Electrodiagnostic Variations in Guillain-Barré Syndrome - Retrospective Analysis of 95 Patients

Chilvana Patel, Surya Murthy Vishnubhakat***

Abstract :

Introduction : Guillain-Barré syndrome (GBS) is a common cause of acute peripheral neuropathic disease. Electrodiagnostic studies (EDX) are important in diagnosis, classification, treatment and prognosis. **Objective :** To evaluate & define the early and common parameters of EDX for diagnosis of GBS. **Methods :** EDX of total 95 patients with clinical diagnosis of GBS were reviewed & analyzed. **Results :** Out of total 95 patients of GBS, 75 were demyelinating, 13 were axonal and 7 were of mixed type. In demyelinating group, there were 42 men and 33 women from ages 8 to 86; Hoffman reflex was absent in 100% patients; median sensory nerve action potential (SNAP) amplitude was abnormal in 66.6%patients compared to sural SNAP in 19.6%; F wave abnormalities, temporal dispersion and conduction block were found in 64%, 42.2% and 45% respectively. In axonal group, there were 7 men and 6 women from ages 11 to 83; compound motor nerve action potential (CMAP) amplitude was abnormal in (84%) studies & most commonly in tibial nerve. **Conclusion :** In demyelinating GBS, abnormal Hoffman reflex was found to be the most sensitive test and sural nerve sparing is frequently noticed. In axonal GBS, low CMAP in lower extremity was found the most sensitive test for diagnosis of GBS.

Key words : Axonal GBS, CMAP, Demyelinating GBS, Electrodiagnostic study, H reflex

Introduction :

Guillain-Barré syndrome (GBS) is an immune-mediated polyradiculoneuropathy and is the foremost cause of acute, generalized, peripheral neuropathic disease. Electrodiagnostic studies (EDX) are important ancillary method in diagnosis, classification, treatment and prognosis of this illness. Prompt diagnosis of GBS is imperative, as early treatment has shown to improve outcomes.[1,2] However due to varying nature of demyelination and /or axonal involvement, electrical abnormalities may not be extensive or specific enough for a definitive diagnosis in the first two weeks.[3] Common findings in early EDX within 10 days of clinical presentation have been abnormal late responses.[4,5] However, distal temporal dispersion, partial motor conduction block, abnormal blink reflex, presence of multiple A-waves and sural-sparing have been described in many previous studies. [4-9] The objective of our study was to evaluate & define the early and common parameters of electrodiagnostic variations for diagnosis of GBS.

* Assistant Professor

** Vice chair , Dept of Neurology, NS-LIJ health system, NY, 11030, U.S.A.

Correspondence to : Dr. Chilvana Patel,
e-mail: chilvana@gmail.com

Methods :

A retrospectively study of total 95 patients who were presented with clinical diagnosis of GBS over the period of 2005 to 2014 was done. Only those patients who underwent EDX within 2 to 28 days after onset of symptoms were selected for this study. EDX of all these patients were reviewed & analyzed.

Electrophysiological studies were carried out by the two electromyography instrument & by standard methods described by Kimura and Preston and Shapiro. Skin temperature was at or above 32°C when involved limb temperature was raised and maintained. Motor nerve conduction studies (NCS) were performed on upper and lower extremities with use of surface electrodes; these included stimulation of median and ulnar nerves at the wrist and forearm while recording from the abductor pollicis brevis muscle and abductor digitiminimi muscles of the hand. In the lower extremity, stimulation was done at deep peroneal and posterior tibial nerve at the ankle and knee, while recording was done from the extensor digitorum brevis muscle and the abductor hallucis muscle. Sensory NCS were performed with use of antidromic techniques of the median, ulnar, superficial peroneal and sural nerves. F waves were measured with each motor NCS for which a compound

muscle action potential (CMAP) was obtained. H reflex was recorded from gastrocnemius and /or soleus muscles after stimulation of the posterior tibial nerve at the knee. Blink reflex studies and monopolar needle electrode examination was performed in some of the patients.

Statistical Methods:

Descriptive statistics (e.g. mean and standard deviation for continuous variables, proportions and frequencies for categorical variables) were calculated for the entire sample and for each GBS type. Comparisons among categorical variables (e.g. GBS type and gender) were carried out using the Fisher's exact test, and comparisons on continuous variables (e.g. Tibial M percent, age) between the 3 GBS groups was performed using the Kruskal Wallis test. We have also performed frequency analysis of abnormal findings with different nerve conduction parameters.

