

Outcome of Guillain - Barré Syndrome in Children: A prospective cohort study in a tertiary hospital in Upper Egypt

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Abstract

Introduction: Guillain-Barré syndrome is the most common cause of acute flaccid paralysis in children, and defined as an acute inflammatory polyneuropathy. The objective of this study was to assess the clinico-laboratory profile, and outcome of Guillain-Barré syndrome in children at Sohag University Hospital.

Methods: This prospective cohort observational study was conducted in 2014-2015. The included children were subjected to through medical history and detailed systemic and neurological examination. Nerve conduction studies and cerebrospinal fluid analysis were done for all patients. Follow up was done at three and six months both clinically and by nerve conduction studies.

Results: This study included 50 patients (27 males / 23 females) with median age of 2.92 years. Upper respiratory tract infections were the most common antecedent infections (50%) and the neurological findings were weakness of both lower limbs and pain in all patients (100%) followed by sphincteric dysfunction (26%) while cranial neuropathies were found in 4%. Nerve conduction study revealed that acute inflammatory demyelinating polyradiculoneuropathy was found in 52% of cases, acute motor axonal neuropathy in 36% of cases, whereas acute motor-sensory axonal neuropathy was found in 6% of cases. The outcome was good in about 78% of cases, Hughes motor scale revealed that 58% were healthy, 18% had minor signs or symptoms, 12% walked without support, 6% walked with support, and 6% were bed ridden.

Conclusion: The outcome was favorable, although a minority of patients suffered neurological deficit. Immediate administration of intravenous immunoglobulin reduced mortality and disability.

Keywords: Guillain-Barré syndrome (GBS); Nerve conduction study; Intravenous immunoglobulin (IVIg)

1. Introduction

Guillain-Barré syndrome (GBS) is the most common cause of acute flaccid paralysis in children, and defined as an acute inflammatory polyneuropathy characterized by rapidly progressive, essentially symmetric weakness and areflexia in a previously otherwise healthy child (1, 2). The incidence of GBS has been estimated to be between 0.34 and 1.34/100 000. GBS in children and adolescents is a disease affecting mainly the younger age groups (3). It is associated with a mortality rate of 5–15% and approximately 30% of the patients require mechanical ventilation some time during their illness (4, 5). The diagnosis of GBS is based primarily on the clinical evaluation and the exclusion of important possible alternative diagnoses. Classically in GBS the weakness starts in the lower limbs then follows an ascending course over hours or days (6). Supportive investigations include CSF examination, and nerve conduction studies (NCS). Both intravenous immunoglobulins (IVIg) and plasma exchange have been the first-line therapy for GBS patients (7). About 5 to 10% of GBS patients deteriorate after initial improvement or stabilization following IVIg treatment, a condition named “treatment-related clinical fluctuation” (8, 9). Pediatric GBS is

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generally associated with a shorter illness and more complete recovery than is typical in adults (10-12). Studies in Upper Egypt about GBS are few, so the objectives of this study were analysis of the clinical and laboratory findings, in addition to evaluating the outcome of 50 children having GBS at Sohag University Hospital.

2. Material and Methods

2.1. Study design

This was a prospective cohort observational study carried out for a period of one year (from the 1st of October 2014 to the end of September 2015) at the Pediatric department, Sohag University Hospital, Sohag, Upper Egypt.

2.2. Selection criteria

2.2.1. Inclusion criteria

All infants and children presented with acute flaccid paralysis and suspected to have GBS were included.

2.2.2. Exclusion criteria

Children with other causes of acute flaccid paralysis, such as transverse myelitis, hypokalemic paralysis. Also central nervous system infections were excluded from the study depending on absence of any encephalopathy or CSF characteristics.

2.3. Ethical consideration

The protocol of the study was approved by the Research Ethics Committee at Sohag Faculty of Medicine. Informed consent was obtained from parents of all enrolled subjects. The work has been carried out in accordance with The Code of Ethics of The World Medical Association (Declaration of Helsinki) for experiments on humans.

