Demographics, Clinical Features, Outcome and Prognostic Factors of Guillain-Barre Syndrome in Thai Children

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Objective: *To describe demographics, clinical profiles, management, outcomes and to determine factors associated with severity in Guillain-Barre Syndrome (GBS).*
Material and Method: *Medical records of GBS patients in Queen Sirikit National Institute of Child Health during 2000-2009 were searched. The data included demographics, clinical features, management and outcomes after 6 months to determine prognostic factors.*
Results: *Forty-eight patients with GBS were studies. Mean age of onset was 5 years. Male and female ratio was 1.4:1. History of antecedent infection was 73 %. Clinical presentations included limb weakness 100%, respiratory distress 27%, facial palsy 27%, autonomic nervous dysfunction 22% and ataxia 17%. Nerve conduction study revealed demyelinating process in 57%, axonopathy in 26% and mixed type in 17%. Clinical outcomes were satisfactory in most of the patients except three patients who still had disability eighteen months after onset. Autonomic nervous dysfunction was a significant factor to determine the severity.*
Conclusion: *The demographic and clinical features of GBS were similar to other published studies. The autonomic nervous dysfunction was a significant predictor for adverse clinical course. All but three patients had complete, full recovery.*

Keywords: *GBS, Prognostic factors, Outcome*

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Guillain-Barre Syndrome (GBS) is an acquired immune-mediated polyneuropathy, with typical findings of rapidly progressive symmetrical weakness of limbs, decreased/absent deep tendon reflex (DTR) and albuminocytological dissociation of CSF. Currently it is known as the most frequent cause of acute flaccid paralysis in the pediatric population[1]. Several subtypes of GBS have been defined by clinical manifestations and nerve conduction studies[2,3]. It is unresolved whether the natural history of GBS in children is more variable and benign than in adult[4,5]. Although several studies of childhood GBS have been reported from different countries there have been only a few reports from Thailand[6-9]. Therefore, the purposes of this study were to describe demographics, clinical characteristics, treatment intervention, potential prognostic factors, and long-term outcomes of GBS in Thai children.

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Material and Method

The authors reviewed the medical records of the patients in QSNICH who had been diagnosed as GBS or acute inflammatory demyelinating polyradiculoneuropathy (AIDP) over a 10-year period between January 2000 and December 2009. The inclusion criteria included: 1) age between 1-16 years, 2) acute symmetrical motor weakness of extremities with maximum weakness within 4 weeks, 3) decreased or absence deep tendon reflexes, 4) cerebrospinal fluid albuminocytological dissociation or acquired neuropathy detected from nerve conduction studies and 5) follow-up for longer than 6 months.

The patients' medical records were reviewed for demographic data, clinical characteristics, cerebrospinal fluid profiles, nerve conduction studies, treatment interventions, condition at discharge, potential prognostic factors and long-term outcomes.

The severity of weakness was assessed using Hughes' disability scale. The SPSS program was used as an analysis tool. The Fisher exact and Chi-square test were used to determine the association between potential prognostic factors and outcomes.

Results

Sixty-two patients were diagnosed with GBS during the present study period of which forty-eight patients fulfilled with the inclusion criteria. Male to female ratio was 1.4:1. The mean age of onset was 5 years with a range of 1.3-12.6 years. The age of onset was less than 12 years in 96% of patients. Seventy-three percent of patients had antecedent infection including: respiratory tract 60.8%, gastrointestinal tract 8.7%, and skin infection 2.1%. There was no preceding vaccination history in any patients.

Sixty-one percent of patients had weakness of extremities as the initial symptom, the others were pain or paresthesia in 28% and respiratory distress in 11%.

During hospital admission, all patients had limb weakness, 28.3% had respiratory distress or failure, 28.3% had facial muscle weakness and 21.7% had autonomic nervous dysfunction, e.g. changes in blood pressure, bladder dysfunction and 17.4% had ataxia (Table 1).

At nadir of the disease, the severity of weaknesses, classified by Hughes' functional disability scale, is shown in Table 2. Forty-seven patients (98%) were unable to walk independently. No child could live independently: of these, 52% ambulated with support, 31% were confined to the bed and 13% required assisted ventilation (Table 2).

Thirty patients received 2 gram/kg intravenous immunoglobulin (IVIG) over 2-5 days. All of these patients had been diagnosed with grade 3, 4 and 5 disability before IVIG treatment. After IVIG, 26 patient improved; the disability grade decreasing by at least 1; however, there were four patients in disability grade 3, 4, who showed no change. Eighteen patients did not receive IVIG (two patients in disability grade 2 and 4 and the rest in disability grade 3). Of this group, fourteen patients showed improvement at discharge decreasing the disability grade by at least 1, except for three patients in grade 3 who had no change (Table 3).

