ELECTRODIAGNOSTIC FEATURES IN CLINICALLY SUSPECTED GUILLAIN BARRE SYNDROME

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Abstracts: **BACKGROUND AND OBJECTIVE:** The study was undertaken for electrophysiological confirmation of the diagnosis of Guillain Barre Syndrome (GBS) in patients presenting with bilaterally symmetrical progressive weakness of both limbs not exceeding two weeks and inability to walk, following respiratory/gastrointestinal infections suggestive of GBS.**MATERIAL AND METHOD:** 35 patients (mean age= 6.62 ±3.70 years) were referred from the Department of Paediatrics. Nerve Conduction Study adopting standard techniques were carried out using RMS–EMG EP MK II. Distal latency (DL), Amplitude(CMAP and SNAP), conduction velocity (CV) and F-wave of median, ulnar, deep peroneal, posterior tibial, superficial peroneal and sural nerves were recorded. **RESULT AND INTERPRETATION:** 21 patients were confirmed electrodiagnostically as having GBS. In 13 patients, decreased distal CMAP amplitude (<90% of LLN), with no evidence of demyelination confirmed the presence of Primary Axonopathy. 8 patients with normal or decreased distal CMAP amplitude, increased motor DL(>110% of ULN) and decreased motor CV (<90% of LLN), absent or delayed F waves(>120% of ULN) in at least 2 nerves were classified as demyelinating polyneuropathy (Ho et al,1995;1997).**CONCLUSION:** Study supports clinical utility of early electrophysiological confirmation of diagnosis and heterogeneity of GBS.

Key words: Guillain Barre Syndrome, Nerve conduction, Axonopathy, Demyelination

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Introduction:

GBS is an immune mediated disorder characterized by both axonal and demyelinating polyneuropathy. It is an acute polyneuropathy presenting with ascending paralysis, areflexia with or without sensory, autonomic and brainstem abnormalities [1]. Amato et al in 2005, reported earliest features of GBS as oedema of proximal nerves and degeneration of myelin sheath within the first week of illness[2].

Several studies on Human autoimmune neuropathies[3], pathogenesis of GBS[4] have explained immunological attacks on different antigens of peripheral nerves along with diversity of antecedent infection[5] as the cause of heterogeneity of the syndrome as demyelinating (AIDP), motor axonal (AMAN) and motor sensory axonal (AMSAN). Antecedent infection with Campylobacter jejuni results in sharing of identical epitope (molecular mimicry) between infectious agent and neural antigen triggering an autoimmune response against the peripheral nerve, has been found to be associated with AMAN subtype in Northern China[3][4][6]. Immunological attacks of anti - ganglioside IgG antibodies involves compliment activation and phagocytic activity against peripheral nerves resulting in demyelination of nerve sheath or damage to nerve axon or motor end plate[7].

Distinguishing the various subtypes of GBS is difficult on the basis of clinical features alone; emphasizing the importance of electrophysiological studies [8,9]. This study was aimed at electrophysiological confirmation of clinically suspected GBS and identifying demyelination and axonal forms of the disease in our patient population.

Material and Methods:

35 patients (mean age= 6.62 ±3.70 years) reviewed clinically by the treating neurologist were referred for electrophysiological confirmation of the diagnosis of GBS. Cerebrospinal fluid examination was carried out in the Department of Paediatrics. All patients presented with history of fever and respiratory/gastrointestinal infection. The presenting symptoms were bilaterally symmetrical muscle weakness beginning in lower limbs ascending upwards and inability to walk. Electrophysiological studies were performed using RMS EMG EP MK II in Neurophysiology unit. Conduction studies for four motor and four sensory nerves of both limbs bilaterally were done

using supramaximal and subminimal percutaneous stimulation with surface and ring electrodes respectively. Prior to the study the procedure was explained to attendants and informed consent was taken.

Chloral Hydrate or trichlofos was used for sedation in non - cooperative patients.

Electrophysiological variables recorded were Distal Latency (DL), Amplitude, Conduction velocities (CV) of motor and sensory nerves. F-wave studies for motor nerves were also done.

Reference, active and ground electrodes were placed using standard nerve conduction techniques[10].

