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Research Article

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Outcome of Acute Flaccid Paralysis in Children Experience of Tripoli Children Hospital 2012-2017

Seham Eshrif[@1], Mabruka Ramadan[1] and Abdulmagid Almejresi[2]

[1] Department of Pediatric. Faculty of Medicine. University of Tripoli
[2] Department of Pediatric, Tripoli Children Hospital, Libya

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ABSTRACT

Acute flaccid paralysis in children is an emergency demanding prompt diagnosis and treatment without delay to prevent life-threatening complications. Guillain-Barré Syndrome (GBS) is the most common cause of acute flaccid paralysis in children, it is an acute monophasic demyelinating neuropathy, Etiology of GBS is incompletely understood, prognosis is usually good with early detection and prompt treatment. This retrospective study was done to assess the clinico-laboratory profile of children admitted to Tripoli Children Hospital with acute flaccid paralysis.

In this study, we performed a clinical analysis and reviewed the data of 58 infants/children presented with AFP and admitted to Tripoli Children Hospital in the period from July 2012 – July 2017 medical records were reviewed for the demographic data (age, sex), seasonal distributions, history of preceding events, time from onset to nadir, co-morbid conditions, clinical features, need of mechanical ventilation, results of CSF examination, spinal MRI, electrophysiological data, mode and results of the treatment.

Study group of 58 patients consisted of 25 (34.1%) males and 33 females (56.9%), with male to female ratio 0.76:1. Mean age of onset was 4.2± 3.5 years (range from 8 months-14years) 23 patients (39.9%) presented at summer season. Upper respiratory tract infections were the most common antecedent infections (55.2%). and the neurological findings were weakness of both lower limbs in all patients (100%), while cranial neuropathies were found in 31%. Nerve conduction study revealed that acute inflammatory demyelinating polyradiculoneuropathy was found in 16% of cases, acute motor axonal neuropathy in 36% of cases, whereas acute motor-sensory axonal neuropathy was found in 40%. The outcome according to Hughes motor scale (HMS) the majority of patients (79.3%) were healthy while 12.1 have minor weakness and one mortality (1.7%).

Conclusion: Guillain-Barre syndrome (GBS) is the commonest cause of acute flaccid paralysis in children. The diagnosis of GBS is based primarily on the clinical evaluation and the exclusion of important possible alternative diagnoses. In this study two patients were diagnosed as transverse myelitis, one as paraspinal collection, other as spinal canal ependymoma. Cranial neuropathy is common in GBS and bulbar palsy is an indicator for need of ventilatory support.

Key words *– Knowledge; Attitude; Practices; Type 1 Diabetes.*

INTRODUCTION

Acute flaccid paralysis (AFP) is a clinical syndrome characterized by rapid onset of weakness, including (less frequently) weakness of the muscles of respiration and swallowing, progressing to maximum severity within several days to weeks. The term "flaccid" indicates the absence of spasticity or other signs of disordered central nervous system motor tracts such as hyperreflexia, clonus, or extensor plantar responses.[1-3] Etiologies of AFP are diverse including infectious agents, trauma or autoimmune reaction.[3] Guillain-Barré Syndrome (GBS) is the most common cause of acute flaccid paralysis in children, it is an acute monophasic demyelinating neuropathy.[4] The disease is characterized by progressive motor weakness of limbs with areflexia. Preceding antecedent infections, mostly viral, are seen in half of the cases. One third of patients required ventialatory support in the past with about ten percent mortality. Immunoglobulins and plasmapharesis have made a significant change in the course of the illness.[5] The incidence of GBS has been estimated to be between 0.34 and 1.34/100 000.[6] 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

@ Author to whom correspondence should be addressed. Dr. Seham Eshrif,; Tel.+218925442682; E. mail sehesharif@yahoo.com

