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Original Article

Study of Cerebrospinal Fluid (CSF) and Clinical and Electrophysiological Features of Hospitalized Patients with Gullain-Barre´ Syndrome

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Abstract

***Background**: Since the elimination of poliomyelitis from most part of the world Gullain-Barre' Syndrome (GBS) has been the leading cause of acute flaccid paralysis which leads to substantial morbidity and mortality. Though GBS has received a lot of attention in developed countries, there is a paucity of reports on the GBS from the developing world including Bangladesh. **Objective**: The objective of the study was to correlate clinical, cerebrospinal fluid (CSF) and electrophysiological findings of hospitalized Gullain-Barre´ syndrome patients for early diagnosis and appropriate management. **Materials and Methods**: A total of 47 clinically diagnosed GBS patients admitted in Neurology, Medicine and Pediatrics departments of Dhaka Medical College Hospital (DMCH) were included in this quasi-experimental study. Biochemical, cytological and bacteriological studies of CSF of these patients were done. Electrophysiological studies of all subjects were done and values were compared with upper and lower limits of normal. **Results**: In this study, antecedent event were present in 55.30% cases and upper respiratory infection (23.40%) and gastroenteritis (21.30%) were the commonest antecedent disorders. All the study patients had numbness or paresthesia and limb weakness, and muscle pain was in 44.7% cases, facial weakness in 36.2% cases, ophthalmoplegia or ptosis in 6.4% and bulbar involvement was in 6.4% cases. Most of the patients (95.7%) had deep tendon hypo/areflexia followed by respiratory distress (21.3%), and ataxia (19.1%). Majority of the study patients (57.4%) required one week time to develop maximum deficit. Maximum subjects (70.2%) had motor type GBS followed by sensori-motor type (21.3%), Miller-Fisher type (6.4%) and sensory type (2.1%). Eighty three percent of the study patients had CSF protein concentration >45 mg/dL with mean ± SD of 71.32 ± 20.20 mg/dL (37–112 mg/dL). The cell count in CSF was <5 per mm^3 in 95.7% of the study patients with mean ± SD cell count of 3.2 ± 1.80/mm^3 (2–15 cells per mm^3). The mean ± SD time to perform EMG was 9.4 ± 3.6 days with a range from 5–17 days and the mean ± SD disability grade at that time to EMG was 3.6 ± 0.9 with a range from 2–5. Regarding the electrodiagnostic types, the commonest pattern (40.40%) was found AIDP, AMAN was 29.80%, AMSAN 19.15% and mixed pattern was in 10.65% of the patients. **Conclusion**: This study reveals that clinical, CSF and electrophysiological findings accurately diagnose the GBS patients along with typing of GBS.*

***Key words**: Gullain-Barre´ syndrome; Cerebrospinal fluid; Electrophysiology*

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Introduction

Guillain-Barré syndrome (GBS) remains one of the most fascinating yet challenging conditions despite considerable advances in its understanding and treatment over the past 10 years.[1] Current epidemiolo-

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gical studies suggest an incidence of between 1 and 2/100 000 with marginally more males affected than females.[2] The incidence rises with age although there is a minor peak among young adults.[3]

Although Guillain, Barré, and Strohl did not comment on the association of this illness with infection, extensive clinical observations supported by epidemiological studies suggest that about 75% of patients have a history of preceding symptoms of infection.[4] Serological studies reveal evidence of antecedent infection in about 30%[5-7] to 50% of cases.[8] Case controlled studies confirm a significant association with Campylobacter. jejuni[9], cytomegalovirus[10] and probably Epstein-Barr virus[10].

Guillain-Barré syndrome is part of a spectrum of diseases, identified by its rapid presentation, but closely allied to more chronic diseases such as subacute inflammatory demyelinating polyneuropathy and chronic inflammatory demyelinating neuropathy. Required criteria for the diagnosis of Guillain-Barré syndrome include progressive weakness of more than two limbs, areflexia, and progression for no more than four weeks. Other causes of an acute neuropathy such as lead poisoning, vasculitis, botulism, and porphyria require exclusion. Supportive criteria include relatively mild sensory signs, raised protein in the cerebrospinal fluid (CSF) with a relatively normal cell count, and neurophysiological evidence of conduction block. The CSF protein may be normal in the first week of the illness[11] but may then rise to several g/dL. The CSF cell count usually remains below 500 cells/L. Oligoclonal bands are sometimes found in the CSF.