2.4. Data collection methods

Diagnosis of GBS was made clinically by a pediatrician and a pediatric neurologist based on the history given by the parents, and observation of clinical data. Patients with clinical diagnosis of GBS were subjected to the following; thorough clinical history, full clinical examination with detailed neurological examination focusing on (the conscious level, cranial nerves, reflexes, muscle tone, muscle power, motor and sensory system). The following investigations were done for all patients; cerebrospinal fluid analysis (CSF), electrophysiological studies, and magnetic resonance imaging of the dorsolumbar spine to exclude spinal lesions and transverse myelitis. Electrophysiological studies were done using Neurosoft Mod: Neuro-EMG MI CRO-Russian during one to two weeks after initiation of symptoms. Motor nerve conduction study conducted by stimulating the common peroneal nerve (CPN), posterior tibial nerve (PTN), median and ulnar nerves to assess compound muscle action potentials (CMAPs), which include onset latency, amplitude and conduction velocity. Sensory nerve conduction study was done to estimate sural, median and ulnar sensory nerve action potentials (SNAPs). F wave latency was also defined. The electrophysiological diagnosis of GBS was based upon the criteria suggested by many researchers (13-15). According to nerve conduction study (NCS), the patients were classified into acute inflammatory demyelinating polyradiculoneuropathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor-sensory axonal neuropathy (AMSAN), and normal nerve conduction study (13-15). All patients received intravenous immunoglobulin 400 mg/kg/day for five days (16). Outcome at 3 and 6 months was assessed both clinically (by detailed neurological examination), and by electrophysiology. Evaluation of motor disability was done using Medical Research Council (MRC) scale and Hughes motor scale (HMS) (17).

2.5. Statistical analysis

The data was subjected to statistical analysis and tabulation using SPSS version 18 (SPSS Inc., Chicago, Illinois, USA). P-value is considered significant if less than 0.05 then the results were presented to fulfill the objectives of the study.

3. Results

The study included 50 patients with median age of 2.92 years (range from 7 months to 11 years). Out of them 27 (54%) were males and 23 (46%) were females with male to female ratio 1.1:1. Twenty-three cases (46%) came from urban areas while 27 (54%) cases from rural areas, and urban to rural ratio was 1:1.1. Antecedent infections were found in 33 patients (66%), of them, 25 (76%) had upper respiratory tract infection, gastroenteritis was present in seven patients (21%) while urinary tract infection was present in only one patient (3%) (Table 1). Concerning clinical presentations of the patients; weakness of both lower limbs and pain were the main complaints in almost all patients. Both urinary and stool incontinence were present in 26% of patients (Table 1). Initially, cranial nerve examination was abnormal in two cases (4%) while at 6 months follow up only one case had abnormal cranial nerve

examination. Hypotonia was initially present in all patients, at 3 months interval about 98% of patients were hypotonic whereas at 6 months interval about 96% of patients were hypotonic (Table 2).

Table 1 Socio-demographic characteristic of studied population

Variables		Summary statistics	
Age (year)	Mean (SD)	3.07 (1.97)	
	Median (range)	2.92 (0.58-11)	
Sex; n (%)	Females	23 (46.00)	
	Males	27 (54.00)	
Residence; n (%)	Urban	23 (46.00)	
	Rural	27 (54.00)	
Antecedent infections (In 33 patients only)	Gastroenteritis	n (%)	7 (21.00)
		Mean duration (SD)	4.14 (3.53)
	Respiratory infections; n (%)	25 (76.00)	
	Urinary tract infection; n (%)	1 (3.00)	
Weakness of lower limb	Acute onset; n (%)	2 (4.00)	
	Gradual onset; n (%)	48 (96.00)	
Pain (Acute Onset); n (%)		50 (100)	
Autonomic dysfunction (Urine and stool incontinence); n (%)		13 (26.00)	
Nerve conduction study; n (%)	AIDP	26 (52.00)	
	AMAN	18 (36.00)	
	AMSAN	3 (6.00)	
	Normal	3 (6.00)	

Table 2. Examination of the nervous system in the studied population

Variables	Initial; n (%)	At 3 months; n (%)	At 6 months; n (%)	p-value
Cranial neuropathy	2 (4.00)	2 (4.00)	1 (2.00)	0.81
Muscle bulk (Normal)	50 (100.000)	50 (100.000)	50 (100.000)	1.00
Fasciculations or involuntary movements	1 (2.00)	1 (2.00)	0	0.60
Hypotonia	50 (100.00)	49 (98.00)	48 (96.00)	0.36
Muscle power	2/5	2 (4.00)	1 (2.00)	<0.0001
	3/5	41 (82.00)	39 (78.00)	
	4/5	7 (14.00)	9 (18.00)	
	Normal	0	1 (2.00)	
Impaired coordination	50 (100.00)	50 (100.00)	50 (100.00)	1.00

