

Electrophysiologic Findings in Pediatric Guillain Barre Syndrome

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ABSTRACT

Objective: To describe electrophysiologic findings in the pediatric Guillain Barre syndrome (GBS).

Study design: Comparative prospective study.

Place and Duration of Study: Department of Neurology, The Children's Hospital and Institute of Child Health, Lahore Pakistan, from Jun to Dec 2015.

Methodology: Children below 18 years of age, presenting in medical emergency/neurology OPD and fulfilling the clinical case definition of GBS were included for the study. Electrophysiologic studies were performed within 24 hours of admission in all patients.

Results: Out of 83 patients with GBS, 59% were male and 80% were between 3-12 years of age. According to the electrophysiological findings, acute inflammatory demyelinating polyradiculoneuropathy (AIDP) was the most common subtype followed by acute motor axonal neuropathy (AMAN). Reduced CMAP and absent F-response were the most common electrophysiologic findings presented in 70% and 57.8% of patients respectively. However, absent F-response was not specific for any subtype ($p>0.05$). Prolonged motor DL, reduced NCV, temporal dispersion and abnormal F-wave latency were characteristic electrophysiologic features of demyelination ($p\leq 0.001$). However, prolonged motor DL and absent F-wave occurred early in the course of disease while reduced NCV and temporal dispersion observed later.

Conclusion: Electrophysiologic studies were useful in making the appropriate diagnosis to initiate immunotherapy, particularly during first week after onset of weakness when albuminocytologic dissociation may not be present.

Keywords: Acute inflammatory demyelinating polyradiculo neuropathy, Acute motor axonal neuropathy, Guillain Barre syndrome.

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INTRODUCTION

Guillain-Barre syndrome (GBS), an acquired autoimmune mediated polyneuropathy, is classically characterized by an acute, non-febrile, post-infectious illness which usually manifest as symmetrical ascending weakness and areflexia with and without paresthesias.¹ However, sometimes sensory, autonomic, and brainstem abnormalities may be seen. The annual incidence of GBS estimated to be 0.6 cases per 100,000 per year in children.²

The diagnosis of Guillain-Barré syndrome (GBS) is clinical, typically based on the presence of a progressive symmetrical weakness with areflexia. Findings on lumbar puncture support the diagnosis, however, albuminocytologic dissociation do not develop until days to weeks after onset of symptoms.¹

On the basis of electrophysiological criteria, GBS can be classified into following major subtypes: acute inflammatory demyelinating polyradiculoneuropathy (AIDP), acute motor axonal neuropathy (AMAN) and

acute motor sensory axonal neuropathy (AMSAN). In different studies, it was found that AIDP is the more prevalent variety of GBS in children.^{3,4} Prolonged motor DL, reduced NCV, temporal dispersion and abnormal F-wave latency are characteristic electrophysiologic features of demyelination.¹ Although enough data of electrophysiological findings in adult GBS has been reported in literatures, however, there was small data of electrophysiological findings in pediatric GBS particularly from Pakistan. Hence, we planned this study to evaluate the electrophysiological findings in different types of GBS, as early diagnosis of GBS patients can improve outcome by early initiation of immunotherapy.

METHODOLOGY

The comparative prospective study was carried out at the Department of Neurology, The Children's Hospital and Institute of Child Health, Lahore Pakistan, from June to December 2015, after ethics committee approval of the institute. The sample was collected by consecutive sampling. Eighty three children below 18 years of age, presenting in medical emergency or neurology OPD of The Children's

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Hospital, Lahore and fulfilling the clinical case definition

Inclusion Criteria: Children below 18 years of age, presenting in Medical Emergency/Neurology OPD with progressive symmetrical paralysis of both legs and arms associated with areflexia or hyporeflexia with or without limb paresthesias, autonomic dysfunction or cranial nerves involvement of GBS were included.

Exclusion Criteria: All children with an alternating diagnosis for the weakness (hypokalemia, periodic paralysis, botu-lism, spinal cord disease, encephalopathy/encepha-litis) and previous history of GBS were excluded from the study.

Sociodemographic data (age and gender) as well as time from the onset of disease and performing electrophysiologic findings were collected. Lumbar puncture was done following standard protocols and CSF analysis was performed. Electro-physiologic study, including nerve conduction study (NCS) and

spontaneous activity (fibrillations, sharp waves) and motor unit action potential's (MUAP) abnormality (duration, polyphasia, recruitment and interference pattern).