Electrophysiology testing is important in confirming the diagnosis and in predicting outcome: prolonged distal motor latency, reduced compound motor action potential amplitude, reduced conduction velocity and abnormal spontaneous denervation activity are associated with incomplete recovery.[1-3,12-14] In addition, the recognition of primary axonal motor form of GBS has led to the discovery of several distinctive subtypes using electrophysiological criteria: acute inflammatory demyelinating polyradiculopathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor and sensory axonal neuropathy (AMSAN) and Miller-Fisher syndrome.[11,15] Experience from Europe, North America and Australia has shown that AIDP is the most common form of GBS, with Miller-Fisher syndrome occurring in 2–7% cases.[8,11,15-18]

In Bangladesh, GBS is the commonest cause of polyradiculopathy in hospitals.[19] A case-control study in Bangladesh reports an unusually high frequency of an axonal form of GBS in Bangladesh associated with preceding Campylobacter-associated infections, serum antibodies against GD1a and GM1, slow recovery, and severe residual disability.[20] Considering the importance of early diagnosis to achieve best benefit from immunomodulatory therapy and usefulness of only electrophysiological study rather than CSF study which may be normal in early period, it is an utmost necessity to determine the pattern of clinical and laboratory profile including CSF and electrophysiological pattern of the patients with GBS in our country.

This study is intended to evaluate the clinical pattern, CSF and electrophysiological features of Guillain-Barré syndrome in context of Bangladesh for early diagnosis and proper management and to find any variation of presentation of patients.

Materials and Methods

This cross sectional study was conducted at Dhaka Medical College Hospital which is a tertiary care hospital in Bangladesh during the period from January to December 2008 among the population admitted in Neurology, Medicine and Pediatrics departments of the hospital. Clinically diagnosed 47 GBS patients were enrolled in the study by purposive sampling. Patients with other neurological abnormalities like diabetic neuropathy, or preexisting peripheral neuropathy due to alcohol, poliomyelitis, drug, chemicals or other diseases and patients with stroke were excluded. Detailed history, thorough physical examination including follow-up regarding muscle power, respiratory function and autonomic involvement were obtained and recorded in semi-structured questionnaire. CSF was obtained by lumbar puncture within 10 to 14 days of onset of illness and then sent for examination (biochemical, bacteriological and cytological). Electrophysiological study was done irrespective of duration of illness. Nerve conduction parameters were measured by a standard electromyogram (EMG) machine in a room with a temperature of 37˚C. All patients underwent testing of sural, peroneal, posterior tibial, median and ulnar nerves. A monopolar needle EMG was performed in all patients on leg muscles. Nerves were stimulated using 1ms electrical pulses at a repetition rate of one per second with intensity sufficient to elicit maximum amplitude of compound muscle action potential

(CMAP) and sensory nerve action potential (SNAP). In addition to distal latency, amplitude and conduction velocity of nerves were tested for F wave. The values for each variable were compared with upper and lower limits of normal for National Institute of Neurosciences (NINS), DMCH with adjustment of age for the child cases. Data were analyzed by computer with the help of SPSS version 16.0 software package.

Results

In this study the patients of all age groups were found affected, majority (27.7%) of the patients were in the 41–50 years age group; 61.7% of the patients were male and 38.3% were female with male female ratio 1.6:1. The cases presented in a sporadic fashion and did not demonstrate any variation in incidence throughout the year. Antecedent events were present in 55.30% cases. Upper respiratory infection (23.40%) and gastroenteritis (21.30%) were the commonest antecedent disorders. All the study patients had numbness or paresthesia and limb weakness; muscle pain was in 44.7% of the cases. Facial weakness was in 36.2% cases, ophthalmoplegia or ptosis in 6.4% and bulbar involvement was in 6.4% cases. Most of the patients (95.7%) had deep tendon hypo/areflexia followed by respiratory distress (21.3%), and ataxia (19.1%). Majority (57.4%) of the study patients developed maximum deficit within one week, 34.0% within two weeks and 8.5% within three weeks. In this study it was found that maximum patients (70.2%) had motor type GBS followed by sensori-motor type (21.3%), Miller-Fisher type (6.4%) and sensory type (2.1%). Eighty three percent of the study patients had CSF protein concentration >45 mg/dL with mean ± SD of 71.32 ± 20.20 mg/dL (37–112 mg/dL). The cell count in CSF was <5 per mm^3 in 95.7% of the study patients with mean ± SD cell count of 3.2 ± 1.80 mm^3 (2–15 cells per mm^3). The mean ± SD time to perform EMG was 9.4 ± 3.6 days with a range of 5–17 days and the mean ± SD disability grade at that time to EMG was 3.6 ± 0.9 with a range of 2–5. The results of electrophysiological study and classification according to EPS are given below.