over hours or days.[7] Supportive investigations include CSF examination, and nerve conduction studies (NCS). Magnetic resonance imaging (MRI) and computed tomography (CT) scanning of the spine, may be more helpful in excluding other diagnoses, such as mechanical causes of myelopathy. Both intravenous immunoglobulins (IVIg) and plasma exchange have been the first-line therapy for GBS patients.[8] About 5 to 10% of GBS patients deteriorate after initial improvement or stabilization following IVIg treatment, a condition named "treatment-related clinical fluctuation" .[9,10] Etiology of GBS is not completely understood but believed to be due to autoimmune cause where majority of cases are triggered by infection stimulating anti-ganglioside antibodies production. Approximately 70% of cases of GBS occur 1-3 weeks after an acute infectious process. The organisms thought to be involved are Campylobacter jejuni (diarrhea), Mycoplasma pneumonia, Haemophilus influenzae, Cytomegalovirus, Epstein-Barr virus and influenza.[11] Administration of outmoded anti-rabies vaccines and A/New Jersey (swine) influenza vaccine, given in 1976, was associated with a slight increase in GBS incidence. New influenza vaccines appear to confer risk of <1 per million and are relatively safe. The earliest description of GBS dates to 19th century regarding an afebrile generalized paralysis by Wardrop and Ollivier in 1834. Other important landmarks are Landry's report in 1859[12] about an acute, ascending, predominantly motor paralysis with respiratory failure, leading to death and Osler's (1892)[13] description of afebrile polyneuritis. Guillain, Barré, and Strohl (1916) described a benign polyneuritis with albumino-cytological dissociation in the cerebrospinal fluid (CSF)[14] and the first report regarding pathology of GBS was by Haymaker and Kernohan in 1949 who reported that edema of the nerve roots was an important change in the early stages of the disease.[15] Asbury, Arnason and Adams (1969) established that the essential lesion is due to perivascular mononuclear inflammatory infiltration of the roots and nerves.[16]

The current study was aimed to assess the clinico-laboratory profile of children admitted to Tripoli Children Hospital with acute flaccid paralysis.

MATERIALS AND METHODS

This case series study carried by analyzing the data of all infants and children presented with acute flaccid paralysis and admitted to Tripoli Children Hospital in the period from July 2012 – July 2017, The medical records were reviewed for the demographic data (age, sex), seasonal distributions, history of preceding infections (mainly for upper respiratory infection and diarrhea), time from onset to nadir (the maximum degree of disability), co-morbid conditions, clinical features: sensory disturbances/pain, cranial nerve deficits, autonomic dysfunction(e.g. Arrhythmias, blood pressure abnormalities, sphincter instabilities and abnormal sweating), need of mechanical ventilation, results of CSF examination, spinal MRI when available, electrophysiological data, mode and results of the treatment and complications of the procedures during hospitalization. An AFP surveillance program is conducted to increase case yield of poliomyelitis for all cases. According to the WHO guidelines adequate stool samples were collected within 14 days of the onset of paralysis, two specimens – taken 24-48 hours apart. Stool specimens were sealed in containers and stored immediately inside a refrigerator or packed between frozen ice packs at 4-8°C in a cold box, and shipped to the national laboratory in Tunisia within 72 hours of collection. Medical Research Council (MRC)[17] sum score was used for valuing the muscle strength from 0 to 5 in proximal and distal muscles in upper and lower limbs bilaterally; score ranged from 40 (normal) to 0 (quadriplegic) and the functional disability was evaluated by Hughes score[17] which was defined as follows 0 = healthy state; 1 = minor symptoms and capable of running; 2 = able to walk 5m or more without assistance but unable to run; 3 = able to walk 5m across an open space with help; 4 = bedridden or chair-bound; 5 = requiring assisted ventilation for at least part of the day; 6 = dead (Table 1). The nadir of disease was defined as the highest Hughes score or the lowest MRC sum score.

The collected data coded and SPSS software version 16 used for analyses. Frequency, percentage, mean. *Chi – square* used to find the difference between categorized data, P value < 0.05 considered significant.

RESULTS

Study group of 58 patients consisted of 25 (34.1%) males and 33 females (56.9%) , all were have acute flaccid paralysis. With male to female ratio 0.76:1. Mean age of onset was 4.2 ± 3.5 years (range from 8 months–14years) 23 patients (39.9%) presented at summer season,12 (20.7%) and 13 (22.4%) at autumn and winter season respectively and 10 patients (17.2%) at spring. Initially all were diagnosed and treated as cases of GBS but later (after MRI findings) the diagnosis changed for four (6.9%) of them (Figure1). Antecedent events were found in 53 patients (91.4%) of them, 32 (55.2%) had upper respiratory tract infection, gastroenteritis was present in 12 patients (20.7%), eight patients (13.8%) have history of preceded fever while history of trauma was present in only one patient (1.7%) (Table 2). Concerning clinical presentations of the patients; weakness of both lower limbs were the main complaints in almost all patients, twelve patients (20.7%) have only lower limbs weakness, 43 patients (74.1%) got ascending weakness and three patients (5.2%) have a typical presentation in form of descending weakness. Time from onset to nadir was rapid (within two days) in 16 (27.2%) patients and gradual (>2days – 4weeks) in 42 (72.4%), Lower limbs pain and back pain was present in 30 patients (51.7%), sixteen patients (27.6%) were have ataxia (truncal or unsteady gait) at initial presentation, about autonomic manifestations were found in19 patients (33%), four patients (6.9%) have hypertension, constipation was present in twelve (20.7%), only one patient (1.7%) has urine retention, were excessive sweating present in two patients (3.4%). About cranial nerves involvement occurred in 18 patients (31%), four of them (22.2%) have unilateral lower motor facial nerve palsy, 13(72.2%) patients have bulbar palsy (dysphasia & nasal intonation voice), one patient (5.6%) presented with bilateral facial palsy and bulbar palsy. All our patients haven't any chronic illness except one was known case of bronchial asthma and other patient had history of hospital admission about 6 months before because of acute weakness of both

