Original Article

Electrophysiological patterns in patient with Guillain-Barre syndrome

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ABSTRACT

Background: *Guillain-Barre syndrome (GBS) is an acute, frequently severe and fulminant polyradiculoneuropathy that is autoimmune in nature. Incidence and predominant subtypes of GBS differ geographically. Electrophysiology has important role in subtyping GBS. This study aimed to evaluate the electrophysiological findings in patient of GBS.*

Methods: *This was a hospital based cross-sectional descriptive study and conducted at the Department of Neurology in Sir Salimullah Medical College & Mitford Hospital, Dhaka and National Institute of Neurosciences and Hospital, Dhaka during July 2017 to June 2018. Clinically diagnosed 53 patients with GBS were enrolled according to prefixed selection criteria. Detail history taking, clinical examination, nerve conduction study and cerebrospinal fluid (CSF) examination was performed in all cases. Clinical findings, nerve conduction study (NCS) parameters, CSF findings and demographic profiles were evaluated.*

Results: *Mean ± SD age of presentation was 41.64 (±14.56) years and median age was 42.0 years. There were total 33(62 %) males and 20 (38 %) females with male: female ratio of 1.7:1. Clinically two-thirds(62.3%) of patients had both upper and lower limb involvement (62.3%), facial weakness was in 32.1% and 13.2% had bulbar involvement. Acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN) and acute motor sensory axonal neuropathy (AMSAN)were found to be 51%, 32% and 17% respectively. CSFprotein was elevated in most of the patients with a range of 16-725 mg/dl. Highest CSF protein was found in AIDP.*

Conclusion: *Electrophysiological studies play an important role in the early detection; characterization of GBS.In this study, the commonest type of GBS was AIDP. Higher levels of CSF protein, absent H-reflex and F-response, sural sparing and unexcitable nerves are more frequently present in AIDP.*

Key words:*electrophysiological study, flaccid paralysis, Guillain-Barre syndrome, lower motor neuron disease.*

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INTRODUCTION

Guillain-Barre syndrome (GBS) is an acute, frequently severe and fulminant polyradiculoneuropathy that is autoimmune in nature. GBS usually manifests as a rapidly evolving areflexic motor paralysis with or without sensory disturbance. The usual pattern is an ascending paralysis.[1]Although clinical and laboratory findings have an important role in the diagnosis of GBS, electrodiagnostic study (EDS) is the basis for classification of different types of the disease. Based on electrophysiological findings, GBS has three major types: acute inflammatory demyelinating polyne-uropathy (AIDP), acute motor axonal neuropathy (AMAN) and acute motor sensory axonal neuropathy (AMSAN).[2] True and early diagnosis of GBS could impact on its prognosis, as the benefit of immunotherapy is greatest when introduced early, in the first few weeks of disease.

Early electrophysiological confirmation of the diagnosis is even more important as the cerebrospinal fluid (CSF) protein level may frequently be normal within the first week. However, the electrophysiological finding varies in the same patient during the course of disease and characteristic abnormalities may not evolve for several days or weeks.[3] So, the aim of the study was to determine clinical and demographic profile, observation of electrophysiological patterns, comparison of CSF profile among different electrophysiological subtypes of GBS and determination of predominant subtypes of GBS.

METHODS

This study was a hospital based cross-sectional descriptive study and conducted at the Department of Neurology in Sir Salimullah Medical College & Mitford Hospital (SSMC & MH) and National Institute of Neurosciences and Hospital (NINS) during July 2017 to June 2018. Clinically diagnosed 53 GBS patients were enrolled according to selection criteria. Detail history taking, clinical examination, nerve conduction study and CSF examination was performed in all cases. Criteria for entry into the study were follows: (1) adult patients (age> 18 years) who met the Brighton diagnostic criteria for diagnosis of GBS, (2) patients with no preexisting peripheral neuropathy, hypokalemia and transverse myelitis (with shock) and (3) there were no existence of risk factors for peripheral neuropathy like chronic alcohol abuse, connective tissue diseases, chronic kidney disease (CKD) and nutritional deficiency.

Brighton diagnostic criteria for diagnosis of GBS as follows:

a) Bilateral and flaccid weakness of the limbs and
b) Decreased or absent deep tendon reflexes in weak limbs and
c) Monophasic illness pattern and interval between onset and nadir of weakness between 12hours and 28 days and subsequent clinical plateau and
d) Electrophysiologic findings consistent with GBS and
e) Cytoalbuminologic dissociation (i.e., elevation of CSF protein level above laboratory normal value and CSF total white cell count <50cells/μL)

Electrophysiological studies were performed by nerve conduction study (NCS) machine. The standardized techniques and protocols were used.[4] Motor NCS was performed in median, ulnar, tibial and peronealnerve. The distal latency, conduction velocity, amplitude, conduction block (CB) and temporal dispersion (TD)were tested in the same nerves. Sensory study was done in median, ulnar and sural nerves[5] Here amplitude and distal latencies were studied. F-wave study was done in the median, ulnar and tibial nerves. H reflex was studied only in tibial nerve. Study nerves were selected on the basis of clinical data and results of needle electromyography. If both sides were tested, only data from the side with more severe electrophysiological abnormalities were considered.[6-8]