Table I: Results of motor nerve conduction studies of study population

Nerve	Distal latency (ms)		CMAP amplitude (mv)		CV (m/s)		F wave latency (ms)	
	n	%	n	%	n	%	n	%
Median nerve (n=94)								
Unrecordable	0	0.0	0	0.0	0	0.0	34	36.2
Normal	53	56.4	50	53.2	48	51.1	24	25.5
Abnormal	41	43.6	44	46.8	46	48.9	36	38.3
Mean ± SD	5.85 ± 3.88		2.81 ± 2.78		46.83 ± 13.37		33.56 ± 9.36	
Ulnar nerve (n=94)								
Unrecordable	9	9.6	9	9.6	9	9.6	50	53.2
Normal	31	33.0	32	34.0	51	54.3	15	16.0
Abnormal	54	57.4	53	56.4	34	36.2	29	30.9
Mean ± SD	4.54 ± 2.82		2.67 ± 2.33		47.71 ± 14.77		34.26 ± 8.92	
Common peroneal nerve (n=94)								
Unrecordable	17	18.1	17	18.1	17	18.1	60	63.8
Normal	21	22.3	67	71.3	59	62.8	31	33.0
Abnormal	56	59.6	10	10.6	18	19.1	3	3.2
Mean ± SD	7.91 ± 3.22		1.79 ± 1.55		41.32 ± 9.11		51.92 ± 12.44	
Tibial nerve (n=94)								
Unrecordable	16	17.0	16	17.0	16	17.0	59	62.8
Normal	19	20.2	65	69.1	58	61.7	32	34.0
Abnormal	59	62.8	13	13.8	19	20.2	3	3.2
Mean ± SD	7.76 ± 3.13		1.58 ± 1.45		41.73 ± 9.46		52.08 ±12.61	

CV, Conduction velocity; CMAP, Compound muscle action potential

Table II: Results of sensory nerve conduction studies of study population

Nerve	Distal latency (ms)		SNAP amplitude (mv)		CV (m/s)	
	n	%	n	%	n	%
Median nerve (n=94)						
Unrecordable	30	32.4	30	32.4	30	32.4
Normal	55	58.5	52	55.3	24	25.5
Abnormal	9	9.6	12	12.8	40	42.2
Mean ± SD	5.78 ± 3.24		3.25 ± 2.83		52.15 ± 15.40	
Ulnar nerve (n=94)						
Unrecordable	35	37.3	35	37.3	35	37.3
Normal	52	55.3	49	52.1	47	50.0
Abnormal	7	7.4	10	10.6	12	12.7
Mean ± SD	5.10 ± 3.25		2.90 ± 2.55		55.60 ± 17.15	
Sural nerve (n=94)						
Unrecordable	23	24.5	23	24.5	23	24.5
Normal	59	62.8	56	59.6	52	55.3
Abnormal	12	12.8	15	15.9	19	20.2
Mean ± SD	8.45 ± 3.50		1.60 ± 1.48		58.95 ± 17.20	

CV, Conduction velocity; SNAP, Sensory nerve action potential

Table III: Electrodiagnostic types of the study population

	Number	Percentage
AIDP	19	40.40
AMAN	14	29.80
AMSAN	9	19.15
Mixed	5	10.65

AIDP, Acute inflammatory demyelinating polyradiculopathy; AMAN, Acute motor axonal neuropathy; AMSAN, Acute motor and sensory axonal neuropathy

Discussion

In this study the patients of all age groups were affected with 27.7% of the patients in the 41–50 years age group. Alam et al[21] had shown in their series the age of patients from 4–83 years. Similarly, Arami et al[22] and Kundu[23] had observed age from 6–79 years and 12–67 years respectively.

In this study 61.7% cases were male and 38.3% were female with male female ratio 1.6:1. Arami et al[22] found in their studies that 59.2% were male and 40.8% were female and male female ratio was 1.5:1 which closely resembles with this study. Almost similar findings were found by Goh et al[24]; they found male 67.5% and female 32.5% with male female ratio 2:1.

