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ORIGINAL ARTICLES

Electrophysiological Pattern of Guillain Barre Syndrome among Bangladeshi Patients

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Abstract:

Background: *Guillain Barre Syndrome (GBS) is an acute post infectious immune mediated disorder of peripheral nerve with a marked variation in pathology, clinical presentation and prognosis. Electrophysiology has an important role in early diagnosis, electrophysiological patterns and prediction of prognosis.* ***Objective:*** *The aim of the study is to evaluate the electrophysiological pattern of Guillain Barre Syndrome (GBS) among our patients.* ***Materials and methods:*** *An observational, descriptive study was carried out in the Department of Neurology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from March, 2011 to September, 2012. Total 80 patients of GBS were recruited as the study population considering the inclusion and exclusion criteria. On the basis of nerve conduction study, patients were classified into different groups: (1) acute inflammatory demyelinating polyneuropathy (AIDP) pattern with sensory nerve conduction abnormalities (motor-sensory AIDP), (2) acute inflammatory demyelinating polyneuropathy (AIDP) pattern without sensory nerve conduction abnormalities (motor AIDP), (3) acute motor axonal neuropathy (AMAN), (4) acute motor sensory axonal neuropathy (AMSAN).* ***Results:*** *The range of our patients were between 18 to 68 years and 62.5% were male and 37.5% were female. Among 80 patients that are finally included in the study 50% were AMAN, 27.5% were motor AIDP, 12.5% were motor-sensory AIDP and 10% were AMSAN varieties. According to the nerve conduction study acute motor axonal neuropathy (AMAN) was the predominant subtype. In axonal form of GBS (AMAN), the compound muscle action potential (CMAP) amplitude was more than 80% of lower limit of the normal in at least two motor nerves and in AMSAN the compound muscle action potential (CMAP) amplitude was more than 80% of lower limit of the normal in at least two motor nerves and sensory nerve action potential (SNAP) amplitude was more than 80% of lower limit of the normal in at least two sensory nerves. The characteristic findings supportive of acute inflammatory demyelinating polyradiculoneuropathy include prolonged distal motor latencies(>110% of upper limit of normal), reduced conduction velocities (<90% of lower limit of normal), conduction blocks at non-entrapment sites, temporal dispersion and prolonged* F *wave latencies(>120% of upper limit of normal).* ***Conclusion:*** *This study demonstrated a higher proportion of axonal form of GBS in our country.*

Keywords: *Guillain Barre Syndrome (GBS), acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor sensory axonal neuropathy (AMSAN), compound muscle action potential (CMAP), sensory nerve action potential (SNAP).*

Introduction:

Guillain Barre Syndrome is an acute polyneuropathy that is an acquired immune mediated disorder of the peripheral nervous system which is assumed to result from aberrant immune responses of the peripheral nerves directed against component of the peripheral nerves. The classic forms of GBS affects persons of all ages, but men

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are about 1.5 times more likely to be affected than women[1].The mean annual incidence is1.1 to 1.8 per 100000 population[2]. Clinically the disease is characterized by acute flaccid paralysis, areflexia, mild sensory disturbance and albumino-cytological dissociation in the CSF.

Nerve conduction studies (NCS) play an important role in GBS diagnosis and subtype classification[3,4,5]. It is debated whether the GBS subtypes can be diagnosed by a single electrophysiological study; given that GBS pathophysiology is dynamic, serial studies seem to allow a more accurate diagnosis of subtypes[6].

Since the first description of this disorder in France 1916, GBS has regarded as demyelinating neuropathy and was described as the acute inflammatory demyelinating polyradiculo-neuropathy (AIDP). But the concept has changed substantially after the description of axonal subtypes in China.

In northern China, annual epidemics of acute-onset flaccid paralysis diagnosed clinically as Guillain-Barre syndrome have been recognized for at least 20 years. On the basis of an historical analysis of more than 3,200 patients, distinctive features include most cases occurring during the summer months among children and young adults, most of whom reside in rural areas. Of 90 patients with acute flaccid paralysis, 88 had a distinctive pattern that shares clinical and cerebrospinal fluid findings with demyelinating Guillain-Barre syndrome, but that differs from Guillain-Barre syndrome physiologically and pathologically. The clinical course is marked by rapidly progressive ascending tetraparesis, often with respiratory failure, but without fever, systemic illness, or sensory involvement. Cerebrospinal fluid is acellular, and elevations of protein content occur in the second or third week of illness. Electrodiagnostic studies show normal motor distal latencies and limb conduction velocities, but reduced compound muscle action potential amplitudes. Sensory nerve action potentials and, when elicitable, F waves are within the range of normal[7].