We found significant improvement of superficial reflexes (abdominal, anal, cremasteric, and planter reflexes) on follow up. Also significant improvement in muscle stretch reflexes of lower limbs (knee, Achilles reflexes) was noted (Table 3). Regarding CSF analysis, the mean white blood count (WBCs)/mm³ was 1.8 (1.91), while mean CSF protein (mg/dl) was 76.86 (27.68), furthermore the mean CSF glucose was 45.89 (16.43). Electrophysiological study revealed the following subtypes of GBS; acute inflammatory demyelinating polyradiculoneuropathy (AIDP) in 52% of cases, acute motor axonal neuropathy (AMAN) in 36%, acute motor-sensory axonal polyneuropathy (AMSAN) in 6% of cases and 6% of cases had normal NCS study. At 6 months, 2% were AIDP and 98 % had normal NCS (Table 1). Regarding clinical presentations of different subtypes of GBS, weakness of lower limbs was present in all patients. However, autonomic dysfunction including sphincteric problems was found in 23.08% of AIDP cases, 16.67% of AMAN cases, 66.67% of AMSAN cases and in 66.67% of cases with normal electrophysiological study (Table 4). Cranial nerve examination was abnormal in 3.85% of AIDP cases and 5.56% of AMAN cases. However it was normal in all AMSAN cases and all cases with normal NCS (Table 5). All patients treated with IVIg with a mean period between disease onset and treatment was 16.46 ±8.12 days. Recurrence of GBS occurred in 12 (24%) patients. Out of them, 7 (58.33%) were females and 5 (41.67%) were males. After 6 months, MRC sum score showed significant improvement as 74% of the cases reached 60 and the outcome was good in about 78% of cases, moderate in 16% and poor in 6%. Finally Hughes motor scale (HMS) revealed that 58% of cases were healthy, 18% had minor signs or symptoms, 12% walked without support, 6% walked with support and 6 % were bed ridden (Table 6).

Table 3. Reflexes Examination

Variables			Initial; n (%)	At 3 months; n (%)	At 6 months; n (%)	p-value
Superficial reflexes	Abdominal	Normal	0	0	49 (98.00)	<0.0001
		Hyporeflexia	49 (98.00)	50 (100.00)	1 (2.00)	
		Areflexia	1 (2.00)	0	0	
	Anal	Normal	0	0	49 (98.00)	<0.0001
		Hyporeflexia	49 (98.00)	50 (100.00)	1 (2.00)	
		Areflexia	1 (2.00)	0	0	
	Cremasteric in males	Normal	0	0	27 (54.00)	<0.0001
		Hyporeflexia	26 (52.00)	28 (56.00)	0	
		Areflexia	24 (48.00)	22 (44.00)	23 (46.00)	
	Planter	Negative Babinski	41 (82.00)	39 (78.00)	40 (80.00)	0.88
Positive Babinski		9 (18.00)	11 (22.00)	10 (20.00)		
Muscle stretch reflexes (upper limb)	Biceps	Normal	48 (96.00)	48 (96.00)	50 (100.00)	0.73
		Hyporeflexia	1 (2.00)	1 (2.00)	0	
		Areflexia	1 (2.00)	1 (2.00)	0	
	Triceps	Normal	48 (96.00)	48 (96.00)	50 (100.00)	0.73
		Hyporeflexia	1 (2.00)	1 (2.00)	0	
		Areflexia	1 (2.00)	1 (2.00)	0	
	Brachioradialis	Normal	48 (96.00)	48 (96.00)	50 (100.00)	0.73
		Hyporeflexia	1 (2.00)	1 (2.00)	0	
		Areflexia	1 (2.00)	1 (2.00)	0	
Muscle stretch reflexes (lower limb)	Knee	Normal	0	0	49 (98.00)	<0.0001
		Hyporeflexia	49 (98.00)	49 (98.00)	1 (2.00)	
		Areflexia	1 (2.00)	1 (2.00)	0	
	Achilles	Normal	0	0	49 (98.00)	<0.0001
		Hyporeflexia	49 (98.00)	49 (98.00)	1 (2.00)	
		Areflexia	1 (2.00)	1 (2.00)	0	

