



CHANGING PATTERNS OF ELECTROPHYSIOLOGY IN GUILLAIN BARRE SYNDROME, MAKING IT A DYNAMIC PHENOMENON

Neurology

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ABSTRACT

Background: Guillain-Barré Syndrome (GBS) is a rapidly developing autoimmune disorder that affects the peripheral nervous system. Electrophysiological studies play a crucial role in diagnosing this condition. While many previous studies argue against repeated electrophysiological testing in GBS patients, attributing observed changes to the natural progression of the disease, others believe that serial electrophysiology is essential for accurate subtyping and prognostication of the condition. **Aims:** To study the changes in the subtypes in Guillain-Barre syndrome from admission to one month after discharge. **Methods:** This prospective study analysed the electrophysiological changes in Guillain-Barré Syndrome patients at admission and at one month. Motor (Median, Ulnar, Tibial, Peroneal) and sensory (Median, Ulnar, Sural) nerves were tested, identifying and comparing subtypes at both time points. **Results:** Electrophysiological testing in 64 patients showed 19 (29.7%) with AIDP, 19 (29.7%) with an inexcitable subtype, 9 (14.1%) with AMAN, 14 (21.8%) with normal results, and 3 (4.7%) with AMSAN. Out of 64, 8 patients succumbed and the rest 56 were studied with repeat NCS at one month which showed 19(40%) AIDP cases, 11(19.6%) AMAN cases, 6 (10.7%) AMSAN, and 20 (35.7%) inexcitable. The most significant changes occurred in patients with normal NCS at admission. The shift in electrophysiological subtypes over the month was statistically significant ($p = 0.001$). **Conclusion:** This study highlights the dynamic nature of electrophysiological changes in Guillain-Barré Syndrome, emphasizing the need for repeat nerve conduction studies to accurately diagnose the subtypes over time which further helps in better prognostication of the patients.

KEYWORDS

Guillain-Barre syndrome, Serial Electrophysiology, Subtypes of GBS.

INTRODUCTION:

Guillain-Barré Syndrome (GBS) is a rare, rapidly developing autoimmune disorder that affects the peripheral nervous system, typically triggered by a bacterial or viral infection or other preceding events¹. It occurs in 0.9 to 2 out of every 100,000 people worldwide each year, with a slightly higher incidence in males².

Most patients recover well after the acute phase of GBS, with over 80% regaining the ability to walk independently within six months³. The mortality rate during the acute phase is less than 5%⁴. However, about 20% of patients may continue to experience significant disabilities despite receiving standard treatment. The most frequent preceding infection is *Campylobacter jejuni* enteritis, though other infectious agents such as *Mycoplasma pneumoniae*, *Haemophilus influenzae*, Cytomegalovirus, and Epstein-Barr virus can also be triggers⁵.

GBS typically presents with rapidly progressing muscle weakness in both proximal and distal regions of all four limbs, along with sensory loss and areflexia. The maximum weakness is generally reached within four weeks, and most patients reach the maximum disability within two weeks⁶. Cranial nerve involvement, including facial and bulbar muscle palsy and respiratory muscle weakness, is common⁷. Autonomic nerve involvement is also well-documented.

Diagnosis of GBS is primarily clinical, but electrophysiological studies can aid in confirming the diagnosis. The main electrophysiological subtypes are acute inflammatory demyelinating polyradiculoneuropathy (AIDP), which involves both sensory and motor deficits with demyelinating changes, and acute motor axonal neuropathy (AMAN), which is primarily motor and axonal. Another variant, acute motor and sensory axonal neuropathy (AMSAN), involves axonal pathology with sensory involvement⁸.

Most studies advise against serial electrophysiological testing in GBS patients, as the observed changes are considered part of the disease's natural progression⁹. However, some experts argue that repeat electrophysiological studies are crucial for accurately classifying the subtype and predicting the prognosis of GBS patients. Initial nerve conduction studies (NCS) might not effectively distinguish between axonal and demyelinating subtypes due to reversible conduction failure, which is seen in the AMAN subtype and can initially be misdiagnosed as AIDP because of the presence of conduction blocks¹⁰. Additionally, repeating NCS may be justified since initial tests

performed very early in the illness might show normal parameters¹².

Also Electrophysiological parameters may change in the different nerves when performed at different times during the disease course. The motor and sensory conduction are dynamic and may progress even till 3-6 months after the onset of illness¹¹. This study was done with the aim of classifying the study subjects into various subtypes and analyzing the subtypes at admission and at one month of discharge.

METHODS:

Study Design: Prospective study Ethics approval was taken from the Ethics committee.

Duration Of Study: 1 year (may 2023 to may 2024)

Inclusion Criteria: Patients fulfilling Asbury and Comblath criteria were included

Exclusion Criteria: Patients with other neuropathies were excluded

Presence of fever at the time of diagnosis

History of periodic paralysis

A total of 64 study participants were studied. Patients were selected based on specific inclusion and exclusion criteria. clinical history was taken, and a detailed neurological examination was performed on all participants. Electrophysiological tests were conducted on all patients, with follow-up electrophysiological testing performed one month after discharge.