In this study the cases presented in a sporadic fashion and did not demonstrate any variation in incidence throughout the year. Most studies have failed to identify relationship between the incidence of GBS and a season, and the lack of seasonal association may be due to the fact that the most frequent antecedent infections, respiratory and enteric infections, have opposite seasonalities.[10]

In this study a history of antecedent events were present in 26 (55.30%) cases while 21(44.70%) patients failed to give any preceding history of an antecedent event. Most frequent antecedent events in this study were upper respiratory infection (23.40%) and gastroenteritis (21.30%). Bogliun & Beghi[25] had shown in a prospective study that upper respiratory

infection (16.0%), influenza (12.0%), surgery (10.0%) and gastroenteritis (8.0%) were the commonest previous disorders. Upper respiratory infection was the commonest antecedent event in different studies.[22,24,26,27] But the studies done in Asian subcontinent[20,23,28] gastroenteritis was the most frequent previous event. Kundu[23] had found fever alone or in combination with loose motion as the commonest antecedent event (36.66%) followed by loose motion (23.33%). Kalita et al[28] found diarrhea in 37.15% and upper respiratory tract infection in 17.14% of the patients. In the study of Islam et al[20] symptoms of preceding infection were recorded in 69% of the patients, most frequently gastroenteritis (37%) and upper respiratory tract infection (19%).

It was observed in this study that all of the patients had numbness or paresthesia and limb weakness (mainly lower limbs); muscle pain was found in 21(44.7%) patients. Numbness or paresthesia was the commonest type of sensory symptom and limb weakness was more proximal than distal with various degree of motor weakness in all cases. In cranial nerve palsy, facial weakness was in 17 (36.2%), ophthalmoplegia or ptosis in 3 (6.4%) and bulbar involvement was in 3 (6.4%) cases. Most of the patients (95.7%) had deep tendon hypo/areflexia followed by respiratory distress (21.3%) and ataxia (19.1%). Three out of 10 patients with respiratory distress were admitted in intensive care unit, eventually requiring artificial ventilation. Features of autonomic nerve involvement such as sinus tachycardia and bradycardia, hypertension and postural hypotension, constipation, anhydrosis or excessive sweating were present in 7 (14.90%) patients. These features should be considered carefully during patient management to avoid catastrophe.

In this study it was found that more than half (57.4%) of the study patients required one week time to develop maximum deficit, 34.0% two weeks and rest 8.5% three weeks. This is consistent with the study of Hui et al[29] where 45% required one week, 36% two weeks and 20% three weeks to develop maximum deficit. In this study majority of the patients (70.2%) had motor type GBS followed by sensori-motor type (21.3%), Miller-Fisher type (6.4%) and sensory type (2.1%).

In this study 83% patients had CSF protein concentration >45 mg/dL with mean ± SD of 71.32 ± 20.20 mg/dL (37–112 mg/dL). The cell count in CSF was <5 per mm^3 in 95.7% of the study patients with mean ± SD cell count of 3.2 ± 1.80 mm^3 (2–15 cells per mm^3). Hui et al[29] showed in a population based prospective survey of GBS that mean CSF protein concentration was 77 mg/dL when the CSF protein was measured within one week and 100 mg/dL when done after the first week. White blood cell count was below 5/mm^3 in all patients. Similar findings were found by Kundu[23] who observed in his study that cerebrospinal fluid protein was elevated in 90.0% patients and in 93.3% cases cerebrospinal fluid total cell count was up to 5 cells/mm^3 and in only 6.7% patients total cell count was up to 15 cells/mm^3.

In this study it was observed that the mean ± SD time to do NCS and EMG was 9.4 ± 3.6 days with a range of 5 to 17 days and the mean ± SD disability grade at that time was 3.6 ± 0.9 with a range of 2 to 5. Alam et al[21] showed almost identical observations. According to their studies, the mean time to EMG was 13.4 days and the mean disability grade at that time to EMG was 3.9 with a range of 2–5 which supported the present study.

Regarding the electrodiagnostic types of the present study patients, it was observed that the commonest pattern was AIDP (40.40%) followed by AMAN (29.80%), AMSAN (19.15%) and mixed variety (AIDP and AMAN) in 10.65% of the patients. This is almost consistent with the study of Kundu[23] where he observed AIDP 33.3%, AMSAN 26.66%, AMAN and AIDP 26.66% and AMAN 13.33%. But another study in Bangladesh showed that electrophysiologically 67% patients had axonal variant of GBS.[20]

This study reveals that clinical, CSF and electrophysiological findings accurately diagnose the GBS patients along with typing of GBS. The typing of GBS is important not only for diagnosis and treatment but also for the prognosis of the disease. AIDP carries good prognosis and AMAN carries poor prognosis. The others are in between the two. These major patterns of GBS can be difficult to distinguish on clinical grounds alone heightening the importance of electrophysiological studies.

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