Electrodiagnostic (*EDx*) criteria for types Guillain-Barré syndrome (*GBS*):Following diagnostic criteria were used during the study:

EDx criteria for AIDP

Patient must have one of the following in two or more nerves during the first 2 weeks of illness:

Nerve	Muscle	Motor findings				
		>DL(ms) nCMAP	<CV(m/s) ↓CMAP(≤50%)	nCMAP	↓CMAP(≤50%)	>F/H(m/s)(>120%)
Median	APB	4.84	5.28	45	42.5	37.2
Ulnar	ADM	3.63	3.96	45	42.5	38.4
Radial	EIP	3.19	5.4	45	42.5	
Tibial	AHB	6.38	6.96	36.9	34.85	67.2
Peroneal	EDB	7.15	7.8	39.6	37.4	67.2

Dx criteria for AMAN

No evidence of demyelination as defined in AIDP.

Nerve	Muscle	Motor findings			
		<80%d-CMAP(vM)	<DL(MS)90%	>CV(m/s)90%	<F/H(m/s)120%
Median	APB	3.2	5.28	45	37.2
Ulnar	ADM	4.8	3.96	45	38.4
Radial	EIP	1.6	5.4	45	
Tibial	AHB	3.2	6.96	36.9	67.2
Peroneal	EDB	1.6	7.8	39.6	67.2

EDx criteria for AMSAN

No features of demyelination as defined in AIDP.

Nerve	Muscle	Motor findings				Sensory findings
		<80%d-CMAP(mV)	<DL(ms) 110%	>CV(m/s) 90%	<F/H(m/s) 120%	<50%SNAP(uv)
Median	APB	3.2	5.28	45	37.2	10
Ulnar	ADM	4.8	3.96	45	38.4	8.5
Radial	EIP	1.6	5.4	45		7.5
Tibial	AHB	3.2	6.96	36.9	67.2	
Peroneal	EDB	1.6	7.8	39.6	67.2	
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Ethics statement

Informed written consent was taken from patients in a consent form before collecting data. Proper permission was taken from the concerned departments and local ethical committee.

Data analysis plan

Exploratory data analysis were carried out to describe the study population where categorical variables were summarized using frequency tables while continuous variables were summarized using measures of central tendency and dispersion such as mean, median, percentiles and standard deviation. All statistical analysis was performed using SPSS 23.0 for Windows (SPSS Inc., Chicago, Illinois, USA) level of significance was set at 0.05 and p value <0.05 was considered significant.

RESULTS

Total patients were 53 with a mean age of 41.6 (range18 – 80) years. About two-thirds patients (62.3%) presented with both upper and lower limbs weakness whereas one-third (32.07%) complained of facial weakness and 16.98 % had bulbar paralysis. AIDP was the predominant type (51%). Others are shown in Table I. Patterns of weakness is shown in Table II.

Table I Electrophysiological types of GBS (N=53)

Electrophysiological defined types	Frequency	Percentage
AMAN	17	32
AMSAN	9	17
AIDP	27	51

Table II Clinical findings of the patients (N=53)

Clinical parameters	Frequency	Percentage
Limb weakness		
Upper	8	15.09
Lower	12	22.64
Both	33	62.26
Facial weakness	17	32.07
Bulbar weakness	7	13.2
Extra-ocular muscle weakness	9	16.98
Respiratory failure	6	11.32
Sensory deficit	4	7.55

Cerebrospinal fluid protein was elevated in most of the patients with a range of 16-725 mg/dl. Highest CSF protein was found in AIDP patients. The differences in mean values of CSF proteins were found to be statistically significant (p<0.001).

Table III CSF findings of different types of GBS(N=53)

Types of GBS	Protein (mg/dl)		
	Mean ±SD	Range	p-value*
AIDP (n=27)	122 ± 208	16-725	<0.001
AMAN (n=17)	95 ± 38	30-139	
AMSAN (n=9)	93 ± 46	21-152	

*p-value was calculated by one-sample t-test

Motor distal latencies of median, ulnar, peroneal and tibial nerves were increased in AIDP patients, whereas it was within normal limit in AMAN and AMSAN patients (Table IV). Mean CMAP amplitudes were reduced in all subtypes of GBS patients. Reduction of amplitude was more marked in tibial and peroneal nerve and AMAN variant (Table V). Mean motor nerve conduction velocities were reduced in AIDP, whereas it was normal in AMAN and AMSAN (Table VI).

