Original Article

Electrophysiological evaluation of Guillain–Barre syndrome subtypes in childhood

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Abstract:

Background: Guillain-Barre syndrome (GBS) is the most common cause of acute motor paralysis in children where most of electrophysiological findings reveal demyelinating neuropathy. However, an axonal form of Guillain-Barre syndrome had been reported too.

Objectives: Assess the role of neurophysiological study (EMG and NCS) in the diagnosis of Guillain-Barre syndrome subtypes in children and estimate the frequency of subtypes whether demyelinating or axonal form of Guillain-Barre syndrome.

Subjects and methods: Two study groups of either sex was involved, thirty (30) Guillain-Barre patients with different ages and thirty(30) normal healthy subjects matched for age and gender served as control group. Each subject submitted to sensory and motor nerve conduction study (NCS) and electromyography (EMG) of both upper and lower limbs.

Results: The results of this study revealed that 24 (80%), 5 (16.7%), 1 (3.3%) had Acute inflammatory demyelinating polyneuropathy, Acute motor axonal neuropathy and Acute motor sensory axonal neuropathy respectively. The most affected age group was (3-6) years, and the majority of patients had a preceding infection in the past 3 months. Furthermore, 29 patients out of 30 had lost deep tendon reflexes and the H-reflex was absent in 22 (73.3%), however, the F-wave was absent in lower limbs more than upper limbs (46.6%) and (26.6%) respectively. The distal motor latency was abnormal in 121 (82.3%) nerves out of 147 total examined nerves.

Conclusion: Acute inflammatory demyelinating polyneuropathy (AIDP) is the most frequent subtype of GBS, the change in sensory and motor NCS parameters was higher in lower limbs than upper limbs. Proximal segments are more vulnerable to demyelination rather than intermediate or distal nerve segments.

Keywords: GBS (guillain – barre syndrome), NCS (nerve conduction study), AIDP (acute inflammatory demyelinating polyneuropathy), AMAN (acute motor axonal neuropathy), AMSAN (acute motor sensory axonal neuropathy).

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Introduction:

Peripheral neuropathy is a commonly encountered, generalized, non-traumatic disorder affecting multiple peripheral nerves,most severely involving the nerve fibers distally. Ideally it is symmetrical and frequentlyinfluences both motor and sensory fibers virtuallyin equal degree. However, it may also affecteach one selectively or very disproportionately (1). Guillain-Barré syndrome is an autoimmune inflammatory polyneuropathy characterized by flaccid areflexic paralysis and albuminocytologic dissociation in the CSF (2). Male are 1.5 times more likely to be affected than female(3).The acute onset and monophasic disease course can be explained by the preceding infection that triggers a transient immune response to peripheral nerves (4).

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Distal paresthesias evolve into symmetric progressive ascending areflexic motor weakness often in association with facial weakness and (limbs pain and backache) (5). Recovery period of GBS is shorter in children than adults and the mortality rate in children is about 3-5%. Respiratory insufficiency is an ominous event in GBS and can lead to death in these patients if it is not managed properly.Autonomic dysfunction is another main cause of mortality in affected children (6). Diagnosis is based on certain characteristic clinical criteria and exclusion of other causes of polyneuropathy (6). Guillain-Barre syndrome can be classified histopathologically into 2 main types: demyelinating and axonal-degenerating forms. Motor nerves are more vulnerable to be affected than sensory nerves(7). Electrodiagnostic studies are necessary in the estimation of a peripheral neuropathy; and different nerves can be bilaterally compared in order toascertain if there is an actual asymmetry. In addition, confirmingmultifocality (the predilection of one nerve involvement over another one in the same anatomic

area) and length dependence are remarkable principles in electrodiagnostic studying of peripheral neuropathies (8).

Patients and Methods:

Two groups of subjects of either sex were involved in this study, thirty healthy children as the control group and thirty GBS patients as the patient groups of comparable age and sex distribution.Electrophysiological tests of both upper and lower limbs were performed in the first weeks after disease onset which consist of; sensory nerve conduction study (SNCS) for median, ulnar and medial plantar nerves. Distal sensory latency (DSL), sensory nerve action potential amplitude (SNAP) and sensory nerve conduction velocity (SNCV) were performed for each nerve. Furthermore, motor nerve conduction study (MNCS) for median, ulnar and common peroneal (fibular) nerves were performed, which includes; distal motor latency ,compound muscle action potential amplitude (CMAP), motor nerve conduction velocity (MNCV), mean F-wave latency, conduction block (CB%) and temporal dispersion (TD%). Needle EMG was performed for distal and proximal muscle involving: 1st dorsal interosseous muscle for the upper limb,tibialis anterior and extensor digitorum brevis muscles for the lower limb.Insertional activity, spontaneous activity, motor unit action potential (duration, amplitude, and polyphasia %) and interference pattern were considered and evaluated for each muscle.

Statistical analysis:

Chi-Square test was used to test association between dependent and independent variables. Independent sample student Test and one sample T test were used to analyze the continuous data, P value < 0.05 was considered significant.

