Original Article

Pediatric Guillain-Barré syndrome: Indicators for a severe course

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Abstract

Objectives: This study aims to retrospectively evaluate pediatric Guillain-Barré syndrome cases in a tertiary center in Istanbul, Turkey. **Materials and Methods:** The data of 40 patients with Guillain-Barré syndrome who had been admitted to the Department of Pediatrics at the Istanbul University Medical Faculty between 2005 and 2011 were collected. Mann-Whitney U, Kruskal-Wallis, chi-square, and Fisher's exact tests were used for statistical analysis. **Results:** Mean patient age was 5.4 ± 3.0 years; 20 out of 40 patients (50%) were female and 20 (50%) were male. Preceding infection was detected in 32 cases (80%). Six patients had speech impairment. Out of eight patients with respiratory distress (20%), five required respiratory support (12.5%) of which three of them had speech impairment as well. According to nerve conduction studies, 21 patients (52.5%) had acute inflammatory demyelinating polyradiculoneuropathy, 14 (35%) had acute motor axonal neuropathy, and five (12.5%) had acute motor-sensory axonal neuropathy. Thirty-three patients (82.5%) received intravenous immunglobulin, 3 (7.5%) underwent plasmapheresis and 4 (10%) received both. Time until recovery ($P = 0.022$) and time until aided ($P = 0.036$) and unaided ($P = 0.027$) walking were longer in patients with acute gastrointestinal infection than in those with upper respiratory tract infection ($P < 0.05$). Time until response to treatment ($P = 0.001$), time until aided ($P = 0.001$) and unaided ($P = 0.002$) walking, and time until complete recovery ($P = 0.002$) were longer in acute motor axonal neuropathy cases as compared to acute inflammatory demyelinating polyradiculoneuropathy cases. **Conclusion:** Recovery was longer with acute gastrointestinal infection and acute motor axonal neuropathy. Speech impairment could be a clinical clue for the need of mechanical ventilation.

Key Words

Guillain-Barré syndrome, intravenous immunoglobulin, mechanical ventilation, plasmapheresis

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Introduction

Guillain-Barré syndrome (GBS) is an inflammatory polyneuropathy characterized by rapidly progressing symmetrical muscle weakness and loss of deep-tendon reflexes (DTR). There are four main subtypes of GBS according to clinical and pathological features: Acute inflammatory demyelinating polyradiculoneuropathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor-sensory axonal neuropathy (AMSAN), and Miller Fisher syndrome (MFS).[1] Diagnosis is made based on medical history and physical examination as well as cerebrospinal fluid (CSF) analysis, magnetic resonance imaging (MRI), and nerve conduction studies.[2] GBS is treated with intravenous immunoglobulin (IVIG) and/or plasmapheresis.[1]

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Our aim was to evaluate clinical features, treatment schedules, and prognosis of our GBS patients' from a tertiary center with pediatric intensive care unit.

Materials and Methods

The study population comprised 40 patients (20 male, 20 female) who applied to the Division of Pediatric Neurology at the Children's Health and Diseases Department of the Istanbul University Medical Faculty between 2005 and 2011 and were diagnosed with GBS. The study received approval from the Istanbul University Medical Faculty ethics committee (20.04.2011/687-541).

We recorded patients' age and sex at diagnosis, complaints upon admission, physical examination findings, upper respiratory tract infections (URTI), and acute gastrointestinal infections (AGI) detected in the month prior to admission. We analyzed the findings of nerve conduction studies, spinal

cord MRI, CSF analysis, electrocardiography (ECG), and echocardiography (ECHO). The beginning, duration, and form of treatment, side effects, time until response to treatment, and complete recovery were evaluated.

Furthermore, the correlations between GBS subtypes and preceding infection, forms of treatment, and response to treatment were evaluated. In those cases where intensive care was required, it was noted whether the patient was put on respiratory support and if so, its duration and the duration of intensive care stay were noted. Duration of hospital stay, clinical course after treatment and time until recovery were retrospectively analyzed. For patients who had gait disturbance, time until they began walking aided and unaided during physical therapy was determined.

Statistical Package for Social Sciences (SPSS) for Windows 13.0 was used for statistical analysis of obtained data. The Mann-Whitney U and Kruskal-Wallis tests were used for group comparisons of non-normally distributed variables. For comparisons of qualitative data, chi-square and Fisher's exact tests were used. Confidence interval was set at 95% and a *P* value of <0.05 was considered statistically significant.

