Electrophysiological Patterns of Guillain Barre Syndrome in Iraqi Children...A Hospital Based Study

Muhi Kadhem Al-janabi ,Ahmed Mustafa Kamal ,Nadia Aziz Nasir, Safaa H. Al-Shemmary

ABSTRACT:

BACKGROUND:

Guillain-Barre syndrome (GBS) is an acute idiopathic progressive ascending weakness and considered the most common cause of acute flaccid paralysis in healthy infants and children. It is now known to be a heterogeneous syndrome with several variant forms. In addition to the demyelinating form, which is the most common type, axonal forms of GBS are now well recognized.

OBJECTIVE:

To estimate frequency, demographics, clinical characteristics and complications of GBS subtypes from nerve conductive study (NCS) and electromyography (EMG) in patients were admitted to Children Welfare Teaching Hospital.

PATIENTS& METHODS:

Fifty three children with GBS admitted to Children Welfare Teaching Hospital Medical City-Baghdad from January 2009 till August 2010 was enrolled in this study. Clinical data were obtained; electrophysiological studies (NCS, EMG) were performed to determine GBS subtypes.

RESULT:

Out of 53 children studied, eleven patients (20.6%) were diagnosed as axonal subtype and 42 (79.4%) were of demyelinating subtype.

Axonal subtype was more frequent in rural than urban (8/11 patients 72.7% and 3/11 patients 27.3% respectively), where as demyelinating subtype was more frequent in urban residency compared to rural area (33/42 patients 78.6% and 9/42 patients 21.4% respectively) with a P value=0.0025.

Although gastroenteritis was higher in axonal subtype (3/11 patients 27.3%) compared to only (5/42 patients, 11.9%) in demyelinating subtype, it did not reach the statistical significant. History of upper respiratory tract infection was reported more in demyelinating compared to axonal subtype (25/42 patients 59.6% and 3/11 patients 27.7% respectively).

Cranial nerve involvement was found in 8 patients (72.7%) of the axonal subtype while it was found in 24 patients (57.1%) of demyelinating subtype.

Respiratory failure was reported as complication in 4 patients (36.4%) of axonal subtype, compared to 7 patients (16.7%) of demyelinating subtype. Ventilator support was recorded in 3 patients (27.3%) of axonal, compared to only 1 patient (2.4%) in demyelinating subtype (p value=0.024).

CONCLUSION:

The demyelinating subtype was the predominant type of GBS followed by the axonal. Gastroenteritis was the predominant recorded antecedent event in axonal subtype and more frequent in rural residency. Cranial nerves involvement was reported more frequently in axonal subtype and has been a significant factor for future assisted ventilation.

KEYWORD: gbs, demyelinating, axonal,children.

INTRODUCTION:

Guillain-Barre syndrome (GBS) is an acute idiopathic polyneuropathy characterized by symmetrical progressive ascending weakness, loss of deep reflexes, variable sensory complaints, and elevated cerebrospinal fluid (CSF) protein without pleocytosis. The disorder is thought to result from a post-infectious event [(1)]. Guillain-Barre syndrome is the most common cause of acute flaccid paralysis in children [(2)]. It is now known to be a heterogeneous syndrome with several variant forms. In addition to the demyelinating form, which is the most common type, axonal forms of GBS are now well

*Pediatric Pulmonologist, Baghdad Medical College.
** pediatrician, Medical City Baghdad.
***Community Medicine specialist, Baghdad Medical College.
**** Neurophysiologist,Medical City Baghdad.

recognized [3,4]. GBS is classified into 3 major forms: Acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor-sensory axonal neuropathy (AMSAN).

AMAN distinguished from AIDP by its involvement of predominantly motor nerves and an electrophysiologic pattern suggesting axonal damage. AMSAN has more sensory symptoms. The course tends to be prolonged [5]. This form of GBS is recognized infrequently in children. In the motor and motor sensory variants, the axon are affected without an inflammatory response [6]. The primary immune process is directed at the nodes of Ranvier. The motor nerves are involved at the ventral roots and peripheral nerve [1,5].

In AIDP a focal inflammatory response develops against myelin-producing Schwann cells or peripheral myelin causes segmental myelin degeneration throughout the nerve. Demyelination blocks electrical conduction along the nerve [1]. Patients with GBS who do not meet the required criteria will typically have one of the other GBS variants such as AMAN. *NCS* and *EMG* are the most specific and sensitive tests for diagnosis of the disease [7].

AIM OF STUDY:

To estimate the frequency of GBS subtypes from nerve conductive study (NCS) and electromyography (EMG) each with its demographics, clinical characteristics and complications in patients who were admitted to Children Welfare Teaching Hospital.