Results:

A total of 30 patients were admitted to hospital and discharged with the diagnosis of GBS during the study period. Patients were 63.3% male (n=19) and 56.7% female (n=11) figure (1). The most frequent age group affected was (3-6) years (53.3%) and the mean age was (5) years. The most common type of GBS was AIDP (80%) followed by AMAN (16.6%) and AMSAN (3.3%).CSF protein analysis was performed in all patients and the results showed no significant difference between GBS subtypes, table (1).The facial nerve involvement was 33.3% and bulbar was 23.3%.

Table (1): Cerebro-spinal fluid protein analysis among children with GBS Subtypes.

AIDP (24)	Axonal (6)	P-value
Mean ± SD	Mean ± SD	
151 ± 84	172 ± 92	0.8

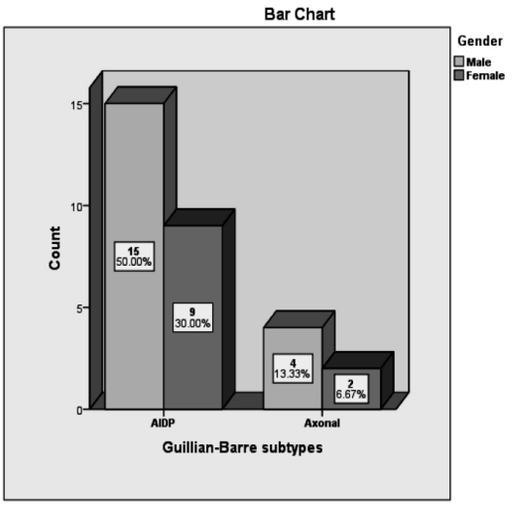

Figure (1): Gender Distribution of GBS subtypes.

The NCS study was revealed that the sensory nerve conduction study showed significant changes when compared to the control group in terms of prolonged distal sensorylatency,reduced SNAP amplitude and slowing of SNCV. The reduction of sensory amplitude in median, ulnar and medial plantar nerves was significant (P=0.001), and the SNCV was significant in lower limbs (medial plantar nerve) (P=0.001). In this study, the sensory motor discrepancy was present in just 8 patients out of 30 GBS patients (26.6%), and it was highest in right ulnar nerve (26.6%) and lowest in right median nerve (16.6%). Concerning motor nerve conduction study, prolonged DML, reduced CMAP amplitude, slowing of MNCV, prolonged mean F-wave latency and prolonged or absent H=reflex were detected in patients subjects compared with control subjects. The differences were statistically significant except for the temporal dispersion of median nerve and left common peroneal nerve as demonstrated in table(2).Analysis of data from different nerve segments whether distal, main nerve trunk or proximal portions of various nerves was applied in this study to find which segment is more affected by demyelination. Therefore, DML, MNCV and F- wave were studied as shown at table (3). The nerve segment with the highest percentage of involvement was the proximal segment 93.19% while the distal segment had the lowest percentage.Regarding EMG study there were several abnormalities in patient group compared to control group in form of reduced recruitments in both subtypes and spontaneous activity (positive sharp waves and fibrillation) which was higher in axonal type compared to demyelinating type especially in the distal lower muscles.

Table (2): motor nerve conduction study of right median and left common personal nerves.

parameter	Study group	Right median nerve Mean ± SD	P-value	Left common peroneal nerve Mean ± SD	P-value
Distal motor latency (m/sec.)	control	1.6 ± 0.7	0.01	2.0 ± 0.1	0.01
	patients	6.2 ± 4.2		7.8 ± 6.5	
CMAP(mV)	control	9.7 ± 0.8	0.01	6.3 ± 0.6	0.01
	patients	8.5 ± 2.4		4.5 ± 2.5	
MNCV (m/sec.)	control	62.4 ± 1.4	0.1	47.1 ± 1.5	0.01
	patients	42.5 ± 17.5		22.7 ± 15.9	
F–wave latency(msec.)	control	19.6 ±1.7	0.01	18.9 ± 1.7	0.02
	patients	36.0 ± 21.8		37.0 ± 29.0	
CB%	control	1.7 ± 0.4	0.01	3.0 ± 0.6	0.01
	patients	21.9 ± 16.4		14.0 ± 12.0	
TD%	control	2.0 ± 0.6	0.6	1.5 ± 0.7	0.1
	patients	4.2 ± 2.8		4.8 ± 2.8	

Table(3): Frequency ofnerve segments involved by demyelination in GBS patients.