Results

Patient age and sex

Out of 40 patients diagnosed with GBS, 20 were female (50%) and 20 were male (50%). Mean age was 5.4 ± 3.0 years (median: 4.2 years, range: 1-12.5 years).

Complaints upon admission and clinical findings

At the time of admission, all patients had lower limb muscle weakness, gait disturbance, and decreased or absent DTR. There was sensory loss in nine (22.5%), speech impairment in six (15%), and respiratory distress in three patients (7.5%).

Vision impairment related to cranial nerve involvement was observed in two patients (5%), difficulty in swallowing in three (7.5%), bladder dysfunction related to autonomic failure in four (10%), and increased heart rate and high blood pressure in two (5%).

Infection

Review of patient histories showed infection preceding GBS in 32 patients (80%), 21 of whom (52.5%) had URTI, and 11 (27.5%) AGI. URTI was common in patients with the AIDP subtype while AGI was common in patients with AMAN, but the correlations were not statistically significant ($P > 0.05$).

Patients with AGI took significantly longer to recover and begin walking aided and unaided as compared to patients with URTI ($P < 0.05$) [Table 1].

Intensive care

Out of 40 patients, 15 (37.5%) required intensive care. On an average, patients were admitted to intensive care after 2.1 ± 1.8 days (median: 1.0 day, range: 1-7 days) and stayed there for 15.1 ± 18.8 days (median: 9.0 days, range: 2-75 days). Out of eight patients (20%) who had respiratory distress, five (12.5%) required ventilatory assistance. One patient who had AMAN (2.5%) underwent a tracheostomy. Out of six patients with speech impairment, three required respiratory support.

GBS subtypes

According to nerve conduction studies, 21 (52,5%) had AIDP, 14 (35%) had AMAN, and five (12.5%) had AMSAN. There was no significant difference in clinical features between patients with AIDP and AMAN ($P > 0.05$).

Table 1: Correlations between infection type and several variables

Variables	Statistics	GBS *n* = 40	URTI *n* = 21	AGI *n* = 11	No infection *n* = 8	*P*
Hospital stay (days)	Mean	15.1	13.4	16.1	18	>0.05
	SD	12.5	6.9	11	23.4	
	Median	11.0	10.0	16.0	11.0	
	IQR	7.8-16.3	7.0-17.5	10.0-17.0	11.0-14.8	
Recovery begins (days)	Mean	8.8	8.1	11.3	7.5	0.022
	SD	5.7	5.4	6.8	4.0	
	Median	7.0	7.0	8.0	6.5	
	IQR	6.0-10.0	5.0-8.5	7.0-13.0	4.3-10.0	
Walking aided (months)	Mean	2.1	1.7	3.1	1.4	0.036
	SD	1.7	1.7	1.8	0.7	
	Median	1.0	1.0	3.0	1.0	
	IQR	1.0-1.3	1.0-2.0	1.0-5.0	1.0-1.9	
Walking unaided (months)	Mean	3.7	3.1	5.8	2.4	0.027
	SD	2.9	2.8	3.0	0.8	
	Median	2.3	2.0	6.0	2.0	
	IQR	2.0-4.5	2.0-3.0	2.0-7.0	2.0-2.9	
Complete recovery (months) *n* = 33	Mean	7.4	7.6	8.6	5.6	>0.05
	SD	6.3	7.7	4.7	2.2	
	Median	6.0	6.0	7.0	6.0	
	IQR	4.0-8.0	4.0-7.0	5.0-13.0	4.0-8.0	

GBS = Guillain-Barré syndrome, URTI = Upper respiratory tract infection, AGI = Acute gastrointestinal infection, SD: Standard deviation, IQR: Interquartile range

Imaging and laboratory examination

CSF sampling was performed in 20 patients (50%). In seven cases (33%) there was albuminocytological dissociation that pointed to GBS. There were findings consistent with GBS in 26 out of 37 patients (70%) who underwent spinal-cord imaging.

Treatment

Out of 40 patients, 33 (82.5%) were treated with IVIG only (2 g/kg/day), three (7.5%) underwent plasmapheresis (50 ml/kg/day for 4-5 days), and four (10%) received both IVIG and plasmapheresis. All patients who required combination treatment had AMAN. No patient died. Beginning of treatment and time until response to treatment is given in Table 2. No patient died. No *P* value for form of treatment, treatment beginning time and response time could be calculated in patients who underwent plasmapheresis due to their low number.