The average disability score at nadir of disease was 3.54 while at discharge it was 2.46. Patients treated with IVIG had an average improvement in these disability scores of 1.27, while those without IVIG treatment had an average improvement of 0.84.

Table 1. The demographics, clinical features, cerebrospinal fluid profile and nerve conduction study result

Characteristics	Number (%)
Sex	
Male	28 (58.33)
Female	20 (41.67)
Age onset (years)	
<3	19 (39.6)
3-6	11 (22.9)
>6-9	11 (22.9)
>9-12	5 (10.4)
>12	2 (4.1)
Antecedent infection (73%)	35 (72.9)
Respiratory tract	30 (62.5)
Gastrointestinal tract	4 (8.3)
Skin	1 (2.1)
Duration weakness before diagnosis (day)	
1-7	32 (66.7)
8-14	12 (25)
15-21	4 (8.3)
Initial symptoms	
Limb weakness	30 (62.5)
Pain	13 (27.1)
Respiratory distress	5 (10.4)
Clinical features	
Extremity weakness	48 (100)
Respiratory symptom/failure	13 (27.1)
Facial palsy	13 (27.1)
Autonomic involvement	10 (20.1)
Ataxia	8 (16.7)
Ophthalmoplegia	2 (4.2)
CSF WBC (46)	
0-5	36 (78.3)
6-50	10 (11.7)
>50	0
Asthma	
CSF Protein (46)	
<45	7 (15.2)
45-120	19 (41.3)
>120-300	17 (37)
>300-800	3 (6.5)
NCS result (35)	
Demyelination	20 (57.2)
Axonopathy	9 (25.7)
Mixed	6 (17.1)

NCS = nerve conduction study; CSF = cerebrospinal fluid; WBC = white blood cell

Ten patients, however, did not show any improvement in the disability grading: six patients were in disability grade 3 in non-IVIG treatment group, three patients in disability grade 4 and one patient in disability

Table 2. Compare Hughes's disability scale on admission and discharge date

Disabilities grade	Function	Admission with nadir of weakness (n)	%	Discharge (n)	%
0	Healthy	0	0	0	0
1	Minor symptom or sign, able to run	0	0	8	16.7
2	Able to walk 5 m independently	1	2.1	16	33.3
3	Able to walk 5 m with a walker or support	26	54.2	18	37.5
4	Bed or chair bound	15	31.2	6	12.5
5	Require assisted ventilation	6	12.5	0	0
6	Death	0	0	0	0

Table 3. Comparison of the disability grade at nadir of disease and at discharge, with or without received IVIG

Received IVIG (n)	Disability Severity	
	At admission (n)	At discharge (n)
No (18)	Grade 2 (1)	Grade 1 (1)
	Grade 3 (16)	Grade 1 (3)
		Grade 2 (7)
		Grade 3 (6)
	Grade 4 (1)	Grade 3 (1)
Yes (30)	Grade 3 (10)	Grade 1 (4)
		Grade 2 (5)
	Grade 3 (1)	
	Grade 4 (14)	Grade 2 (4)
		Grade 3 (7)
		Grade 4 (3)
	Grade 5 (6)	Grade 3 (3)
		Grade 4 (3)

grade 3 in the IVIG treatment group.

Throughout the hospitalization, six patients needed artificial ventilation due to respiratory failure from pneumonia and one patient had urinary tract infection.

The autonomic nervous dysfunction was the only factor that was associated with the severity of diseases. There were no statistically significant associations with gender, age of onset, antecedent infection, duration of weakness before diagnosis, initial symptoms, presence of facial muscle weakness, ataxia, ophthalmoplegia, CSF white blood cell, CSF protein and nerve conduction study result (Table 4).

In comparison with the possible factors associated with the improvement of disability grading, there was no statistical significance in gender, age of onset, duration weakness before diagnosis, antecedent infection, initial symptoms, presence of facial muscle weakness, ataxia, ophthalmoplegia, autonomic nervous system involvement, respiratory involvement, CSF white blood cells, CSF protein or nerve conduction study result, and were treated with IVIG (Table 5).

At six, twelve and eighteen months follow-up after discharge, 79.16%, 91.67% and 93.75%, of patients respectively could ambulate without support. Three patients could not ambulate independently even at 2.5 years after treatment.