Gullian Barre syndrome (GBS) is classically a clinical diagnosis but electrophysiology and nerve conduction studies (NCS) help in supporting the diagnosis, making a distinction between axonal and demyelinating variants as well as helping in prognostication. The characteristic findings supportive of acute inflammatory demyelinating polyradiculoneuropathy include prolonged distal motor latencies, reduced conduction velocities, conduction blocks at non-entrapment sites, temporal dispersion and prolonged *F* wave latencies. Among the demyelinating variants of GBS two primary subtypes have been described: acute inflammatory demyelinating polyneuropathy (AIDP) pattern with sensory nerve conduction abnormalities (motor-sensory AIDP) and acute inflammatory demyelinating polyneuropathy (AIDP) pattern without sensory nerve conduction abnormalities (motor AIDP). Among the axonal varients two primary subtypes have been described: acute motor axonal neuropathy (AMAN) and acute motor sensory axonal neuropathy (AMSAN). Each subtypes has specific clinical feature, immunopathogenesis, prognosis and have different response to treatment.

In 1859, Landry first described the clinical features of GBS[8]. Gullian, Barre and Strohl subsequently in 1916 suggested the characteristic cerebrospinal fluid (CSF) examination findings of albumin-cytological dissociation in two French soldiers. The role of plasma exchange and intravenous immunoglobulins as efficient treatment modalities was established in the 1980s and 1990s, respectively[9,10].

Gullian Barre syndrome (GBS) has been classically described as an acute inflammatory demyelinating polyradiculoneuropathy (AIDP). However, an increasing number of variants and subtypes have been recognized over the past few decades. The rubric term “Gullian Barre syndrome” also includes axonal and the more restricted variants like Miller Fisher syndrome, which is characterized by a triad of ataxia, ophthalmoplegia and areflexia. Other variants include the so-called pharyngeal-brachial variant, which is characterized by pharyngeal and cervicobrachial weakness; and, the paraparetic variant, in which the weakness is limited to the lower limbs and later progresses to involve the arms.

The abnormalities in NCS may be recorded by the end of first week of illness and are most pronounced by the second week after the onset of weakness. To increase the certainty of diagnosis with NCS and to increase the diagnostic yield, recordings at least four motor nerves, three sensory nerves, *F* waves and H- reflexes should be obtained[11].

One valuable electrophysiological characteristic of GBS is "sural sparing" that denotes a normal sural sensory nerve action potential with abnormal upper extremity sensory nerve responses[12]. This pattern is very unlikely for neuropathies other than AIDP. Sural sparing, persists even the later part of the disease as. Similarly, a high i.e., greater than one, sensory ratio (sural + radial sensory nerve action potentials (SNAPs)/median + ulnar SNAPs) is quite helpful in distinguishing GBS from other polyneuropathies[13]. Another role played by NCS in GBS is in prognostication and in assessing the need and duration of ventilatory support in patients presenting with a severe disease. Low compound muscle action potentials (CMAPs) are most predictive of a poor prognosis[11].

In this study, we have used the criteria of Hadden et al.[3], and Uncini et al.[5], to differentiate the various electrophysiological subtypes of GBS. There are many previous works, which demonstrate the predominance of different subtypes of GBS in different parts of the world. Thus this study was done to know about the frequency and various Electrophysiological pattern of GBS in order to raise the awareness in physicians resulting in an opportunity to avert the sufferings of these patients.

Materials and Methods: This is an observational and descriptive study, which was performed in the Neurology ward, Peripheral Neuropathy Clinic and Neurophysiology laboratory of BSMMU, Dhaka, conducted from March, 2011 to September, 2012. All patients who were diagnosed as GBS were taken as study population. Patients were selected according to the inclusion and exclusion criteria.

Inclusion criteria: 1) Clinically diagnosed GBS patients referred for nerve conduction study.

Exclusion criteria: 1) Known case of diabetes mellitus, 2) Patients with chronic kidney disease(CKD), 3) Patients with chronic liver disease(CLD), 4) H/O toxin exposure or alcoholism, trauma, 5) Muscle disease, motor neuron disease or other genetic disorders affecting nerves and muscles.

Patients were selected from in patient of neurology ward and peripheral neuropathy clinic of neurology OPD. Clinical diagnosis was done by history, physical examination and neurological examination by expert neurologist. Then some routine and relevant investigations were done. Nerve conduction study were performed at least one week after the onset of symptoms. It was performed in the neurophysiology lab. of BSMMU using the NIHON KOHDEN model machine by neurophysiologist.