PATIENT AND METHOD

Fifty three patients with GBS who were admitted to Children Welfare Teaching Hospital Medical City-Baghdad from January 2009 to August 2010 were enrolled in this cross sectional study. They fulfilled the Asbury and Cornblath clinical criteria for the disease; Required features: Progressive weakness in both arms and legs and areflexia (or hyporeflexia). Features supportive of diagnosis: Progression of symptoms over days to 4 weeks, relative symmetry, mild sensory signs or symptoms, cranial nerve involvement, especially bilateral facial weakness, recovery beginning 2 to 4 weeks after progression ceases, autonomic dysfunction, absence of fever at onset, typical CSF (albuminocytologic dissociation), EMG/nerve conduction studies with characteristic signs of a demyelinating process in the peripheral nerves [8]. Data collected including age, sex, residence, date of onset, antecedent event, clinical features including sensory involvement, cranial nerves affected and autonomic involvement, complications including respiratory failure & RCU admission, laboratory investigations including CSF examination, and electrophysiological study**.** Nerve conduction studies (NCS) were undertaken using conventional procedures. Needle EMG was done for any denervation and motor unite action potential changes in all patients in at least two proximal and two distal limb muscles. Graph-pad program used to calculate fisher exact and Chi square values. P values less than 0.05 were considered significant.

RESULTS:

Eleven out of 53 (20.6%) children had a diagnosis of axonal pattern of GBS and 42 (79.4%) children were diagnosed with demyelinating form, of axonal subtype {9 patients out of 11 (16.9%) had AMAN and 2 (3.7%) had AMSAN}. For patients with axonal type, the mean age was 4.78±2.7 years and 4.7 ±3.1years for patients with demyelinating subtype. The male to female ratio for patients with axonal was 1.75:1 compared to a ratio of 2:1 for children for demyelinating. Concerning residency (urban or rural), demyelinating type were more common within urban residency than axonal representing 33 versus 9 patients (78.6%versus 21.4%) which was statistically significant with a p-value of 0.002.

Events gastroenteritis (GE) and upper respiratory tract infection (URTI) prior to onset of neurological symptoms were showed GE in 3 (27.3%) of axonal patients where as it was only 5 (11.9%) in demyelinating subtype patients although statically not significant (p=0.33), and URTI was more in demyelinating compared to axonal 25 (59.6%) and 3 (27.3%) respectively with a non-significant P value 0.089, (table-1).

Table-2 shows that respiratory failure is the most serious short term complication of GBS and may require mechanical ventilation .Four patients out of 11 (36.4%) with axonal type were admitted to RCU with a mean time to reach peak disability was 5±2.94 days ,3/4 patients 27.3% has assisted ventilation for a mean duration of 14.3±13.6 days, 7/ patients 16.7%with demyelinating type were admitted to RCU with mean time to reach peak disability was 5.28±4.68 days ,one out of seven patients 2.4% has assisted ventilation for a 20 days, axonal and demyelinating types showed no difference to RCU admission where assisted ventilation was highly associated to axonal subtype (P value = 0.024).

Cranial nerve involvement was found in 32 out of total studied patients (60.3%), 8/11 (72.7%) of

the axonal patients were affected and 24/42 (57.1%) of demyelinating patients were affected. By comparing axonal with demyelinating type, no significant difference was found (table 2).

Table-3 shows distribution of demyelinating and axonal form in regards to cranial nerves involvement. It shows that 28 (87.5%) patients had got bulbar involvement facial nerve involvement was second in order of frequency.

CSF study were conducted in 44 patients; because of concept (over the days 4-19 of onset); mean level of CSF protein concentration was 97.64 ±49.64 mg/dl for axonal and 98.12±65.29 mg/dl for demyelinating type, while in 80% it was more than 45 mg/dl, in 16.6% of patients whose CSF done in the first week of illness, protein levels were normal. Comparing the axonal and demyelinating form no significant difference was found in CSF protein level (p=0.61).

Table 1: General characteristic of GBS according to subtype.

		Axonal	Demyelinating	Total	P- value
	Age Mean (SD) year	4.78 (2.7)	4.7 (3.1)		0.5
Sex	Male	7	28	35	1.0
	Female	4	14	18	
Residence	Urban	3 (27.3%)	33 (78.6%)	36	0.002
	Rural	8 (72.7%)	9 (21.4%)	17	
G.E	Yes	3 (27.3%)	5 (11.9%)	8	0.3
	No	8	37	45	
URTI	Yes	3 (27.3%)	25 (59.6%)	28	0.08
	No	8	17	25	

Table 2: Clinical characteristic of GBS subtype.