Table IV Results of distal motor latencies in patients with GBS (N=53)

Nerve	Normal control	AIDP, n=27 (mean±SD)	AMAN, n=17 (mean±SD)	AMSAN n=9 (mean±SD)
Median (ms)	≤4.4	6.3± 1.2	3.8±0.4	3.1±0.8
Ulnar (ms)	≤3.3	4.1±1.1	3.1±0.2	3.2±0.4
Peroneal (ms)	≤6.5	9.2 ± 1.8	5.4±0.7	4.6±0.5
Tibial (ms)	≤5.8	7.1±0.8	7.3±0.9	5.0±0.8

Table V Results of proximal CMAP amplitude of GBS patients (N=53)

Nerve	Normal control	AIDP n=27 (mean±SD)	AMAN, n=17 (mean±SD)	AMSAN, n=9 (mean±SD)
Median (mV)	≥4.0	3.4 ± 1.8	2.9 ± 1.7	3.3±1.7
Ulnar (mV)	≥6.0	4±2.0	3.6 ± 1.9	5.6 ±1.2
Peroneal (mV)	≥2	1.2±1.6	0.9±1.1	0.5 ± 0.3
Tibial (mV)	≥4	2.5±1.9	1.5 ± 1.1	1.5 ± 0.9

Table VI Results of motor nerve conduction velocity of GBS patients (N=53)

Nerve	Normal control	AIDP, n=27 (mean±SD)	AMAN, n=17 (mean±SD)	AMSAN, n=9 (mean±SD)
Median(m/s)	≥49	47.8±7.5	53.6±4.2	52.7±2.1
Ulnar (m/s)	≥49	45±8.2	60 ± 4.6	67.5±1.1
Peroneal (m/s)	≥44	33±9.3	44.8 ± 2.6	35 ± 3.2
Tibial (m/s)	≥41	28 ± 11.4	45 ± 3.1	45.8±1.7

DISCUSSION

GBS is a widely distributed disease throughout the world that affects all ethnic and age groups, but the predominant electrophysiological subtype may differ geographically.[9,10]The study is conducted in a tertiary referral center in Dhaka where subjects who are referred from different areas of the country. So, this study has given some idea about the demographic profile and varieties of GBS in tertiary care hospital at Bangladesh. GBS patients in this study shows a wide range of age(18years to 80 years) with mean age of presentation is 41.64 years (±14.56) and median age of 42.0 years. Maximum incidence of GBS is found in 4th decade followed by 5th and 3rd decade. In addition, mean age of patients is lower in AMAN (2nd decades) and AMSAN (3rd decades) than AIDP in this study.[11-14]About two-thirds patients (62.86%) presented with both upper and lower limbs weakness whereas one-third (31.43%) complained of facial weakness and 13.2% has bulbar paralysis. Antecedent events are present in two thirds of the patients (66%) in preceding weeks (one to four weeks).[15]

A more recent study in India found AIDP being the most prevalent variety (38%) followed by AMAN (36%) and AMSAN (24%).[16] Consequently, the main type of GBS in Middle East and South Asia is probably AIDP. But National Institute of Neurosciences and Hospital, Dhaka, Bangladesh observed AMAN to be the predominant variant and Habib in BIRDEM noted AMSAN to be the predominant type in Bangladesh.[17] Along with the predominance of demyelinating pattern in this part of the world, the axonal variants of GBS seems more prevalent than North America and Europe which include only 5% of GBS and less common than

East of Asia, Japan which have reported AMAN in 45-48% of their GBS.[18,19] Albumino-cytological dissociation (ACD) in CSF analysis showed significant difference between demyelinating and axonal types of GBS in this study but we could not find a cut-off to split these types based on CSF protein.[20] However, the amount of CSF protein in AIDP is significantly higher than axonal variants and very high levels of protein is detected only in demyelinating form. Hence, beside the rise in CSF protein without cell, which may be found in AMAN, the amount of protein should be considered in interpretation of CSF finding in GBS.[21-23]

CB and TD are present in 48.1% and 40.7% of NCS in AIDP whereas no AMAN or AMSAN patient had conduction block or temporal dispersion. Between motor nerves, CB was more frequent in lower limbs especially tibial nerve, which could be related to long length of these nerves.[24] In this study, prolonged F-wave latency is observed only in AIDP cases. In addition, median of F-wave persistency was prominently reduced in this subtype of GBS. In this study absent H reflex is the most common finding in AIDPs, which could reflect its high sensitivity, but since some patients with axonal GBS also represented this feature, specificity is probably low. Unexcitable nerves are more common among examined sensory nerves, especially those evaluated after 2 weeks. The reason is probably related to the time that takes Wallerian degeneration to occur, which is longer for sensory than motor nerves and subsequently results in SNAP amplitude reduction to its nadir later than CMAP amplitude.[25] Lower amplitude of CMAP in the median and tibial nerves in the early phase of AIDP compared to axonal variants may be due to proximal CBs. With progression of time, CMAP amplitudes are decreased more in axonal types which reflected axonal degeneration.[26] This study showed that the most common type of GBS is AIDP. Higher levels of CSF protein, absent H-reflex and F-response, sural sparing and unexcitable nerves are more frequent in this subtype.

Conclusion

In this study, the commonest type of GBS was AIDP followed by AMAN and AMSAN. Higher levels of CSF protein, absent H-reflex and F-response, sural sparing and unexcitable nerves are more frequently present in AIDP.

Limitations

This study has small sample size and study populations were confined to two tertiary care hospitals. Time of NCS and CSF study was not same for all cases and EMG was not done in all cases to confirm axonal involvement.

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