Table 4. Comparison among different types of nerve conduction velocity according to presenting symptoms of studied population

Variables		AIDP (n=26)	AMAN (n=18)	AMSAN (n=3)	Normal NCS (n=3)	p-value
Weakness of lower limb; n (%)	Acute onset	1 (3.85)	0	0	1 (33.33)	0.06
	Gradual onset	25 (96.15)	18 (100)	3 (100)	2 (66.66)	
Pain (acute onset) ; n (%)		26 (100)	18 (100)	3 (100)	3 (100)	1.00
Urine and stool incontinence; n (%)		6 (23.08)	3 (16.67)	2 (66.67)	2 (66.67)	0.11

Table 5. Comparison among different subtypes of GBS according to motor system examination

Variables		AIDP (n=26)	AMAN (n=18)	AMSAN (n=3)	Normal (n=3)	p-value
Cranial nerves; n (%)	Normal	25 (96.15)	17 (94.44)	3 (100)	3 (100)	0.95
	Abnormal	1 (3.85)	1 (5.56)	0	0	
Muscle bulk (normal)		26 (100)	18 (100)	3 (100)	3 (100)	1.00
Fasciculations or involuntary movements; n (%)	Not present	25 (96.15)	18 (100)	3 (100)	3 (100)	0.82
	Present	1 (3.85)	0	0	0	
Hypotonia; n (%)		26 (100)	18 (100)	3 (100)	3 (100)	1.00
Muscle power; n (%)	2/5	2 (7.69)	0	0	0	0.07
	3/5	16 (61.54)	18 (100)	3 (100)	3 (100)	
	4/5	8 (30.77)	0	0	0	
Coordination (Impaired)		26 (100)	18 (100)	3 (100)	3 (100)	1.00

Table 6. Outcome after 6 months

Variables		n (%)			
Good outcome	Full recovery	33 (66)			
	Minor deficit upper limb	0			
	Minor deficit lower limb	6 (12)			
Moderate (Moderate and independent) outcome		8 (16)			
Poor outcome	Chair bound	3 (6)			
	Bed ridden	0			
Hughes motor scale (HMS)	(0) Asymptomatic	29 (58)			
	(1) Mild signs or symptoms but able to run	9 (18)			
		6 (12)			
	(2) Able to walk unaided for 5 meters	3 (6)			
	(3) Able to walk 5 meters with support	3 (6)			
	(4) Bed ridden or chair bound	0 (0.0)			
	(5) Requiring ventilatory assistance	0 (0.0)			
(6) Death					
Medical Research Council (MRC) sum-score	Score	Initial	At 3 months	At 6 months	p-value
	51-60	0 (0%)	1 (2%)	37 (74%)	< 0.0001
	41-50	7 (14%)	9 (18%)	9 (18%)	
	31-40	41 (82%)	39 (78%)	4 (8%)	
≥30	2 (4%)	1 (2%)	0 (0%)		