Outcome Variables:

GBS – Demyelinating, Axonal, or Combined type

Continuous Variables :

• Age (years),	Height (inches)	
• MedianS DL	MedianS CV	MedianSNAP
• UlnarS DL	UlnarS CV	UlnarSNAP
• SupPeroneal DL	SupPeroneal CV	SupPeroneal SNAP
• SuralS DL	SuralS CV	SuralSNAP
• MedianM CV Median F	MedianM DL	MedianCMAP MedianM CB (%)
• UlnarM CV Ulnar F	UlnarM DL	UlnarCMAPUlnarM CB (%)
• PeronealM CV Peroneal F	PeronealM DL	PeronealCMAP PeronealM CB (%)
TibialM CV Tibial F	TibialM DL	TibialCMAP TibialM CB (%)

Categorical Variables :

- Gender
- Median M Disp, Ulnar M Disp, Peroneal M Disp, Tibial M Disp
- Blink reflex (abnormal or normal)
- H Reflex (absent or present)
- Unilateral H (abnormal or not)
- Bilateral H (abnormal or not)
- EMG (reduced recruitment or Normal)

For statistical analysis, the Fisher's exact test, Chi-squared test, Kruskal-Wallis test and analysis of variance (ANOVA) were applied as and where appropriate to get inference of data.

Results :

A total of 95 patients were analyzed. Out of these 95 patients of GBS, 75 (79%) were demyelinating, 13 were axonal (13.7%) and 7 were of combined type (7.4%). About 46% were female (n=44). Median sensory nerve was done on 66% of these patients (n=63), ulnar sensory nerve was done for 61% (n=58). Further, 89 patients (94%) had SupPeroneal, 68 (72%) had Sural, 69 (72.6%) had Median M, 59 (62%) had Ulnar M, 92(97%) had TibialM, 93 (98%) had PeronealM, 69 (72.6%) had MedianF, 59(62%) had UlnarF, 90 (94.7%) had Peroneal F, and 90 (94.7%) had Tibial F studies. For H-reflex, 58 (61%) had it done (though only 52 had H-reflex value being present or absent). Among the 52 with H-reflex values, 1 was Present and the other 51 were absent. Fifty-four patients (56.8%) had EMG done, and 14 (15%) had Blink reflex done. Average height among 94 patients was 66.27 inches and mean age was 52 years. The mean Median SDL was 3.21ms, mean Median SCV was 48.83m/sec and Median SNAP amplitude was 20.96 microvolt, as examples of summary statistics.

The Fisher exact tests results showed evidence of statistical significant associations between type of GBS and each of the following categorical variables: Tibial M Disp (p=0.0063) and H-reflex (p=0.0385). Total 80 patients were presented with valid Tibial M Disp measurements. 66.7% of the demyelinating GBS whereas only 22.2% of the axonal and 20% of the combined type were presented with valid Tibial M Disp measurements. Among subjects with a valid H-reflex value performed (n=52), 50 patients with demyelinating GBS, H reflex were absent, the 1 patient with axonal, H-reflex was present, and the 1 patient

with combined presentation, H reflex was absent.

The results from the Kruskal-Wallis tests provided evidence to suggest a significant difference existed, on a $p<0.05$ scale, on the following continuous measurements among the three groups (e.g. at least one group's median measurement is different from at least one other group's median measurement): Median SCV ($p=0.0175$) and Peroneal CMAP amplitude ($p=0.0094$). The median for Median SCV among demyelinating patients was 48.35, compared with 53.35 in the axonal group and 36.10 in the combined group. The median Peroneal CMAP amplitude among demyelinating patients was 2.6, compared with 0.75 in the axonal group and 1.9 in the combined group.

There are several variables with p-values >0.05 but less than 0.07, which indicates there may significant differences between the groups, but this study may not have been powered enough to detect small differences.

Statistical Sub analysis :

We also performed pair wise comparisons of Median SCV and Peroneal CMAP amplitude measurements to assess if any significant differences exist for either of these measurements among pairs of the differing types of GBS diagnose types (demyelinating, axonal or combined type)

The non-parametric test, Wilcoxon rank sum test (also known as Mann-Whitney U test), was used to perform pair-wise comparisons of measurement differences among the three GBS types. These tests were used as they do not assume the differences or the outcome are normally distributed. Due to the small sample size within 2 of the three GBS types (combined and axonal), the exact test (or the Monte Carlo estimation for the Exact test) was performed as part of each analysis. Further, to adjust for multiple comparisons, the Bonferroni correction method was applied. As such, only results yielding a p-value <0.01667 were considered statistically significant on the two-sided tests. All analyses were carried out in SAS Version 9.3 (Cary, NC).

The results from the Wilcoxon tests provided evidence to suggest a significant difference existed, on a p-value <0.01667 scale, on the following continuous measurements for the following pair wise comparisons:

- Median SCV was significantly different between demyelinating and combined, and between axonal and combined (exact p-value=0.0115 and 0.0022, respectively).
- Peroneal CMAP amplitude was significantly different only between Demyelinating and Axonal ((MC estimate for the exact p-value =0.0024)).