The cases were classified into AIDP, AMAN and AMSAN based on electrophysiologic criteria by Hughes,^{6,7} (see Appendix). However, patients not fulfilling the criteria were classified as equivocal. Student's t test was used for comparative analysis and *p*-value ≤0.05 was considered significant.

RESULTS

A total of 83 patients fulfilling the inclusion criteria were enrolled after informed consent. About of 59% patients were male and the mean age was 6.0±3.16 years (range 1.5-13 years) with the highest frequency (80%) occurring between 3-12 years of age. 80% of children presented within 14 days of illness with median interval of 7 days. According to the electrophysiological findings, the most common type of GBS was AIDP (48%) followed by AMAN (34%) and

Table-I: Clinical profile of the patients at the time of EMG (n=83)

Clinical Profile		AIDP (n=40)	AMAN (n=29)	AMSAN (n=2)	Equivocal (n=8)	Inexcitable (n=4)	<i>p</i> -value AIDP vs AMAN
Duration of weakness at time of EMG	≤14 days	29(72.5%)	25(86.2%)	2(100%)	7(87.5%)	4(100%)	0.173
	>14 days	11(27.5%)	4(13.8%)	-	1(12.5%)	-	
CSF done	Yes	33(82.5%)	16(84.21%)	1(50%)	1(12.5%)	1(25%)	0.807
	No	7(17.5%)	3(15.78%)	1(50%)	7(87.5%)	3(75%)	
CSF albuminocytologic dissociation		24/33(72.7%)	7/16(43.7%)	1/2(50%)	1/3(33.3%)	1/2(50%)	0.048

AIDP= Acute Inflammatory Demyelinating Polyradiculoneuropathy; AMAN= Acute Motor Axonal Neuropathy; AMSAN= Acute Motor Sensory Axonal Neuropathy; GBS= GuillainBarre Syndrome.

needle electromyography were performed within 24-48 hours of admission in all patients by following standard protocol, using surface electrodes and maintaining skin temperature above 32°C. Motor NCS were performed in upper and lower limbs and amplitude, conduction velocities as well as distal latencies were recorded for tibial, peroneal, median and ulnar nerves. Sensory NCS were performed on median and sural nerves by using antidromic techniques and amplitude, conduction velocities as well as distal latencies were measured. Late responses (F- reflex) were performed on tibial/peroneal nerves as well as median/ulnar nerves and their persistence, conduction velocities and shortest F response latencies were measured. Needle electrode examination (NEE) was conducted in deltoid & abductor digiti minimi (upper limb) and tibialis anterior & gastrocnemius (lower limb) as well as lumbar paraspinous muscles; and observed for

AMSAN (2.4%), while 8(9.6%) were equivocal and 4 had inexcitable nerves in all four limbs. For each GBS subtypes clinical findings are summarized in Table-I.

CSF analysis was done in 56 children and albumino-cytologic dissociation was observed in 33(58%). Out of which 72.7% was present in AIDP and 43.7% in AMAN subtype (*p*>0.05). EMG was performed within first 2 weeks of onset of symptoms in 67(81%) children and after 2 weeks in 16(19%) children. The mean duration between onset of symptoms and performing EMG was 9.49±0.5 with range 3-30 days. The results of motor and sensory NCS are summarized in Table-II & III. Respective-ly. Reduced CMAP and absent F-response were the most common findings presented in 70% and 57.8% respectively. However, in AIDP variant, prominent CMAP amplitude reduction was observed in testing nerves of lower limbs, while in AMAN, this reduction was the same in lower as well

as upper limbs ($p<0.001$). Prolonged motor DL and reduced NCV were observed in 100% and 80% cases of AIDP respectively ($p<0.001$). However, DL prolongation was seen early as compared to reduction of

most frequent inexcitable sensory nerve was median nerve 33(40.0%) followed by sural nerve 26(31.0%). Overall, inexcitability was more frequently seen in sensory (36%) than motor nerves (16.8%).

Table-II: Motor Nerve conduction studies in GBS Patients (n=83)

Electrophysiological features	AIDP (n=40)	AMAN (n=29)	AMSAN (n=2)	Equivocal (n=8)	p-value AIDP vs AMAN
Low CMAP amplitude	26(65%)	29(100%)	2(100%)	2(50%)	<0.001
Prolonged Motor DL	40(100%)	-	-	3(37.5%)	<0.001
Reduced NCV	32(80%)	-	-	1(12.5%)	<0.001
CB	18(45%)	5(17.2%)	-	2(50%)	0.001
TD	16(40%)	-	-	-	<0.001
F-wave absent	27(68%)	17(58.6%)	1(50%)	3(37.5%)	0.449
Prolonged F-wave latency	6(15%)	-	-	1(12.5%)	0.029