upper and lower limbs witch completely recovered after few weeks "Relapsing course". Table 3 demonstrate nadir function disabilities for our patients evaluated by Hughes scale, all of them were have distal muscle strength less than grade five. Table 4 provides the summary statistics for CSF & MRI and electrodiagnostic studies where lumber puncture was done for twelve patients (20.7%) only 50% of them shows cytoalbuminologic dissociation in cerebrospinal fluid, 33% have normal CSF, and two patients (16.7%) shows high cells and protein. MRI of full spine or lumbar spine with gadolinium infusion was obtained in 26 patients (45%), 21 (81%) of them was normal, one patient (3.8%) has spinal nerve roots thickening, other one has paraspinal cord collection, another patient has finding of lumber spinal canal ependymoma, and two 7.7% shows findings of transverse myelitis ,brain MRI done for 7 (12.1%) patients who presented with consciousness alternation all were normal except one (14.3%) patient shows white matter changes. Electrodiagnostic studies were done for 25 (43%) patients where 9 (36%) for acute motor axonal neuropathy AMAN, 10 (40%) have acute motor sensory axonal neuropathy AMSAN findings and four (16%) have NCV findings of acute inflamatory demyelinating polyneuropathy AIDP and two patients (8%) have normal studies. Workup for poliovirus was negative for all cases. All our patients treated by IVIg alone or in combinations with plasma exchange/ methylprednisolone/ antimningioencephaltis drugs, one patient had surgical interventions (Table 5). 86.2% of them have no significant complications, 3 patients (5.2%) developed fever during Ig infusion, two (3.4%) got transient hypertension, one patient (1.7%) had hypotension and another one developed severe headache. At least 3 months after onset 46 (79.3%) of patients got complete recovery, 7(12,1%) have mild weakness and one patient (1.7%) lifted bed ridden with sever lower limb weakness, one patient dead after discharge against medical a advice and no data available for three patients.

Table 1: Guillain-Barré Syndrome Disability Scale (Hughes)

0	Healthy
1	Minor symptoms or signs of neuropathy but capable of manual work/capable of running
2	Able to walk without support of a stick (5m across an open space) but incapable of manual work/running
3	Able to walk with a stick, appliance or support (5m across an open space)
4	Confined to bed or chair bound
5	Requiring assisted ventilation (for any part of the day or night)
6	Death

Table 2: Frequency of antecedent event

Antecedent event	No. of pts	%
No antecedent event	5	8.6
URTI	32	55.2
Diarrhea	12	20.7
Fever	8	13.8
Trauma	1	1.7

Table 3: Patients Nadir Function Disabilities at initial presentation (Hughes Scale)

Function disabilities	Hughes scale	No. of patients	%
Walk with support	3	11	19
Confined to bed	4	44	75.8
Requiring assisted ventilation	5	3	5.2

Table 4: Frequency of CSF, MRI and NCV findings

Investigation	Frequency	%
CSF		
Normal	4	6.9
High protein	6	10.3
High cells and protein	2	3.4
Not done	46	79.3
Spinal MRI Findings		
Normal	21	36
Thickening of nerve roots	1	1.7
Paraspinal cord collection	1	1.7
Features of acute transverse myelitis	2	3.4
Lumber spinal canal ependymoma with retropertoneal extension	1	1.7
Not done	32	55.2
Brain MRI		
Normal	6	10.3
Demyelinating white matter	1	1.7
NCV		
Normal	2	3.4
AIDP	4	6.9
AMAN	9	15.5
AMSAN	10	17.2
Not done	33	56.9

Table 5: Frequency of treatment modalities

Treatment	Frequency	%
IVIG	46	79.3
IVIG + exchange	1	1.7
IVIG+methylprednisolone	1	1.7
IG+antimeningioencephalitis	4	6.9
IVIG+antimeningitic +surgical drainage	1	1.7
IVIG+antimeningioencephalitis+ventilatory support	3	5.2
IVIG+ antimeningioencephalitis+methylprednisolone	1	1.7
IVIG+plasma exchange+methlprednisolone	1	1.7
Total	58	100