The other pair wise comparisons on the above measurements were not significantly different using the Bonferroni-corrected p-value.

Frequency analysis for abnormal finding for different nerve conduction parameters

In demyelinating group, there were 42 men and 33 women from ages 8 to 86. Hoffmann reflex (H-reflex) was absent in 50 of 50 (100%) patients. Median sensory nerve action potential (SNAP) amplitude was abnormal in 32 (66.6%) of 48 patients, and Sural SNAP amplitude was abnormal in 10 (19.6%) of 51 patients. 132(64%) of 204 F wave studies were abnormal and Median nerve was the most abnormal (35) (67.3%) of 52 studie). Temporal dispersion was found in 103 (42.2%) of 244 studies and conduction block was found in 110 (45%) of 244 studies.

In axonal group, there were 7 men and 6 women from ages 11 to 83. Compound motor nerve action potential (CMAP) amplitude was abnormal in 37 (84%) of 44 studies, of Tibial nerve CMAP amplitude was the most abnormal (13 of 13 patients).

Figure 1: H reflex study in demyelinating group

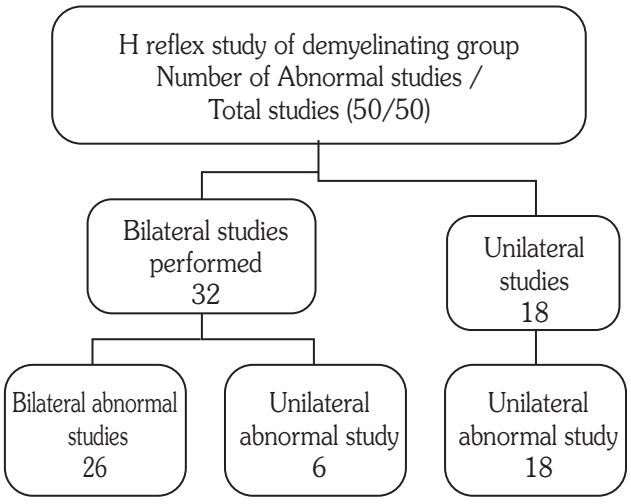

Table 1: NCS abnormalities noted in GBS patients

Nerve studies		Demyelinating	Axonal
Median Sensory	Distal Latency	45.3%	40%
	Conduction Velocity	66.6%	60%
	Amplitude	66.6%	60%
Ulnar Sensory	Latency	31.1%	42%
	Conduction Velocity	51.1%	57.1%
	Amplitude	51.1%	71.4%
Superficial Peroneal Sensory	Latency	17.6%	53.8%
	Conduction Velocity	23.5%	53.8%
	Amplitude	23.5%	46.1%
Sural Sensory	Latency	13.7%	50%
	Conduction Velocity	31.3%	50%
	Amplitude	19.6%	70%
Median Motor	Conduction Velocity	52.8%	63.6%
	Distal Latency	30.1%	54.5%
	Amplitude	37.7%	72.7%
	Temporal Dispersion	24.5%	45.4%
	Conduction Block	73.5%	9%
	F wave	67.3%	37.5%
Ulnar Motor	Conduction Velocity	32.6%	42.8%
	Distal Latency	26.0%	28.5%
	Amplitude	56.5%	57.1%
	Temporal Dispersion	10.8%	42.8%
	Conduction Block	41.3%	14.2%
	F wave	59.0%	60%
Peroneal Motor	Conduction Velocity	43.8%	61.5%
	Distal Latency	53.4%	38.4%
	Amplitude	46.5%	92.3%
	Temporal Dispersion	56.1%	53.8%
	Conduction Block	53.4%	15.3%
	F wave	66.0%	42.8%
Tibial Motor	Conduction Velocity	43.0%	30.7%
	Distal Latency	62.5%	53.8%
	Amplitude	68%	100%
	Temporal Dispersion	61.1%	23%
	Conduction Block	18%	7.6%
	F wave	65.3%	71.4%

Discussion :

The purpose of this study was to identify most common early electrodiagnostic abnormalities found with GBS. Elevation of Cerebrospinal fluid protein and abnormalities in motor nerve conduction studies usually does not occur till 1st week of GBS. However, early diagnosis of GBS is important, because early treatment has shown to improve outcome. [1, 10, 11] We reviewed 95 patients studies who underwent EDX studies from 2 to 28 days after onset of symptoms. Patients were further divided in three groups according to EDX data: demyelinating group (75), axonal group (13) & combined group[7]. Descriptive statistics were calculated for the overall sample and for each GBS type. Comparisons among categorical variables were also performed. We also performed frequency analysis for abnormal finding on EDX data with different GBS types.