AIDP= Acute Inflammatory Demyelinating Polyradiculoneuropathy; AMAN= Acute Motor Axonal Neuropathy; AMSAN= Acute Motor Sensory Axonal Neuropathy; CB= Conduction Block; CMAP= Compound Muscle Action Potential; DL= Distal Latency, GBS= Guillain Barre Syndrome; NCV= Nerve Conduction Velocity; TD= temporal dispersion

Table-III: Sensory nerve conduction studies in GBS Patients (n=83)

Electrophysiological features	AIDP (n=40)	AMAN (n=29)	AMSAN (n=2)	Equivocal (n=8)	p-value AIDP vs AMAN
Median Nerve					
Low SNAP amplitude	10(25%)	-	-	4(50%)	0.004
Reduce NCV	-	-	-	-	--
Unexcitable nerves	27(67.5%)	-	2(100%)	-	<0.001
Sural Nerve					
Low SNAP amplitude	5(12.5%)	-	-	2(25%)	0.048
Reduce NCV	-	-	-	-	--
Unexcitable nerves	20(50%)	-	2(100%)	-	<0.001

NCV= Nerve Conduction Velocity; SNAP= Sensory Nerve Action Potential

nerve conduction velocities.

In sensory NCS, prominent difference was seen in each subtype. In case of AIDP, the sensory nerve action potential (SNAP) amplitude showed reduction in 9% ($p=0.004$) and inexcitability in 28% of examined sensory nerves ($p<0.001$), especially when EMG was performed after 2 weeks. However, SNAP amplitude remained preserved in AMAN, while showed inexcitability in all AMSAN cases. Moreover, abnormality in SNAP amplitude was less common in examined sensory nerves of lower limbs (occurring in 40%) than upperlimbs (occurring in 56%).

The most frequent inexcitable motor nerve was peroneal nerve 21(25.3%) followed by ulnar 19(22.8%), tibial 13(15.6%), and median 9(10.8%) nerves. While the

CBs were present in 45% and TD in 40% of cases in AIDP subtype. However, both were seen more frequently when EMG was performed after 2 weeks. Furthermore, 17% of patients with AMAN also had CB but TD was exclusively seen in AIDP patients ($p<0.001$).

Abnormal F-responses (reduced or absent F-wave, prolonged latency of F-wave) were observed in 55.7% of patients. These abnormalities were more commonly present in demyelinating type as compared to axonal type. F-responses were absent in 68% with AIDP and 58% with AMAN and AMSAN ($p>0.05$). Moreover, F-wave latency was prolonged in 9.6%; out of which, 15% were observed in AIDP and 25% in equivocal subtype.

Table-IV: Needle Electrode Examination results in GBS patients (n=83)

Electrophysiological Features	AIDP (n=40)	AMAN (n=29)	AMSAN (n=2)	Equivocal (n=8)	p-value AIDP vs AMAN
Spontaneous activity	1(2.5%)	9(31%)	-	1(12.5%)	0.001
Abnormal MUAP	29(72.5%)	22(75.8%)	2(100%)	5(62.5%)	0.754
Reduced Recruitment	40(100%)	29(100%)	2(100%)	8(100%)	--
Reduced interference pattern	40(100%)	29(100%)	2(100%)	8(100%)	--

MUAP= Motor Unit Action Potential

NEE was performed in all patients and showed fibrillations in 14.4%, which were more frequently observed in axonal variety ($p=0.001$), especially when EMG was performed after 15 days of illness. Table-IV summarises the NEE findings. Furthermore, MUAPs were reduced or absent in 74% of patients but recruitment and interference pattern were reduced in all patients. However, abnormality in MUAPs showed no specific pattern for any subtype ($p>0.05$).

DISCUSSION

GBS is an acquired polyneuropathy that is widely distributed and affects all age groups. In our study, male to female ratio was 1.4:1 with an overall male preponderance of 59% which is comparable to that cited in other studies.^{4,8-11}

In our study, AIDP is the major subtype of GBS accounting for 48% followed by AMAN (34%) and AMSAN (2.4%). This is in accordance with the studies done in Pakistan,^{5,10} and other Asian countries,¹⁰⁻¹³ where AIDP preponderance reported but contrary to that in Japan and some areas of India,^{14,15} where AMAN had been documented the major subtype. Frequency of AMAN variant in our study closely correlate with that of studies in Northeast China,¹² while in others frequency of 10-27% has been reported.