STIMULUS SITES [10]

NERVE	COMPONENT	DISTAL STIMULATION	PROXIMAL STIMULATION
Median	Motor	Wrist	Elbow
Median	Sensory	Wrist	-------
Ulnar	Motor	Wrist	Elbow
Ulnar	Sensory	Wrist	--------
Tibial	Motor	Behind and proximal to medial malleolus	Popliteal Fossa
Peroneal	Motor	Ankle	Neck of Fibula
Sural	Sensory	Laterally at junction middle and lower third of leg	--------
Superficial Peroneal	Sensory	10-15 cm proximal to lateral malleolus	--------

F-waves were recorded by stimulating at distal motor stimulation site and minimal latency of 10 consecutive stimulation in upper limb and 15 consecutive stimulation in lower limb were recorded.

Based on the results of electro diagnostic study the subtypes of GBS were classified as acute inflammatory demyelinating polyneuropathy (AIDP) Acute Motor Axonal Neuropathy (AMAN) and Acute Motor Sensory Axonal Neuropathy (AMSAN) using criteria adopted from Ho et al (1995,97).

Electrophysiological criteria for classification of Guillain-Barre syndrome (adopted from Ho et al 1995, 97)

Diagnosis of Demyelination:

Present in two or more nerves-

1.Conduction velocity <90% of lower limit normal if amplitude is >50% of lower limit normal; <85% if amplitude <50% of lower limit of normal

2. Distal latency >110% of upper limit of normal if amplitude normal ; >120% of upper limit of normal, if amplitude is less than lower limit of normal

3. F-latency >120% of normal

Diagnosis of primary axonopathy :

1.AMAN subtype

No evidence of demyelination as above

(i) Decrease in CMAP (compound muscle action potential) to <80% of lower limit of normal

2. AMSAN subtype

(i) no evidence of demyelination

(ii) Distal CMAP amplitude <= 80% LLN in ≥2 nerves or inexcitable nerves.

(iii)Sensory nerve action potential(SNAP) amplitude < 50% LLN

Result:

According to clinical and electrophysiological findings, 21 patients had GBS and in remaining 14 patients no evidence of peripheral neuropathy could be diagnosed. Out of 35 patients, 19 patients gave informed consent of lumbar puncture for CSF analysis. In 11 patients albuminocytological dissociation was reported by the referring paediatrician.

In 61.9% patients of GBS electrophysiological findings were similar in proximal and distal segments of the motor nerves studied, in rest of the patients the pattern of electrophysiological findings varied. Out of 21 patients, 13 patients

(61.9%) were classified as AMAN and 8 patients (38.1%) as AIDP subtype of GBS

Table 1: ELECTROPHYSIOLOGICAL FINDINGS OF MOTOR NERVES

	MEDIAN				ULNAR			
	RIGHT		LEFT		RIGHT		LEFT	
	AMAN (n=13)	AIDP (n=8)	AMAN (n=13)	AIDP (n=8)	AMAN (n=13)	AIDP (n=8)	AMAN (n=13)	AIDP (n=8)
DL	1.5 ±0.3	**9.2 ±6.4**	1.8 ±0.6	**10.5 ±5.6**	1.6 ±0.5	**8.6 ±3.5**	1.5 ±0.4	**6.4 ±4.1**
CMAP	**0.9 ±2.2**	3.3 ±0.8	**0.4 ±0.7**	1.5 ±0.9	**0.6 ±1.1**	**2.8 ±2.8**	**0.5 ±0.8**	**2.4 ±2**
MNCV	61 ± 13.5	45 ±7.3	59.5 ±24.2	**33.7 ±15.3**	57.7 ±11	**17.1 ±14.9**	61.9 ±13.5	**25.3 ±18**
	TIBIAL				PERONEAL			
	RIGHT		LEFT		RIGHT		LEFT	
	AMAN (n=13)	AIDP (n=8)	AMAN (n=13)	AIDP (n=8)	AMAN (n=13)	AIDP (n=8)	AMAN (n=13)	AIDP (n=8)
DL	4.2 ±1.9	**8.9 ±5.3**	3.2 ±2.1	**8.9 ±5.6**	1.8 ±1	**5.4 ±4.2**	1.5 ±0.4	**5.9 ±4.2**
CMAP	**0.9 ±2**	**1.5 ±1.25**	**0.9 ±2**	2.1 ±2.4	**0.2 ±0.5**	1.3 ±1.7	**0.4 ±1.04**	**1 ±1.9**
MNCV	74.7 ±22.7	**34.2 ±16.7**	71.2 ±18	**29.9 ±12.5**	73.6 ±10.4	**24.3 ±15.1**	74.6 ±16.6	41.5 ±22.2

***** DL in ms; CMAP in mV; MNCV in m/sec**

F-wave study showed absence of F-wave in 17 patients and delayed F-wave (F - min latency > 31 ms in upper limb and > 61 ms in lower limb) in 4 patients.