In demyelinating group Hoffmann reflex (H-reflex) was absent in 50 of 50 (100%) patients. The results from the Fisher exact tests, show evidence of statistical significant associations between type of GBS and H-reflex (p=0.0385). Among subjects with a valid H-reflex value, all 50 patients with demyelinating GBS were absent, the 1 patient with Axonal was present, and the 1 patient with combined was absent. Literature review revealed an absent H reflex was the most common finding in AIDP patients, with a sensitivity of 95 %.[4] Our study suggests that performing " H" reflex bilaterally also increases ability to diagnose early GBS. Thus, "H" reflex assessment should become part of standard repertoire in early diagnosis of GBS.

In present study, amongst demyelinating group, median sensory nerve action potential (SNAP) amplitude was abnormal in 32 (66.6%) of 48 patients, and Sural SNAP amplitude was abnormal in 10 (19.6%) of 51 patients; the results from the Kruskal-Wallis tests provided evidence & revealed a significant difference existed on a $p<0.05$ scale for the following continuous measurements among the three groups: Median SCV (p=0.0175). The Median SCV among demyelinating patients was 48.35m/sec, compared with 53.35m/sec in the axonal group and 36.10m/sec in the combined group. As per the previous studies, Sensory nerve action potentials were frequently found abnormal in early GBS;[12,13] reduced SNAP amplitudes in association with variable slowing of the sensory distal latencies were the most common abnormalities according to sensory NCS;[14,15,16] a normal sural SNAP amplitude with absent or reduced median and ulnar SNAP amplitudes (sural sparing pattern) was the most specific sensory abnormality in AIDP because it suggests a lack of length-dependent involvement as seen in axonal polyneuropathy;[15, 16, 17] median nerve conduction velocity involvement was likely related with predisposition for entrapment syndrome in patients with GBS (underlying nerve disorder).

F wave studies- As per our data, 132(64%) of 204 F wave studies were abnormal and Median nerve was the most abnormal (35 (67.3%) of 52 studies). Previous studies have shown abnormality of F waves (prolonged latency or absent response) & that was detected in 26 patients (84%).[4]

Temporal dispersion – As per our data, temporal dispersion was found in 103 (42.2%) out of 244 studies. The Fisher exact tests results show evidence of statistical significant associations between type of GBSand each of the following categorical variables: Tibial M Disp (p=0.0063). Among 80 patients with valid Tibial M Disp measurements, 66.7% were presented with demyelinating GBS whereas only 22.2% of the axonal and 20% of the combined type. In the previous studies, dispersion of CMAP was found in 58% (1 nerve in 10% and multiple nerves in 48%). Distal CMAP dispersion may be associated more commonly with demyelination of distal segments and segmental motor conduction slowing across the forearm or foreleg than it is with partial motor conduction block or abnormal distal–proximal temporal dispersion. When added as an "and" criterion, the presence of DCMAP dispersion improves the specificity of the most sensitive criteria (e.g., Albers et al.) [3], albeit with a corresponding decrease in sensitivity. [4]

In axonal group, compound motor nerve action potential (CMAP) amplitude was abnormal in 37 (84%) out of 44 studies & amongst them, Tibial nerve CMAP amplitude was the most abnormal (13 of 13 patients). The results from the Kruskal-Wallis tests provided evidence of a significant difference existed on a $p<0.05$ scale for the following continuous measurements among the three groups. The median Peroneal CMAP amplitude among demyelinating patients was

2.6milivolt, compared with 0.75milivolt in the Axonal group and 1.9milivolt in the combined group. Furthermore, pair wise comparison revealed that Peroneal CMAP was significantly different only between Demyelinating and Axonal (MC estimate for the exact p-value =0.0024). Other similar research [18-21] carried out also revealed that Electrophysiologic studies, including NCS most commonly demonstrate low or absent CMAP.

Conclusion :

Early diagnosis and treatment of GBS improves outcomes, so it was important to identify sensitive and specific EDX parameters to diagnose GBS. Present study suggests, abnormal "H" reflex and Sural sparing patterns are highly suggestive of demyelinating type of GBS. Dispersion of distal CMAP in at least one motor nerve increases specificity to diagnose demyelinating type of GBS. Reduction in CMAP amplitude is highly suggestive of axonal GBS.

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Abbreviations:

M CV- motor conduction velocity m/sec

S CV- sensory conduction velocity m/sec

SNAP- sensory nerve action potential

CMAP- compound motor action potential

M CB- motor nerve conduction block (50% reduction in amplitude)

M Disp- Motor nerve dispersion

F- F wave latency msec

H – Hoffman reflex latency msec

SDL- sensory nerve distal latency msec

MDL- motor nerve distal latency msec

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