Albuminocytologic dissociation, observed in 74% of patients in our study, was in agreement with other studies.^{12,16} However, statistically significant higher levels of CSF protein were present in AIDP as compared to axonal variant ($p=0.048$).¹⁶ In GBS, the raised protein level of CSF represents the damage of proximal nerve root myelin or axon causing the release of proteins either myelin sheath-associated markers (Myelin basic protein) or axonal damage markers (Neurofilaments, tau, and anti-ganglioside antibodies) into CSF.¹⁷

Reduced CMAP amplitude and absent F-response, the most common findings in our study, are in agreement with other studies.^{12,16} Although reduced CMAP amplitude were observed in both AIDP and axonal variety but these were statistically significant in axonal variety ($p<0.001$). However, CMAP amplitude reduction was more prominent in peroneal and tibial nerves in AIDP while in axonal variants all nerves were equally affected.¹⁸ Lower CMAP amplitude in AIDP cases may be due to proximal CBs.

Prolonged motor DL and reduced NCV, observed in AIDP in our study, also reported in literature reflecting peripheral nerve demyelination.^{12,16} However, DL prolongation was seen early as compared to

reduction of nerve conduction velocities which has also been reported by Yadegari *et al.*¹⁶

Sensory abnormalities were seen in AIDP as well as AMSAN subtype. However, no sensory abnormality was detected in AMAN variant. Moreover, sensory abnormalities were less commonly detected in lower limbs than upper limbs. Other studies have also shown the similar results in sensory NCS.^{12,16}

Inexcitability more commonly seen in sensory nerves as compared to motor nerves, has also been reported by Yadegari *et al.*¹⁶ Low CMAP amplitude or inexcitability seen in early GBS are usually due to either distal CB or axonal degeneration.¹⁹

Although CBs more frequently occurred in AIDP (occurring in 45%), also observed in 18% cases of AMAN. CBs usually indicates segmental demyelination.²⁰ However, it has also been documented in AMAN variant in literature indicating reversible conduction failure at the axolemma of the nodes of Ranvier besides axonal degeneration.^{16,20} Furthermore, temporal dispersion, documented exclusively in 40% of AIDP patients in our study, is highly specific for demyelinating polyneuropathy.²⁰

As mentioned above, abnormal F-responses, the second most common finding after reduced CMAP amplitude in our study, were most frequently observed in AIDP. F-responses were absent in 68% of AIDP and 58% of AMAN and AMSAN patients. However these were not found statistically significant for any subtype ($p>0.05$). Abnormal F-responses have been documented as an important diagnostic finding of acquired polyneuropathy in literature, even in early stages of GBS.²¹ F-wave studies are helpful in evaluation of conduction problems in the proximal part of the nerve. However, abnormal F-responses, more commonly observed in demyelinating polyneuropathy, are not exclusive feature of demyelination. Physiological conduction failure, decreased nerve excitability and axonal degeneration at the level of nerve roots are proposed mechanism for absent F-wave in AMAN subtype.^{22,23} Furthermore, prolonged F-wave latency is the characteristic of demyelination and can be helpful in early diagnosis of AIDP when other features of demyelination (prolonged distal latencies, reduced nerve conduction velocities and temporal dispersion) don't fulfill the diagnostic criteria.²¹⁻²³

Lastly, needle electrode examination showed denervation potentials in the form of fibrillations, which were more common in axonal GBS. Furthermore, these were present in those patients in whom

EMG performed after 15 days of illness. However, abnormal MUAPs, reduce recruitment and interference pattern werenot specific for any subtype.²⁴

CONCLUSION

AIDP was the major subtype of pediatric GBS in our study. Abnormalities of CSF (albuminocytologic dissociation) usually developed after one week of onset of symptoms. During this period, electrophysiologic studies were helpful in making the early diagnosis to initiate the immunotherapy. Prolonged motor DL, reduced NCV, temporal dispersion and abnormal F-wave latency were characteristic features of demyelination. However, prolonged motor DL and absent F-wave occurred early in the course of disease while reduced NCV and temporal dispersion observed later. Conduction block and absent F-wave thoughmore common in AIDP subtype,were also seen in axonal GBS. In equivocal cases repeat study may be helpful for classification of the disease.

LIMITATION OF STUDY

As this study was done in a tertiary care hospital, disease burden and incidence cannot be calculated. To determine the exact incidence multi-institutional studies with large sample size are required. Furthermore, we could not repeat EMG in equivocal and inexcitable groups which might be helpful in further classification of those cases.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

SB: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

TS: Critical review, concept, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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