Physical therapy

Complete recovery was made by 33 (82.5%) patients, while seven patients continued to have sequelae. Time until complete recovery was 7.4 ± 6.3 months (median: Six months, range: 2-36 months).

Due to the small number of patients with AMSAN, no statistical analysis of variables could be performed. In patients with AMAN, time until response to treatment, walking aided/unaided, and complete recovery was significantly longer as compared to AIDP ($P < 0.05$). When other variables were compared (time of GBS onset after infection, beginning of treatment, beginning and duration of intensive care, days of peak symptoms and findings, and duration of hospital stay), the *P* value was >0.05 [Table 3].

Discussion

History of infection that preceded GBS was 80% in our patients, 52% of whom had URTI while 28% had AGI. In their 2004 study of 95 pediatric and adult GBS patients, Rocha *et al.* found antecedent infection in 58 patients (61%), with URTI in 46 (48%), and AGI in 12 (13%)[3] A study by Cuadrado *et al*. reported antecedent infection in 62 out of 98 GBS patients (63%), with URTI in 43 (44%), and AGI in 10 (10%).[4] The relatively high prevalence of infection, particularly AGI, in our study can be attributed to the abundance of rural areas in our country where hygiene conditions are poor and fecal-oral transmission rates are high.

Table 2: Beginning of treatment and time until response to treatment

Feature	*n*	%	Treatment is started (day) Mean ± SD/ median	Response to treatment (day) Mean ± SD/ median
IVIG	33	82.5	1.5±0.8/1.0	6.9±4.8/6.0
Plasmapheresis	3	7.5	2.7±2.1/2.0	5.3±1.2/6.0
IVIG + plasmapheresis	4	10	1.3±0.5/1.0	15.3±10.2/12.0
Total	40	100	1.6±0.9/1.0	7.6±5.8/6.0

SD = Standard deviation, IVIG = Intravenous immunoglobulin

Table 3: Evaluation of GBS subtypes and several variables

Variables	Statistics	AMAN *n* = 14	AIDP *n* = 21	*P*
Gap between URTI and onset of GBS (days)	Mean	12.2	13.7	>0.05
	SD	10.0	5.7	
	Median	7.0	14.0	
	IQR	7.0-20.0	10-14.5	
Gap between AGI and onset of GBS (days)	Mean	15.6	7.6	>0.05
	SD	10.2	5.1	
	Median	10.0	7.0	
	IQR	7.0-30.0	3.5-12.0	
Respiratory distress begins (day)	Mean	2.3	3.8	–
	SD	1.5	2.4	
	Median	2.0	4.0	
	IQR	1.0-4.0	1.5-6.0	
Intubation (days)	Mean	3.0	3.5	–
	SD	1.0	2.1	
	Median	3.0	3.5	
	IQR	2.0-4.0	2.0-5.0	
Intubation duration (days)	Mean	30.5	6.5	–
	SD	20.5	0.8	
	Median	30.0	6.5	
	IQR	10.0-51.0	6.0-7.0	
Intensive care starts (day)	Mean	1.5	2.4	>0.05
	SD	0.8	2.2	
	Median	1.0	1.0	
	IQR	1.0-2.3	1.0-4.0	
Intensive care duration (days)	Mean	18.8	5.4	>0.05
	SD	26	6.0	
	Median	9.5	4.0	
	IQR	1.0-32.8	0-9.8	
Symptom peak (days)	Mean	2.1	2.3	>0.05
	SD	1.6	1.8	
	Median	1.0	1.5	
	IQR	1.0-3.3	1.0-3.0	
Hospital stay (days)	Mean	22.1	11.4	>0.05
	SD	18.3	5.7	
	Median	16.5	10.0	
	IQR	10.0-25.5	7.0-14.0	
Treatment is started (days)	Mean	1.5	1.5	>0.05
	SD	0.7	1.0	
	Median	1.0	1.0	
	IQR	1.0-2.0	1.0-2.0	
Response to treatment is observed (days)	Mean	11.5	5.3	0.001
	SD	8.4	1.7	
	Median	9.5	5.0	
	IQR	5.8-12.5	4.0-6.0	
Walking aided (months)	Mean	3.2	1.5	0.001
	SD	1.8	1.4	
	Median	3.0	1.0	
	IQR	2.0-4.3	1.0-1.5	
Walking unaided (month)	Mean	5.9	2.7	0.002
	SD	3.2	2.2	
	Median	6.0	2.0	
	IQR	3.0-7.8	1.6-2.9	
Complete recovery (months)	Mean	10.1	4.7	0.002
	SD	4.8	1.8	
	Median	9.0	4.5	
	IQR	6.5-14.0	3.0-6.0	

