms after three years were done with different variables. The patient's age did not show any significant correlation with full recovery (P-value = 0.68), nor did the patient's sex (P-value = 0.24). Also, none of the prodromal symptoms were strongly correlated with patients' recovery; whether autonomic dysfunction was present (hypertension, tachycardia, or bradycardia) had no significant impact on their recovery.

Cranial neuropathy or weak DTRs were seen in both groups, and there was no significant difference.

Regarding electromyographic results, there was a significant correlation between the axonal form of EMG and residual symptoms (P-value $< 0.05$).

Analyzing laboratory data between two groups of complete vs. residual symptoms yields no significant difference except for blood urea nitrogen, which upon correction by age and sex (by binary logistic regression), proves to be insignificant to the prognosis (P-value=0.06, OR=1.09 95% CI 0.99 - 1.020).

Of 71 patients, four did not receive IVIG due to lack of parental compliance or consent to treatment; regarding others, whether receiving IVIG alone or alongside plasmapheresis had no statistical significance on prognosis.

## 5. Discussion

While some studies present the male-to-female ratio to be greater than 1, we found an almost equal number of male and female patients (3, 13, 14), which is also suggested by others (4, 15).

We found muscle weakness to be the most common presenting symptom, which agrees with other studies (11, 16, 17).

In prodromal symptoms, most of our cases were preceded by upper respiratory infections (URIs), which is similarly reported by other studies (18, 19), while diarrhea is reported to be the most common preceding infection by van Koningsveld et al., in which URIs are the second most (2). Previously, during SARS-CoV-2 pandemic, we reported 37 patients of GBS, with SARS-CoV-2 infection clues in 18 (48.6%) patients of them (20). In the current study, the preceding URI was recorded in 84.5% of patients. It seems that SARS-CoV-2 infection increases the risk of GBS; however, the risk is probably lower than other viral infections.

Regarding autonomic dysfunctions, we found slightly fewer cases with autonomic abnormalities than some studies (11, 19), while others reported an even higher number of cases with such conditions (10, 17). Furthermore, studies found cardiac rhythm abnormalities as the most common autonomic dysfunction, which is in concordance with our data (10, 11, 17, 19).

As for cranial nerve involvement, some pediatric studies suggest similar involvement rates (13, 14, 19), though others, whether studying children or the general population, reported higher rates (2, 4, 10, 17, 18, 21).

Based on electrophysiologic studies in the second week of our patients' admittance, we confronted mostly demyelinating subtype (AIDP), which comprised 62% of our cases; though different results have been obtained, current data often denotes AIDP as the most common subtype presented. (4, 11, 14, 19, 22, 23). Differences in results are reflected similarly in adults and children alike, yet as Ashrafi et al. suggested, due to racial and ethnic differences, AIDP seems to comprise a higher percentage of cases in the European region than in Asia (17). Furthermore, as Jasti et al. proposed, different proportions of GBS subtypes may result from different antecedent infections (6).

In comparing the duration of hospital stay, our findings were similar to some studies (11, 17) yet differed from others which reported longer durations of hospitalization for their study groups (10, 19).

Unsurprisingly, the illness prognosis was favorable, and most of our cases (74.6%) completely recovered upon follow-up, and in agreement with Gonzalez-Suarez et al., we found the axonal involvement of GBS to predict poor prognosis (4).

Moreover, we could not find any reports of incomplete recovery from GBS with hand tremors as the main sequelae.

### 5.1. Conclusions

Our findings showed that although GBS ordinarily results in a complete recovery of sensory and motor symptoms, in some instances, poor prognoses are observed, and even permanent complications might ensue. Furthermore, while not being the most commonly presented form of GBS, axonal involvement in electrophysiologic tests can predict an unfavorable prognosis in GBS patients.

## Footnotes

**Authors' Contribution:** Study concept and design: Mohammadmehdi Nasehi, Elham Pourbakhtyaran, Acquisition of data: Zahra Khalili, Maryam Rahmannia, Zahra Ahmadi, Drafting of the manuscript: Pooria Ahmadi, Elham Pourbakhtyaran, Mahmoud Reza Zinatzadeh, Critical revision of the manuscript for important intellectual content and supervision: Mohammadmehdi Nasehi.

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