Discussion

This report is similar to a previous report by predominantly in male. This is similar to Visudtibhan A[8] on Thai children in 1998, which showed onset less than 6 years and male predominance. This is different from that of Caitlin WH[6] on American children whose age at onset was greater than 13 years with female predominance. This discrepancy may be due to the

Table 4. Possible prognostic factors associated with severity

Characteristics	Severity (Hughes' disability grade)				*p*-value
	2	3	4	5	
Sex					0.25
Male	1	14	11	2	
Female	0	12	4	4	
Age onset (years)					0.84
<6	1	14	1	4	
6-12	0	10	4	2	
>12	0	2	0	0	
Antecedent infection (73%)					0.97
No	0	8	4	1	
Respiratory tract	1	15	10	4	
Gastrointestinal tract	0	2	1	1	
Skin	0	1	0	0	
Duration weakness before diagnosis (day)					0.22
1-7	1	15	13	4	
>7	0	11	2	2	
Initial symptoms					0.60
Limb weakness	1	16	8	5	
Pain	0	8	5	0	
Respiratory distress	0	2	2	1	
Clinical features					
Facial palsy	1	5	3	3	0.14
Autonomic involvement	0	2	4	4	0.01
Ataxia	0	6	2	0	0.70
Ophthalmoplegia	0	1	1	1	0.41
CSF WBC (46)					0.24
0-5	0	19	13	4	
>5-50	1	5	2	2	
CSF Protein (46)					1.0
0-45	0	4	2	1	
>45-120	1	19	13	4	
NCS result (35)					0.31
Demyelination	1	8	7	3	
Axonal	0	7	0	2	
Mixed	0	4	3	0	

racial differences or the etiology of GBS. There are reports of GBS subtype differences according to geographic distribution. Demyelinating GBS with presence of anti-GM1 antibodies accounts for up to 90% in Europe-North America whereas axonal GBS with anti-GD1a antibodies account for 30-65% in China and Japan[2,10]. Nerve conduction study between ten and twenty days after onset of 35 patients in the present study revealed demyelination 57%, axonopathy 26% and mixed type 17%. This finding implies the axonal GBS 26-43%. This supports the difference in racial strain and etiological organism or antigens that can induce different immune antibodies.

Antecedent infection seen in 73% included respiratory tract infection and gastrointestinal tract infection. This is similar to the other studies. However, we were unable to demonstrate organisms or antibodies regarding *Campylobactor jejuni*, Mycoplasma pneumonia, cytomegalovirus, influenza or Epstein-Barr virus[11-14].

Forty-three patients (89.6%) had initial symptoms of weakness or pain or paresthesia; five (10.4%) complained of respiratory distress as an initial symptom. This is different from Masucci E[15] who reported that the initial symptoms were weakness with or without sensory symptom in 72% and sensory

Table 5. Possible prognostic factors associated with improved disability score

Clinical	Improved disability score		*p*-value
	No (10)	Yes (38)	
Sex			0.17
Male	4	14	
Female	6	24	
Age at onset (years)			0.28
<6	7	23	
6-12	2	14	
>12	1	1	
Duration weakness before diagnosis (days)			0.15
≥7	5	28	
>7	5	10	
Antecedent infection			0.8
No	3	10	
Respiratory tract	7	23	
Gastrointestinal tract	0	4	
Skin	0	1	
Initial symptoms			0.26
Weakness	7	23	
Pain	1	12	
Respiratory dysfunction	2	3	
Facial weakness	2	10	0.52
ANS involvement	2	8	0.69
Ataxia	1	7	0.46
Ophthalmoplegia	0	3	0.49
Respiratory involvement	4	9	0.43
CSF protein (mg%)			0.53
0-45	2	6	
>45	7	30	
WBC in CSF (cell)			0.36
0-5	8	28	
5-50	1	9	
NCV result			0.15
Demyelination	3	16	
Axonopathy	2	7	
Mixed	3	4	
Received IVIG			0.15
Yes	4	26	
No	6	12	

symptoms alone 28%. No respiratory distress was reported. This discrepancy may be due to more than 50% of one patient population being younger than 6 years of age who may not have been able to describe symptoms of weakness or sensory disturbance.

All the patients in the present study had limb weakness, mostly symmetrical, proximal, predominantly lower extremity in 98% were classified by Hughes's functional disability grade as 3, 4 and 5, which meant that the patients could not ambulate without support. Six patients (12.5%) had respiratory failure and needed artificial ventilation. The present study supports the need for GBS patients to receive emergency treatment with careful monitoring[16]. At least 10% of cases can be fatal as a result of respiratory failure, cardiac arrhythmia, dysautonomia and pulmonary embolism. Fortunately, no patient died in the present study.

The presenting symptoms of the present study are in accordance with other reports[17,18]. Extremity weaknesses, pain or paresthesia were the

most common. Cranial nerves involvement e.g. bilateral facial palsy, ophthalmoplegia, ataxia, autonomic nervous dysfunction and respiratory involvement have been frequently reported.