		Axonal	Demyelinating	Total	P –value
Cranial nerve	Yes	8 (72.7%)	24 (57.1%)	32	0.4
	No	3	18	21	
RCU	Yes	4 (36.4%)	7 (16.7%)	11	0.2
	No	7	35	42	
Mean Time to nadir(SD)days		5 (2.94)	5.28 (4.68)	10.28	0.9
Ventilation support	Yes	3 (27.3%)	1 (2.4%)	4	0.02
	No	8	41	49	

Table 3: Cranial nerves involvement.

Cranial nerve	Axonal n=8	Demyelinating n=24	Total n=32
III	1	0	1(3.12%)
VI	1	1	2(6.25%)
VII	1	5*	6(18.75%)
IX,X	8**	20***	28(87.5%)

*3 facial were Rt sided
**there is overlap between bulbar, extra ocular & facial.
***there were two overlaps with facial & trochlear

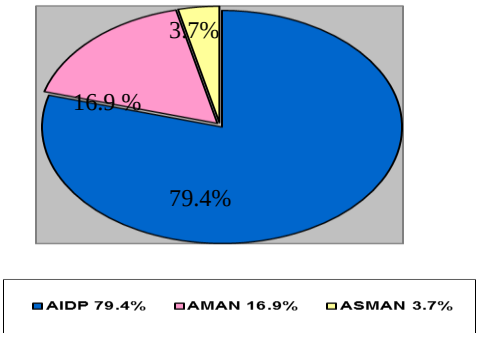

Figure 1: PIE chart demonstrating GBS pattern.

DISCUSSION:

The frequency of the axonal form of GBS varies considerably, from less than 10% of patients with GBS in Western countries by Cosi and Versino study [8] to over 40% in East Asia by Griffin et al [9].Current study shows a frequency of 20.8%.

Demyelinating type was reported in studies done by Ashrafi et al in Iran 84.4%[10], Tekgul et al in turkey 65%[11], Brown et al in North America 90%[12] and Mckhann et al in China 35%[13] ; in current study it was, (79.2%) lower than western country and higher than that mentioned in Chinese study and comparable in that figure observed in Iran.

The mean age of studied patients was 4.78±2.7 years for axonal and 4.7±3.1 years for demyelinating subtype which is less than that reports of childhood GBS in Mckhann et al 9.02±5.17 years in axonal and 7.88±4.86 years in demyelinating [13]. This might be attributed to small sample size of the present study. Boys accounted for a higher proportion of both axonal and demyelinating, particularly pronounced in demyelinating, where the male to female ratio was 2:1. Major differences in gender distribution were also noted in Lee et al study [14]; which was 4:1 in demyelinating subtype compared to 1:1 ratio for axonal subtype. In contrast, there was a lower male to female ratio for demyelinating cases in Paradiso et al study [15] and an equal distribution among axonal subtype.

Antecedent event were distributed between gastroenteritis and upper respiratory tract infection, children with axonal were more likely to have gastroenteritis preceding to development of GBS than children with demyelinating although it was statistically not significant and this result is related mainly to campylobacter jejune by other studies but unfortunately stool culture and serological tests were not available in the current study; which limited our expectations about the role of infectious agent. Comparable result was shown by Nagasawa et al study on Japanese children which showed that gastroenteritis was associated more frequently with axonal cases [16]. Urban residency in this study was highly associated with demyelinating type 78.5% compared to study done in Buenos Aires where half of demyelinating patients lived in urban which is related to air pollution increased frequency of URTI and 72.7% of axonal patients was from rural residency compared to 90% in Paradiso et al study due to more healthy water supply and sanitation [15].

The involvement of cranial nerves in Van der et al was 55.7% of the patients which is similar to this study, facial nerve being the most affected, usually bilateral [17]. That fact is different to that found in current study in which bulbar involvement was more frequent 87.5% followed by facial nerve involvement 18.6% which was asymmetrical (unilateral) in half of cases; cranial nerves involvement were more frequent in axonal than demyelinating form.

Respiratory involvement occurred in 21% of studied patients was similar to that found in Cosi and Versino literature, but mechanical ventilation was needed in 7.5% of patients was less to that found in the same literature [8]

Admission to RCU was more frequent in axonal compared to demyelinating form so as ventilation support which was significantly associated to axonal type of GBS which is similar to Barzegar study, Lawn et al and Durand et al [18-20]. Cranial nerve involvement mostly bulbar palsy was a reported complication in patients required ventilation support which was comparable to Barzegar study, Lawn et al and Durand et al [18-20]. Patients in the studied sample survived because of availability of equipped RCU.