Table 2 F - WAVE FINDINGS

N=21	ABSENT		DELAYED		PRESENT
F-wave	17		04		00
	AMAN(11)	AIDP(06)	AMAN(02)	AIDP(02)	

In present series of early GBS patients sensory conduction studies showed normal distal latency, SNAP and conduction velocity. Involvement of motor nerves with sparing of sensory nerves in conduction studies further confirmed the diagnosis of GBS.

Table 3: ELECTROPHYSIOLOGICAL FINDINGS OF SENSORY NERVES

	MEDIAN				ULNAR			
	RIGHT		LEFT		RIGHT		LEFT	
	AMAN	AIDP	AMAN	AIDP	AMAN	AIDP	AMAN	AIDP
DL	1.9±1.1	1.5±0.7	1.2±0.1	1.4±0.3	1.5±0.4	2.0±1.3	1.4±0.8	1.3±0.2
CMAP	25.7±6.7	39.5±7.7	15.6±9.69	34.6±16.8	14.2±8.3	25.7±18.2	15.3±4.0	29.5±5.2
SNCV	65.7±12.8	73.3±11.6	76.9±16.2	68.5±18.5	55.9±24.0	54.8±13.6	57.6±19.8	60.1±22.0
	SURAL				SUPERFICIAL PERONEAL			
	RIGHT		LEFT		RIGHT		LEFT	
	AMAN	AIDP	AMAN	AIDP	AMAN	AIDP	AMAN	AIDP
DL	1.7±0.87	1.6±1.0	1.2±0.5	1.6±0.8	2.0±1.0	1.6±1.0	2.3±1.7	2.2±1.0
CMAP	8.48±3.88	2.7±1.7	8.9±3.4	7.7±5.5	7.4±2.8	17.4±14.8	7.6±1.6	8.5±7.9
SNCV	50.1±9.0	51.6±17.1	57.6±16.0	50.1±13.0	57.7±17.2	49.4±13.7	51.9±16.8	46.9±12.8

**** DL in msec; CMAP in µV; SNCV in m/sec**

Discussion:

Early confirmation of the diagnosis of polyneuropathy has become very important to decide the therapeutic strategies for the treatment of GBS. GBS has clearly defined subgroups, which includes AIDP, AMAN and AMSAN. Pathologically, AIDP is a segmental demyelinating peripheral neuropathy, manifesting with distal paresthesia's,

symmetric weakness of the limbs. Patient suffering from AMAN presents with abrupt onset of rapidly ascending weakness without sensory symptoms and signs. Patient suffering from AMSAN presents with features similar to AMAN associated with sensory deficits.

In the present study, there were a total of 35 patients, the mean age was 6.62 ±3.70 years, the mean interval between the onset of symptoms of illness to electrophysiological study was 9 days. The criteria proposed by Ho et al was used for distinguishing axonal forms of GBS from the AIDP. Out of 21 patients identified as having GBS, the electrophysiological criteria for detection of AMAN was full filled by 61.9% and for AIDP was fulfilled 38.1% patients.

Distribution of GBS subtypes in a study in South India conducted in 2008 was AIDP in 85.2% and axonal in 10.6%[11] and a review study (2011) reported 44.3% axonal forms of GBS, 30.4% had AMAN and 13.6%had AMSAN, and 38.2% had AIDP subtype[12]. In the north Indian study the distribution of GBS subtypes was: AIDP in 86.3%, AMAN in 7.8% and AMSAN in 6.7%[12]. In our study no case of AMSAN was reported. The difference between present study and other Indian studies is probably due to the fact that our study included mainly children aged 1 to 15 years and the other Indian studies had more adults.