Table 6: Relation between the need of mechanical ventilation and other data

Variable	Frequency	%	Mechanical ventilation	*P* Value
Bulbar palsy	13	22.4	3	.000
Autonomic manifestations	19	33	1	.025
Onset to nadir				.174
Rapid	16	27.6	2	
Gradual	42	72.4	1	
NCV				.138
AIDP	4	16	0	
AMAN	9	36	0	
AMSAN	10	40	2	
Normal	2	8	0	

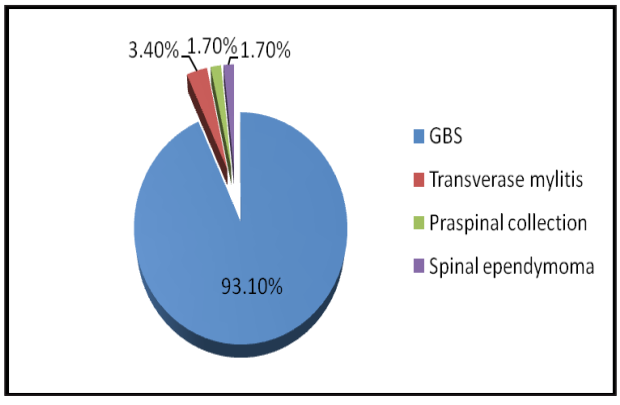

Figure 1: Frequency of causes of AFP

Table 7: Relation between long-term outcome and other data

Character		Long-term outcome					P Value
		Complete recovery		Mild weakness	Sever weakness	Death	
		No	%				
Sex							.008
	Male	16	27.6	6	0	1	
	Female	34	58.6	6	1	0	
Antecedent event							.826
	Nil	4	6.9	1	0	0	
	URTI	26	44.8	3	0	1	
	Diarrhea	10	17.2	1	0	0	
	Fever	5	8.6	2	1	0	
	Trauma	1	1.7	0	0	0	
Onset to nadir							.206
	Rapid	13	22.4	1	1	1	
	Gradual	33	56.9	6	0	0	
Cranial nerves involvement							.000
	Facial palsy	3	5.2	2	0	0	
	Bulbar palsy	10	17.2	1	1	1	
NCV							.234
	Normal	2	3.4	0	0	0	
	AIDP	2	3.4	2	0	0	
	AMAN	6	10.3	2	1	0	
	AMSAN	8	13.8	2	0	0	
IVIG coarse							.748
	2 days	34	58.6	5	1	1	
	5 days	12	20.7	2	0	0	

DISCUSSION

Infants and children presenting with acute flaccid paralysis represent a relatively common emergency in Pediatric department. The aims of evaluation of these patients were to clarify the clinical manifestations, diagnosis, therapy and assess their outcome. 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 58 infants and children presented with AFP. The median age was 3 years and the majority of cases belonged to the youngest age group (1 year to 4years) 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 0.75:1 suggesting a relative female predominance. This finding was inconsistent with other reports.[20–22] In our study, a higher incidence of GBS was found in summer, especially in July and August. Our finding was in accordance with the study by Paradiso and colleagues.[23] antecedent events were encountered in 91.4% of cases and respiratory tract infections were the most frequent (55.2%) followed by gastroenteritis (20.7%). This finding was on line with other reports.[20–24] One of our patients has relapsing course witch