In motor nerve conduction study, compound muscle action potential (CMAP) amplitude and duration, distal latency, nerve conduction velocities, conduction block and F wave latencies were measured. In sensory nerve conduction study, sensory nerve action potential (SNAP) amplitude, distal latency and nerve conduction velocities were recorded.

Hadden et al. (1998)[3] criteria for diagnosis of GBS:

1. Normal (All the following in all nerves tested)
   DML< 100% ULN
   F wave present with latency < 100% ULN
   MCV> 100% LLN
   dCMAP > 100% LLN
   pCMAP > 100% LLN
   pCMAP/ dCMAP>0.5
2. Primary demyelinating:

   (At least one of the following in each of at least two nerves, or at least two of the following in one nerve if all others are inexcitable and dCMAP > 10% LLN)

   MCV<90% LLN(85% if dCMAP<50% LLN)

   DML>110% ULN(120% if dCMAP<50 LLN)

   pCMAP/dCMAP ratio <0.5 and dCMAP>20% LLN

   F-response latency >120%ULN
3. Primary axonal:
   None of the above features of demyelination in any nerve (except one demyelinating feature

allowed in one nerve if dCMAP <10% LLN), and dCMAP <80% LLN in at least two nerves.

4. Inexcitable:
   dCMAP absent in all nerves (or present in only one nerve with dCMAP<10%LLN)
5. Does not exactly fit criteria for any other group. (DML=Distal motor latency, ULN=Upper limit of normal, MCV=Motor conduction velocity, LLN=Lower limit of normal, dCMAP= Compound muscle action potential amplitude after proximal stimulation).

Considering inclusion and exclusion criteria finally 80 patients were selected for study subjects. After selecting patients were divided into four groups: (1) acute inflammatory demyelinating polyneuropathy (AIDP) pattern with sensory nerve conduction abnormalities (motor-sensory AIDP), (2) acute inflammatory demyelinating polyneuropathy (AIDP) pattern without sensory nerve conduction abnormalities (motor AIDP), (3) acute motor axonal neuropathy (AMAN), (4) acute motor sensory axonal neuropathy (AMSAN).

Statistical analysis:
At the end of data collection, all the data were rechecked, coded and entered in standard statistical software used in BSMMU, data base using SPSS software (Version-24). Quantitative data were expressed as mean ±SD and statistical analysis was done by independent sample t test. The P value <0.05 was considered statistically significant.

Results:
Total 80 patients were included in the study. Table-1 shown distribution of patients according to age group and they were further divided in AMAN, AMSAN, motor AIDP and motor-sensory AIDP. In AMAN variety of GBS maximum clustering of the cases were seen between the ages 21-30 years, in motor AIDP and motor-sensory AIDP 41-50 years. In AMSAN variety of GBS maximum clustering of the cases were seen between the ages 21-30 years.

The age range of our patients was 18 to 68 years. Among total 80 patients, 50 were male and 30 were female. Figure 1 shows distribution of patients according to gender. GBS was more prevalent in male (62.5%) than female (37.5%) and male to female ratio was 1.66:1.

Figure 2 showing the distribution of patients according to electrophysiological subtypes. Among the demyelinating variants of GBS two primary subtypes have been described: acute inflammatory demyelinating polyneuropathy (AIDP) pattern with sensory nerve conduction abnormalities (motor-sensory AIDP) and acute inflammatory demyelinating polyneuropathy (AIDP) pattern

Table-I

Distribution of patients according to age groups (n=80) and electrophysiological subtypes.

Ages(years)	AMAN	AMSAN	Motor AIDP	Motor-sensoryAIDP	Total
	No.(%)	No.(%)	No.(%)	No.(%)	No.(%)
>20	4(05.0)	1(01.25)	1(01.25)	0(00.0)	6(07.5)
21-30	12(15.0)	3(03.75)	2(02.5)	1(01.25)	18(22.5)
31-40	6(07.5)	1(01.25)	3(03.75)	1(01.25)	11(13.75)
41=50	8(10.0)	2(02.5)	8(10.0)	3(03.75)	21(26.25)
51-60	6(07.5)	0(00.0)	7(08.75)	4(05.0)	17(21.25)
>60	4(05.0)	1(01.25)	1(01.25)	1(01.25)	7(08.75)
Total	40(50.0)	8(10.0)	22(27.5)	10(12.5)	80(100.0)