No. of Nerves	Nerve	Distal Segment	Main Trunk	Proximal Segment
30	Right Median	25 (83.3%)	24(80.0 %)	26 (86.6%)
29	Left Median	25(86.2%)	22(75.8%)	26 (89.6%)
29	Right Ulnar	25(86.2%)	22(75.8%)	28 (96.5%)
30	Right Common Peroneal	23(76.6%)	29(96.6%)	29 (96.6%)
29	Left Common Peroneal	23(79.3%)	28(96.5%)	28 (96.6%)
Total147		121 (82.3%)	125(85.0)	137(93.2%)

Discussion:

GBS is a rapidly progressive sensory motor disease associated with an absence of reflexes, it presented with sensory symptoms in the lower limbs which marks the onset of the disorder, then it will be followed by rapidly progressive weakness distally that spreads proximally after very short period (9).In this study the male gender was the predominant, male to female was (1.7:1) which is higher than the ratio reported byNachamkin I.et al.(10) which was (1.3:1) in the Mexican population, while it is lower than the ratio reported by Kumar M. et al.2015(11) which was (2.3:1). The mean age for both genderswas 5 years which is higher thanKannan M.et al.2005(5) who reported the mean age was 8 years, the younger age is more associated with infections and vaccinations and this may give the good explanation. According to this study the AIDP is the most frequent type of GBS 80% followed by AMAN then AMSAN 16.7% and 3.3% respectively. In contrast to many reports that showed in China, Japan and Turkey(12, 13, 14) most of GBS patients appear to have AMAN as the commonest type. However another study from Iran reported that AIDP is the most frequent type of GBS among children (15), these findings suggest that, the incidence of AIDP in childhood GBS differs geographically. The reason is unclear but host factors and anteceded infectious agents might be responsible (13).CSF analysisshowedno significant differences between demyelination and axonal form (P=0.8) and this finding was the same as Yadegari S.et al.2014 (15). The elevated protein in the CSF among GBS patients is due to damage of proximal nerve root (myelin or axon) which leads to, release of proteins into CSF(15).In consideration to the NCS; the prolongation of distal sensory and (or) motor latency and slowing of nerve conduction velocity are noted when the fastest and largest conducting nerve fibers are subjected to process of demyelination. While reduction in amplitude of sensory nerve action potential SNAP or compound muscle action potential CMAP mirrors the degree of axonal degeneration and indicates the decline of sensory fibers of nerves, as theaction potential appears to represent the summated action potential of the active fibers under the recording electrodes (16).The discrepancy between sensory conduction study between upper and lower limbs was 6.66% in only 2 patients in which the median nerve was abnormal whilst medial plantar nerve is normal, this result is similar toYe Y.et al.2010 (12) while it is less than what was reported byAlexanderM.et al. 2011(17). This combination of changes between SNAP of upper and lower extremities could reflect an indication of an acquired demyelination disease specifically if it is noted with H-reflex absence (18).Another important parameter is H-reflex which

was absent in 22 patients out of 30 patients (73.3%). However, the remaining 8 patients (26.6%) had prolonged latency .This analysis is lower than that obtained fromGordon P.2001(18) where the absence of H- reflex was 97%, and it is more elevated comparably withYe Y. et al. 2010(19) in which the absence of H-reflex was (62%).Although AIDP has the higher level of H-reflex abnormality than AMAN and AMSAN but there is no significant association between H-reflex and GBS subtypes (P=0.5) and this is the same asYadegari S. et al.2014 (15).Mean F-waves latencies were recorded to detect proximal nerve involvement. F-wave was prolonged or absent in 93.1% of the examined nerves, these results are higher than AlexanderM. et al. 2011(17) who revealed 30.14% and Gordon P.2001 (18) who reported 84%.The main nerve trunk affection was 85.0% of the tested nerves which is considered higher than what was reported from Yadegari S. et al.2014 (15) that was only 33.9%. In this study the distal segment was the least affected by demyelination, where it was (82.3%)in comparison with with proximal and intermediate segments, this finding could be clarified by the fact that, the thick myelinated fibers are more prone to be influenced by demyelination than thin myelinated fibers (20). Therefore, the distal segment may be particularly less affected because of its distance from the cell body whilst, the more proximal segment is more susceptible to be affected by demyelination because of increase in permeability of spinal root blood-nerve barrier owing to the reduction of well-formed perineurium(21).According to needle EMG examination in this study, there were several abnormalities such as appearance of spontaneous activity and reduced recruitment in GBS children. In addition, spontaneous activity (positive sharp waves and fibrillation) predominates in AMAN and AMSAN subtypes rather than demyelinating subtype which is associated with severely ill patients and this finding could be explained by the axonal damage of the tested nerves, this result is similar to other study (18).

Conclusion:

The study concludes that AIDP is the most frequent subtype of Guillain-Barre syndrome followed by AMAN and AMSAN. The more frequent age affected was (5) years with male predominance. The more vulnerable nerve segment that is affected by the process of demyelination is the proximal portion and the least one is distal segment. Late responses (F- wave and H-reflex) affected early in course of disease, in addition the F-wave was absent in lower extremities more than upper extremities while the H-reflex was absent in the majority of patients.

Authors' contributors:

Lamees Mansoor Hussein: MSc. Student who perform this study project including selection of the sample, examination and doing concerned tests also writing the thesis.

Najeeb Hassan Mohammed: Supervisor who design the protocol of the study and support in writing the thesis.

Safaa Hussein Ali: Supervisor who help student in performing the electrophysiological tests and data collection.

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