not going with diagnosis of GBS as it is characterized by a monophasic course, with a clinical nadir within 4 weeks of symptom onset (Van der Meché *et al*., 2001).[4] By contrast, chronic inflammatory demyelinating polyneuropathy (CIDP) typically demonstrates a slowly progressive course with gradual worsening over more than an 4-week period OR with relapsing symptoms Asbury and Cornblath, 1990.[25] Distinguishing patients with AIDP and acute-onset CIDP has been a challenging clinical issue, especially for patients presenting early in the course of disease, where differentiation has not been possible Odaka *et al*.,[26] Although diagnostic criteria are available for both diseases[25,27], a patient may only be classified as having acute-onset CIDP with certainty after progression occurs over 4 weeks or relapse neurological symptoms.[25] Concerning clinical manifestations (74.1%) got ascending weakness, (20.7%) have only lower limbs weakness, (5.2%) have presentation in form of descending weakness, These results are in agreement with Mazen Dimachkie findings which showed most patients present initially with leg weakness and arm weakness (32%) or selective proximal and distal leg weakness (56%) often spreading to the arm while some have onset of weakness in the arms (12%). A descending presentation mimicking botulism, with onset in the face or arms, is less common[28], all were have hyporeflexia / areflexia. One interesting finding is seven (12.1%) of our patients presented by alteration in consciousness this result may be explained by the fact that five percent of typical GBS cases may have Bickerstaff's brain stem encephalitis (BBE).[28] Only one from these seven patients has demyelinating white matter changes found in brain MRI so diagnosis of the association between ADEM and GBS was made and this finding also reported in Isha Deshmukh *et al*., study.[29] Cranial nerves involvement occurred in (31%), this data came to agreement with other reports[20-30], Many of the studies done before quote variable involvement of cranial nerves ranging from 50% to 75%, for example, Lφeffel, *et al*.,[31] have quoted 50% and Dhadke et al., had 62.5% involvement.[32] Bulbar palsy was the most common (72%) in our study, which correlates with other studies.[30] Among bulbar palsy patients majority have dysphagia and few have dysphonia, 23% of them need ventilator support it's less than Amita Bhargava et al., study which was 52.6%.[30] In many of the studies facial palsy was the most common finding with percentage ranging from 45% to 53%. In a study by Winer *et al*.,[33] 53% had bilateral facial palsy, in our patients four (22.2%) have unilateral palsy and one patient (5.6%) had bilateral facial palsy. According to nerve conduction studies, we found that AIDP was present in 16% of patients 50% of them got complete recovery, AMAN in 36% of patients, AMSAN in 40% of patients and complete recovery recorded in 66.7% & 80% respectively only 8% of patients had normal nerve conduction study and all got complete recovery. 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[34], In our study we reported autonomic dysfunctions (hypertension, urine retention, abnormal sweating) in 55.6% of AMAN patients, 70% of AMSAN patients, Comparable results were obtained by Tekgul *et al*.,[35] as mild autonomic dysfunctions were seen in only 20% of the AIDP group and severe autonomic dysfunctions were observed in 80% of the AMSAN group. In the current study only three patients were need mechanical ventilation and all of them have bulbar palsy and they present 23% of patients with bulbar palsy [.000 *P* value]. Table 6 demonstrate the relation between the need of assisted ventilation to other variables. In our study a standard IVIg therapy was administered at hospital admission for all patients with any grade of the disease, total dose was 2 gm/kg 74.1% of patients received it over two days and 25.9% of them were over 5 days course with no significant outcome difference between the two groups was evident (Table 7). Two (3.4%) patients have also plasma exchange because they were severely affected and need ventilatory support however, the findings of Mazen M. Dimachkie study which showed that combined treatment produced no significant difference in patient outcomes compared with either therapy given alone.[28] Methylprednisolone as an add-on therapy were administrated to three of patients whose clinical manifestations deteriorated despite the use of IVIg, two of them diagnosed later by MRI as transverse mylitis, 4 children (6.9%) had treated as meningoencephalitis because of the initial impression was meningioencepalitis however generalized weakness and areflexia along with NCS confirmed the diagnosis of GBS. Surgical drainage of paraspinal collection done for one patient. Data from similar reports[36] 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.[36] 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 was good in 79.3% of cases. According to Hughes motor scale (HMS), the majority of patients (79.3%) were healthy while 12.1 have mild weakness, 1.7% was bedridden and one mortality (1.7%). These findings were consistent with other reports.[36,37] 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% have completely recovered while 27.8% had poor functional outcome.[22]

There are limitations of our study. Due to the retrospective nature of the study and the failure to make follows-up on some patients, the current sample size is too small for the stratified analysis like comparisons of the clinical characteristic between pediatric AMAN and AIDP, as well as the comparisons of different subtypes of GBS between children

CONCLUSIONS

Guillain-Barre syndrome (GBS) is the commonest cause of acute flaccid paralysis in children. The diagnosis of GBS is based primarily on the clinical evaluation and the exclusion of important possible alternative diagnoses. In this study two patients were diagnosed as transverse myelitis, one as paraspinal collection, other as spinal canal ependymoma.

RECOMMENDATIONS

As analysis of cerebrospinal fluid (CSF) and electrophysiological study are essential for accurate diagnosis of GBS so we recommend that at least one of these tools must be done for all cases presented with AFP to confirm GBS diagnosis.

Cranial neuropathy is common in GBS, and bulbar palsy is an indicator of respiratory paralysis careful search for this is highly significant.

Because distinguishing patients with GBS and acute-onset CIDP has been a challenging clinical issue, especially for patients presenting early in the course of disease, close follow-up of GBS patients during the recovery phase is also needed for accurate diagnosis

A detailed case sheath prepared and to be filled for all cases presented with AFP which can be used for a further study on larger sample need to reach more conclusive result.

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