GBS = Guillain-Barré syndrome, AMAN = Acute motor axonal polyradiculoneuropathy, AIDP = Acute inflammatory demyelinating polyneuropathy, URTI = Upper respiratory tract infection; AGI = Acute gastrointestinal infection, SD = Standard deviation, IQR = Interquartile range

Cranial nerve involvement was observed in eight of our patients (20%), while autonomic involvement was observed in six (15%). In a study of 35 patients by Hicks *et al*., 16 (46%) had cranial nerve involvement and 16 (46%) had autonomic involvement.[5] A study in which detailed tests were performed to determine autonomic involvement reported a rate as high as 67%.[6] This result may point to clinically insignificant high-rate autonomic involvement. The presence of cranial nerve involvement is linked to increased disability, while autonomic involvement is linked to increased need for respiratory support.[7,8] Although autonomic involvement can be linked to an increased mortality rate in adult patients,[9] it rarely poses a threat in children. However, as it is an important indicator of the course of the disease, measures must be taken to ensure that it is clinically recognized.

GBS subtypes are determined based on clinical and laboratory features. As compared to western countries, AMAN is more common in the Far East[10] as a latest study from Northern India reported.[11] In our study, AIDP is more prevalent. In a German study by Korinthenberg *et al*., out of 69 GBS cases 48% had AIDP, 11% had AMAN, and 26% had both axonal and demyelinating involvement.[7] A study of 36 GBS patients from Turkey reported AIDP in 69%, AMAN in 28%, and AMSAN in 2.8%.[12] The results we obtained were closer to those reported in western countries.

Pediatric GBS patients require respiratory support in 15-20% of cases.[1] Similar to literature, five of our patients (12.5%) had to be put on respiratory support. Three of them had speech impairment. Bulbar involvement-related palate dysfunction can lead to speech impairment and severe respiratory distress. It has been demonstrated that the need for respiratory support can be foreseen in GBS if there is bulbar involvement and vital capacity of < 20 ml/kg.[8] This confirms that clinical findings are very important in predicting the course of the disease. Among those of our patients who required respiratory support, three had AMAN (7.5%) and two had AIDP (5%). In a study of 56 pediatric patients by Lee *et al*., out of eight patients (14%) on respiratory support, two had AMAN (4%), five had AIDP (9%), and one had AMSAN.[13] In a study by Paradiso *et al*., out of eight patients (13%) who required respiratory support, five had AMAN (8%), and three had AIDP (5%).[14]

In a multicenter study of 150 pediatric and adult patients by Van Der Meche *et al*.,[15] IVIG, plasmapheresis, and their combination were compared and found to be equally effective. In another multicenter study with 383 adult patients,[16] 121 underwent plasmapheresis, 130 — IVIG, and 128 — combination treatment, with similar recovery and sequelae rates in all three groups. In our study, no *P* value for form of treatment, treatment beginning time, and response time could be calculated due to the low number of patients with plasmapheresis.

Patients who received both IVIG and plasmapheresis took much longer to respond to treatment than the rest of the patients, although statistical significance could not be assessed due to the small number of cases. We attribute this need for combination treatment to the fact that these patients had the AMAN subtype of GBS with a poor clinical course.

In our study, it took patients with axonal involvement significantly longer to begin walking aided/unaided and recover completely as compared to those with AIDP. In a study of 23 children with GBS by Tekgül *et al*., recovery was slower in the AMAN group than in the AIDP group but only during the first 12 months, after which the recovery rates evened out.[17] Ogawara *et al*., has reported the correlation between diarrhea secondary to *Campylobacter jejuni* and the GBS subtype AMAN.[18] The fact that those of our patients with history of AGI took significantly longer to recover and begin walking aided/unaided can be attributed to them having the AMAN subtype.

The main limitation of our study was its retrospective nature, due to which we were unable to compare the long-term functional status of our patients. Due to the low number of patients who underwent plasmapheresis, we could not compare them to those who received IVIG.

In conclusion, patients with the AMAN subtype of GBS and AGI take longer to recover than those with the AIDP subtype. According to our findings, speech impairment can be seen as a risk factor for respiratory failure. The presence of speech impairment and the subtypes of GBS were found to be the most important indicators of the clinical course of the disease.

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