4. Discussion

Infants and children presenting with acute flaccid paralysis represent a relatively common emergency in outpatients and inpatients divisions of the Pediatric department. The aims of evaluation of these patients were to clarify the diagnosis and to give an appropriate therapy. Analysis of cerebrospinal fluid (CSF) and electrophysiological study are essential for accurate diagnosis of GBS (18). In the present study, we performed a clinical analysis and reviewed the data of 50 infants and children presented with GBS. The median age was 2.92 years and the majority of cases belonged to the youngest age group (1 year to 2 years) and this was relatively similar to the Arab country study (19) (median age was 3.5 years) and lower than other reports (20, 21). Male to female ratio was 1.1:1 suggesting a relative male predominance. This finding was consistent with other reports (20-22). The prevalence of GBS was sporadic with urban to rural ratio of 1.1:1. This finding was in agreement with other reports (23), furthermore, in the study done by van Doorn et al., they found that GBS was sporadic and small epidemics had been reported (11). In our study, antecedent infections were encountered in 66% of cases and respiratory tract infections were the most frequent (76%) followed by gastroenteritis (21%). This finding was consistent with other reports (4, 20-24). The neurological manifestations were weakness of both lower limbs (100%), hyporeflexia (98%), areflexia (2%), and cranial nerve involvement (2%), this data came to agreement with other reports (20-23). The analysis of CSF showed cytoalbuminous dissociation and this was in accordance with other reports (23) in AIDP subtype but lower in the other subtypes. According to nerve conduction studies, we found that AIDP was present in 52% of patients, AMAN in 36% of patients, AMSAN in 6% of patients and only 6% of patients had normal nerve conduction study. In a similar report, AIDP was present in 44% of patients, AMAN in 35% of patients, AMSAN in 21% of patients and 1% only had normal nerve conduction study (25), furthermore comparable results were obtained by other studies (2, 21, 23) however other reports (22) showed different data as the axonal type was the most frequent pattern. All forms of GBS presented with weakness of lower limbs. Cranial nerve involvement was present in 3.85% of AIDP patients and in 5.56% of AMAN patients, whereas there was no affection of cranial nerves, neither in AMSAN cases nor in cases with normal NCS. Similar data were obtained in other reports (23) meanwhile in other study (21), cranial neuropathies were more common in the axonal subtype. In our study we reported sphincteric dysfunction with urine and stool incontinence in 23.08% of AIDP patients, 16.67% of AMAN patients, 66.67% of AMSAN patients, and 66.67% of patients with normal NCS. Comparable results were obtained by Tekgul et al., (2003) as mild autonomic dysfunctions (urinary dysfunction, abnormal sweating) were seen in only 20% of the AIDP group and severe autonomic dysfunctions were observed in 80% of the AMSAN group (23) however urinary problems were more common in the demyelinating group in other reports (21). Although GBS is a self-limiting illness in many patients, it can be associated with severe morbidity and mortality in patients with fulminant course. In our study a standard IVIg therapy was administered at hospital admission for all patients with any grade of the disease followed by physiotherapy, but there was no consensus as to which patients would benefit from IVIg

treatment and what the effective dose is. Data from similar reports (26) found that IVIg had shortened the time to first improvement and to regain independent walking. They reported that the patients who had just lost the ability to walk had experienced the greatest benefit from IVIg, and the patients who were tetraplegic and/or ventilated did not respond to treatment. They applied a standard IVIg therapy on admission for all patients with any grade of disease (26). In this work, recurrence or treatment-related fluctuation (TRF) was noticed in 12 patients (24%). Our data was higher than other reports (23, 27) that showed recurrence in 3.5% and 9% respectively. This could be explained by higher exposure to infectious diseases in our community that trigger the disease. The prognosis of GBS was usually favorable and the majority of the patients fully recovered or had only minor deficits. In our study, the outcome of GBS was good in 78% of cases, moderate in 16% whereas only 6% had poor outcome. According to Hughes motor scale (HMS), the majority of patients (58%) were healthy while 18% had minor signs or symptoms. These findings were consistent with other reports (26, 28). Furthermore, comparable studies demonstrated almost similar findings. In one report published by Verma et al., they found good functional outcome in 72.2% of patients, of which 30% had completely recovered while 27.8% had poor functional outcome (22). In another report (26), 75% of patients were free of symptoms, 21% suffered minor residual symptoms, while 4% were severely disabled. Although 81.4% recovered satisfactorily, eight were persistently disabled (29). Outcome was excellent in a childhood study (20) with full recovery or minimal symptoms in 87.5% of children at one year, and reached 95% after two years. In a review by van Doorn it was concluded that, after 6 months 20% of patients are still unable to walk (11).

5. Conclusions

GBS should be suspected in all cases presenting with acute flaccid paralysis in different age groups, and immediate intervention by administration of IVIg therapy can reduce morbidity and mortality, and ultimately can reduce chronic neurological disability. We recommend that this idea of research should be repeated in the future on a larger number of cases including different age groups in our locality with better resources, and longer follow up.

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Conflict of Interest:

There is no conflict of interest to be declared.

Authors' contributions:

AS and AA conceived the study, carried out its designing, coordinated the implementation, and drafted the manuscript. WA participated in the design of the study, analysis and interpretation of data. WA was responsible for interpretation of laboratory and radiological data of patients and revision of the manuscript. All authors read and approved the final manuscript.

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