In our series, all patients had normal sural and median nerve neurography. The sural sparing pattern in patients with AIDP had been reported by other authors[13,14] .Some authors have reported abnormal SNAPs in sural and median nerves[15]. Absent or prolonged F-wave were common findings in all the cases. In 80.95% of our cases F-wave were absent, prolonged F-wave were found in 19.04% of cases. Similar findings have been reported by other authors in AIDP[16,17].

Conclusion:

The present electrophysiological study was carried out on 35 patients to facilitate early confirmation of clinically diagnosed cases of GBS within 2 weeks of illness. Out of 35 patients 21 were confirmed as having GBS. Out of these 21 patients 61.9% fulfilled the Ho et al criteria for detection of AMAN and 38.1% for AIDP. Thus the heterogeneity of the syndrome was also identified by the study. The limitation of the study is that at the time of electrophysiological nerve studies EMG could not be recorded and serological examination could not be done. The study concludes that electro-diagnosis plays an important role in early detection and characterization of polyneuropathies.

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References:

1. Sharma G, Sood S, Sharma S. Seasonal, Age & Gender Variation of Guillain Barre Syndrome in a Tertiary Referral Center in India. Neuroscience & Medicine, 2013, 4, 23-28.
2. A. Amato, “Guillain Barre Syndrome & Related Dis-orders,” Revista Mexicana de Neurociencia, Vol. 6, No. 5, 2005, Pg. 455-469
3. Ho TW, McKhann GM and Griffin JW. Human autoimmune neuropathies. Annu Rev Neurosci 1998;21:187-226
4. Hughes RA, Hadden RD, Gregson NA and Smith KJ. Pathogenesis of Guillain-Barré syndrome. J Neuroimmunol 1999;100(1-2):74-97
5. Jacobs BC, Rothbart PH, van der Meche FGA et al. The spectrum of antecedent infections in the Guillain-Barré syndrome. A case-control study. Neurology 1998;51:1110-5.
6. Ho TW, Mishu B, Li CY et al. Guillain-Barré syndrome in northern China. Relationship to Campylobacter jejuni infection and anti-glycolipid antibodies. Brain 1995;118:597-605
7. www.immunopaedia.org.2a/index.php?id=658
8. Guillain G, Barre´ JA, Strohl A. Radiculoneuritis syndrome with hyperalbuminosis of cerebrospinal fluid without cellular reaction. Bull Soc Med Hop Paris 1916 ; 40 : 1462-70.

9. McKhann GM, Cornblath DR, Griffin JW, Ho TW, Li CY, Jiang Z, *et al*. Acute motor axonal neuropathy: A frequent cause of acute flaccid paralysis in China. Ann Neurol 1993;33 : 333 - 42.
10. Misra UK, Kalita J: Clinical Neurophysiology. 3rded Elsevier, 2014: 30,39,76-78
11. Gupta D, Nair M, Baheti NN, Sarma PS, Kuruvilla A. Electrodiagnostic and clinical aspects of Guillain Barre´ Syndrome: An analysis of 142 cases. J Clin Neuromuscular Dis 2008;10:42-51
12. Alexander M, Prabhakar A T, Aaron S, ThomasM, Mathew V, Patil A K. Utility of neurophysiological criteria in Guillain Barre´ syndrome: Subtype spectrum from a tertiary referral hospital in India. Neurol India 2011;59: 722-612.
13. Vucic s, Cairns Kd, Black Kr, Chong Pst, Cros d. neurophysiologic findings in early acute Inflammatory demyelinating polyradiculoneuropathy. Clin neuro-physiol 2004;115:2329-35.
14. Al-shekhiee A, Hachwi rn, Preston dc, Katirji B. New criteria for early electrodiagnosis of acute inflammatory demyelinating polyneuropathy. muscle nerve 2005;32:66-72
15. Ranka Baraba, Ana sruk, Šragalj L and Ivan B. Electrophysiological findings in early guillain-barre syndrome. Acta Clin Croat 2011; 50:201-207
16. Ropper Ah, Wijdicks Efm, shahani Bt. Electrodiagnostic abnormalities in 113 consecutive patients with guillain-Barré syndrome. Arch neurology 1990; 47:881-7.

Gordon Ph, Wilbourn AJ. Early electrodiag-nostic findings in Guillain - Barré syndrome. Arch neurol 2001; 58: 913-7.

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