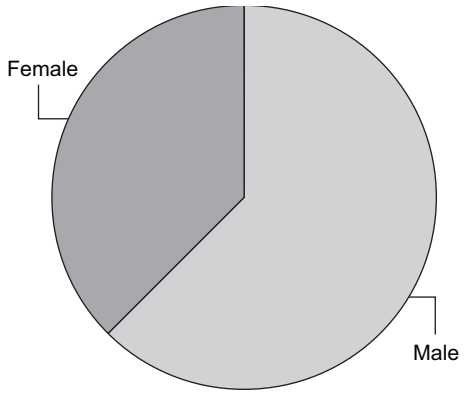

Fig.-1: *Pie chart showing distribution of patients according to gender.*

without sensory nerve conduction abnormalities (motor AIDP). Among the axonal variants two primary subtypes have been described: acute motor axonal neuropathy (AMAN) and acute motor sensory axonal neuropathy (AMSAN). Highest peak of the disease was seen in the AMAN group, which is 50% of total cases and the second peak was seen in the motor AIDP group comprising 27.5%. The third peak of the disease was seen in motor sensory AIDP group comprising 12.5% and the lowest peak was seen in AMSAN variety, comprising only 10%.

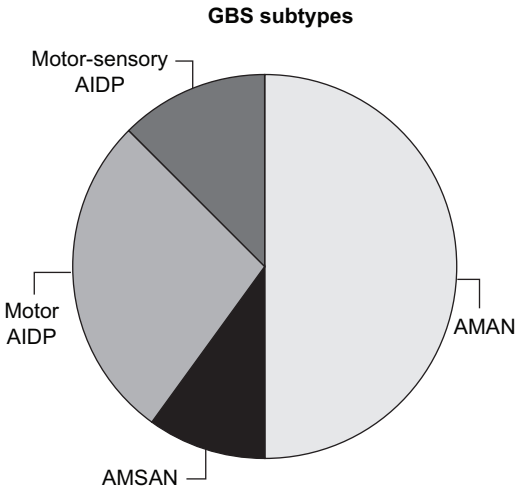

Fig.-2: *Pie chart showing distribution of patients according to electrophysiological subtypes(n=80).*

Discussion:

Our studies showing that axonal subtypes is most common in our country, which is consistent with results from Northern China, where a much higher proportion(65%) of patients had axonal physiology compared with only 24% demyelinating[14]. Guillain Barre syndrome is a widely distributed disease throughout the world, that affects all ethnic and age groups, but the predominant electrophysiological subtypes differs geographically[15].

In our patients 62.5% were male and 37.5% were female and male to female ratio was 1.66:1, which is consistent with previous study where men are about 1.5 times more likely to be affected than women[1]. In the AMAN variety maximum clustering of the cases were seen between the age ranges of 21-30 years. It coincides with study of Yedegari et al.[16] AMAN was observed more in younger ages in many previous study and was mostly reported in epidemics in Northern China[14].AIDP (both motor and motor-sensory) form maximum clustering of cases were seen between age group 41-60, which coincides with previous study of Yedegari et al. [16].

This study was conducted in Bangabandhu Sheikh Mujib Medical University (BSMMU), which is a tertiary referral centre in Bangladesh. So, subjects who are referred from different parts of the country could be a fair representative of the whole population of Bangladesh.

A previous study was done by Islam et al. at 2010 showing highest peak in AMAN variety (56%) followed by AIDP(22%)[17]. In our study highest peak of the disease was seen in the AMAN group, which is 50% of total cases and the second peak was seen in the motor AIDP group comprising 27.5%. The third peak of the disease was seen in motor sensory AIDP group comprising 12.5% and the lowest peak was seen in AMSAN variety, only 10%. So, we have almost similar results with many previous study of our country. A various sets of criteria used in North America and Western Europe have suggested that 56 -87% of GBS patients have AIDP[15]. We have different electrophysiological findings of GBS from Europe and America and similar findings with China, which may due to different pathogenic mechanism.

Conclusion:

In our study AMAN is the most common subtype of Guillain Barre Syndrome (GBS) in Bangladesh, which is 50% of total cases followed by motor AIDP group comprising 27.5% of total cases. The motor sensory AIDP is the third common subtype, comprising 12.5% and AMSAN is the lowest subtype, comprising only 10%. The findings of the study are almost similar to other Asian populations.

Limitation of the study:

The study population was selected from one selected hospital in Dhaka city with limited time of span, so that the results of the study may not be reflect the exact picture of the country. Ideally repeat electrophysiological test should be done for further evaluation. But only a few repeat electrophysiological study could be done for limitation of facilities.

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