Albuminocytological dissociation was present in 39 of 46 patients (84.8%) at the first day of admission. Lumbar puncture was repeated in patients who had absence of typical finding CSF at the end of the second week after onset. Eventually 42 patients (91.3%) demonstrated albuminocytological dissociation. This finding revealed the importance of a CSF profile in supporting the diagnosis of GBS. All patients with suspected GBS should have a CSF examination.

Seventy percent patients who could not ambulate before treatment improved and were able to ambulate after treatment with IVIG. Patients received IVIG had greater improvement in their average disability score than the patients without IVIG, but it was not statistically significant.

There have been previous reports of poor prognostic factors on GBS such as advanced age, duration of onset of maximum weakness less than 7 days, bulbar dysfunction, axonal involvement, Clostridium jejuni infection, cytomegalovirus infection and anti GM1 antibodies. Testing for antibodies to Clostidium, cytomegalovirus and GM1 antibodies was not performed in the present study. Only the autonomic involvement was prognosticated for disease severity, but not the outcome at discharge from hospital. However, the overall prognosis in this series was good, without any mortality. Approximately 94% had good functional recovery 18 months after the onset of illness. However, three patients were still unable to ambulate after 2.5 years.

Conclusion

The present study shows the clinical presentation to be similar to other reports except for a younger age group at the onset of illness. Autonomic nervous dysfunction is a prognostic factor for the severity of disease. However, the overall prognosis is good, without any mortality. Most of the patients had complete functional recovery 18 month after the onset of illness.

Potential conflicts of interest

None.

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ระบาดวิทยา อาการทางคลินิก ผลการรักษาและปัจจัยพยากรณ์โรคของ Guillian Barre Syndrome ในเด็กไทย

สมจิต ศรีอุดมขจร, ศิโรรัตน์ สุวรรณโชติ

วัตถุประสงค์: *เพื่อศึกษาการศึกษาระบาดวิทยา, ผลการรักษา, ภาวะแทรกซ้อนและค้นหาปัจจัยเสี่ยงของโรคกลุ่มอาการ Guillain-Barre (GBS) ในผู้ป่วยเด็กของสถาบันสุขภาพเด็กแห่งชาติมหาราชินี*

วัสดุและวิธีการ: *รวบรวมข้อมูลผู้ป่วยกลุ่มอาการ GBS ที่รับการรักษาที่สถาบันสุขภาพเด็กแห่งชาติมหาราชินี ระหว่างปี พ.ศ. 2543 ถึง พ.ศ. 2552 รวบรวมอาการทางคลินิก การรักษา ผลการรักษาทั้งระยะที่อยู่ในโรงพยาบาลและ 6 เดือนต่อมา*

ผลการศึกษา: *พบผู้ป่วย GBS จำนวน 48 ราย เป็นชาย 28 ราย หญิง 20 ราย อายุเฉลี่ย 5 ปี ประวัติการติดเชื้อที่นำมาก่อนร้อยละ 73 อาการและอาการแสดงได้แก่ อาการอ่อนแรงขาร้อยละ 100 ระบบหายใจอ่อนร้อยละ 27 อาการกล้ามเนื้อหน้าอ่อนแรงร้อยละ 27 อาการทางระบบประสาทอัตโนมัติร้อยละ 20 อาการเดินเซร้อยละ 17 ผลการตรวจทางประสาทสรีรวิทยาพบ demyelination คิดเป็นร้อยละ 57 axonopathy คิดเป็นร้อยละ 26 และแบบ mixed คิดเป็นร้อยละ 17 ผลของการรักษาทางคลินิกอยู่ในระดับเป็นที่น่าพอใจในผู้ป่วยส่วนใหญ่ มีเพียง 3 ราย ที่อาการอ่อนแรงไม่กลับมาเป็นปกติเมื่อติดตามที่ 18 เดือน หลังเริ่มมีอาการอ่อนแรง ปัจจัยการทำนายโรคที่สำคัญ ที่บ่งว่าโรคมีความรุนแรง ได้แก่ อาการแสดงทางระบบประสาทอัตโนมัติ*

สรุป: *จากการศึกษานี้พบว่าผู้ป่วย GBS มีลักษณะระบาดวิทยาและคลินิกไม่ต่างจากการศึกษาอื่น ยกเว้นอายุ ผู้ป่วยที่น้อยกว่าความผิดปกติของระบบประสาทอัตโนมัติมีความสัมพันธ์กับความรุนแรงของโรคติดตามผู้ป่วย ไปอย่างน้อย 6 เดือนพบพยากรณ์โรคดี ไม่มีการเสียชีวิตและอาการดีขึ้นจนปกติเกือบทุกราย*