CSF protein dissociation is one of the most important diagnostic feature in GBS was seen in 80% of studied group which is more than that

seen in Ashrefi et al study [10], the mean CSF protein concentration was 98.9±63.2 mg/dl higher than Barzegar [18] study 85.3±87.8 mg/dl may be due to timing of CSF aspiration all done after two weeks in current study with no difference between axonal and demyelinating type similar to Lee et al [14].

CONCLUSION:

Demyelinating was the predominant subtype of GBS followed by acute motor axonal neuropathy (AMAN) and acute motor sensory axonal neuropathy (AMSAN).

Cranial nerves involvement was frequent in axonal form which might highlight the future need for RCU admission and ventilation support.

No significant difference was found in CSF protein level between the axonal and demyelinating subtypes.

REFFRENCES:

1. Robert PC, Dougglas RN, Sheldon LK, John FD. Overview of Guillain-Barre syndrome in children. In: up to date [CD-ROM] version 17.1[cited 2008 Jan 8]; Basow, DS(Ed), Up to date, MA, 2008.
2. Beghi, E, Kurland, LT, Mulder, DW, Wiederholt, WC. Guillain-Barre syndrome. Clinicoepidemiologic features and effect of influenza vaccine. Arch Neurol 1985; 42:1053.
3. Visser, LH, Van der, Meche FG, Van Doorn, PA, et al. Guillain-Barre syndrome without sensory loss (acute motor neuropathy). A subgroup with specific clinical, electro diagnostic and laboratory features. Dutch Guillain-Barre Study Group. Brain 1995;118:841.
4. Ho TW, Mishu B, Li CY, et al. Guillain-Barre syndrome in northern China. Relationship to Campylobacter jejune infection and anti-glycolipid antibodies. Brain 1995;118:597.
5. Feasby TE, Hahn AF, Brown WF, et al. Severe axonal degeneration in acute Guillain-Barre syndrome: evidence of two different mechanisms? J Neurol Sci 1993;116:185.
6. McKhann GM, Cornblath DR, Griffin JW, et al. Acute motor axonal neuropathy: a frequent cause of acute flaccid paralysis in China. Ann Neurol 1993;33:333.
7. Nachamkin I, Barbosa PA, Ung H, et al. Patterns of Guillain-Barre syndrome in children: results from a Mexican population. Neurology 2007;69:1665.
8. Cosi V, Versino M. Guillain–Barre syndrome. Neurol. Sci. 2006; 27 (Suppl. 1): S47–51.
9. Griffin JW, Li CY, Ho TW et al. Guillain–Barre syndrome in northern China, The spectrum of neuropathological changes in clinically defined cases. Brain 1995; 118:577–95.
10. MR Ashrafi, et al Outcome of Guillain-Barre syndrome in children. Iran J Pediatr. 2008;18:11:58.
11. Tekgul H, Serdaroglu G, Tutuncuoglu S. Outcome of axonal and demyelinating forms of Guillain-Barre syndrome in children. Pediatric Neurol. 2003; 28:295-99.
12. Brown WF, Feasby TE, Hahn AF. Electrophysiological changes in the acute axonal form of GBS. Muscle Nerve. 1993;16:200-5.
13. Mckhann GM, Gornblath DR, Griffin JW, et al. Acute motor axonal GBS in China. Ann Neurol. 1993;33:333-42.
14. JH Lee et al. Childhood Guillain–Barré syndrome Journal of Pediatrics and Child Health 2008; 44:449–54.
15. Paradiso G, Tripoli J, Galicchio S, Fejerman N. Epidemiological, clinical and electro diagnostic findings in childhood Guillain-Barre syndrome: a reappraisal. Ann Neurol 1999; 46:701–7.
16. Nagasawa K, Kuwabara S, Misawa S, et al. Electrophysiological subtypes and prognosis of childhood Guillain-Barre syndrome in Japan. Muscle Nerve 2006; 33:766–70.
17. Van der Linden et al. Guillain-Barre syndrome in children Arq Neuropsiquiatr 2010;68:12-17.
18. M. Barzegar MD childhood Guillain-Barre Syndrome in the Iran's east Azerbaijan province Iran J Child Neurology 2008:25-31.
19. Lawn ND, Fletcher DD, Henderson RD, Wolter TD, Wijdicks EF. Anticipating mechanical ventilation in Guillain-Barre syndrome. Arch Neurol 2001;58:893-98.
20. Durand MC, Porcher R, Orlikowski D, Aboab J, Devaux C, Clair B, et al. Clinical and electrophysiological predictors of respiratory failure in Guillain-Barre syndrome ; a prospective study. Lancet Neurol.2006;5:1021-28.