The analysis included Compound Muscle Action Potential (CMAP), Distal Latency (DL), F Latency, Conduction Velocity, and Sensory Nerve Action Potentials (SNAPS). The tested nerves included motor nerves (Median, Ulnar, Tibial, Peroneal) and sensory nerves (Median, Ulnar, Sural). The Hughes Electrophysiological criteria were applied to diagnose and classify patients into four electrophysiological subtypes: AIDP, AMAN, AMSAN, and Inexcitable. Classification was based on nerve conduction studies conducted at the time of admission and one month after discharge. Changes in the electrophysiological diagnosis from admission to post-discharge were analyzed and evaluated.

Statistical analyses were performed using IBM SPSS Statistics for

Windows, Version 25.0. The Chi-square test compared categorical variables. A p-value less than 0.05 was considered statistically significant.

RESULTS:

A total of 64 study participants were selected for the study. The mean age of the study population was 37.8±15. The population showed slight male preponderance with males constituting 59.4% and females constituting 40.6%. The mean MRC sum score was calculated and was found to be 35.9 and the mean Hughes score was found to be 3. The electrophysiological testing was done in 64 patients at admission and 56 patients at one month (8 succumbed due to serious illness, hence repeat testing couldn't be done).

(i) Electrophysiological subtypes at admission: Among the 64 patients, 19 were diagnosed with the AIDP and Inexcitable electrophysiological subtypes, making them the most frequently observed subtype. The next most common subtype was the Normal pattern, found in 14 patients, followed by the AMAN subtype, which was identified in 9 patients. The least common subtype was AMSAN, observed in just 3 patients.(Figure 1)

(ii) Electrophysiological subtypes at one month : (total cases 56)
At one month, 56 cases were studied, revealing that the most frequent electrophysiological subtype was Inexcitable, found in 20 patients, followed by AIDP in 19 patients. The AMAN and AMSAN subtypes were observed in 11 and 6 patients, respectively. Notably, none of the patients exhibited Normal electrophysiology at the one-month. (Figure 2)

(iii) Change In Electrophysiological Subtype From Admission To One Month (Table 1):

Out of 64 patients, 8 succumbed to severe illness hence, repeat electrophysiological study was conducted on the remaining 56 patients. Of these, 33(59%) showed no change in their electrophysiological subtype from admission. However, 23(41%) patients experienced a change in their subtype. The most common changes occurred in patients who initially had normal electrophysiological studies at admission, with all of them showing a different subtype at the one-month.

Table 1: Comparison Of Groups With CGANGE In Subtypes Vs The Group With No Change In Subtype

	Subtype at admission→ Subtype at one month		Percentage
No change	AIDP→AIDP	33/56	59%
	AMAN→AMAN	3	
	AMSAN→AMSAN	2	
	Inexcitable→Inexcitable	13	
Change in subtype	Shift from Normal Normal to AIDP (2)	23/56	41%
	Normal to AMAN (7)		
	Normal to AMSAN (2)		
	Normal to Inexcitable (2)		
	Shift from AIDP AIDP to AMAN (1)	4	
	AIDP TO Inexcitable (3)		
	Shift from Inexcitable Inexcitable to AIDP (1)	2	
	Inexcitable to AMSAN (1)		
	Shift from AMSAN AMSAN to Inexcitable(1)	1	
	Shift from AMAN AMAN to AIDP (1)	3	
AMAN to AMSAN (1)			
AMAN to Inexcitable (1)			

(iv) Electrophysiological Subtypes At Admission And After 1 Month (Table 2):

Table 2 : Comparison Of All The Subtypes At Admission And One Month

Admission	1 month				
	AIDP	AMAN	AMSAN	DIED	Inexcitable
AIDP(n=19)	15	1	0	0	3
AMAN (n=9)	1	3	1	3	1
AMSAN (n=3)	0	0	2	0	1
Inexcitable(n=19)	1	0	1	4	13
Normal(n=14)	2	7	2	1	2
Total (n=64)	19	11	6	8	20

P=0.001*, Fisher Exact test

SHIFTS IN SUBTYPES:

- AIDP:** At admission the total AIDP cases were found to be 10. Out of these 19 cases, 15 remained AIDP, 1 became AMAN and 3 became inexcitable at one month.
- AMAN:** At admission, the total number of AMAN cases was 9. At one month, 3 remained AMAN, 1 became AMSAN, 1 became inexcitable, and 3 succumbed to serious illness.
- AMSAN:** There were 3 total AMSAN cases at admission, and at the end of one month, 2 remained AMSAN, and 1 became inexcitable.
- INEXCITABLE:** A total of 19 cases with inexcitable subtype were seen at admission and out of these, 1 became AIDP, 1 became AMSAN, 4 died, and 13 remained Inexcitable
- NORMAL:** 14 patients had Normal Electrophysiology at admission. At the end of one month, 2 became AIDP, 7 became AMAN, 2 became AMSAN, 1 died, and 2 became inexcitable. None of the patients had normal electrophysiology at one month

Statistical Analysis:

P-value: 0.001, Fisher Exact test (indicating a statistically significant difference in the distribution of electrophysiological subtypes from admission to 1 month later).

DISCUSSION:

This prospective study found a mean age of 37.8 ± 15 years and indicated a slightly higher male prevalence, a finding consistent with findings from other studies¹³. In our study, two-thirds of the patients had a preceding infection, typically presenting as fever or an upper respiratory tract infection, which had resolved by the time neurological symptoms appeared. Similarly, a study by Verma et al. from northern India also identified upper respiratory tract infection as the most common preceding illness¹⁴.

Electrophysiologically the most common subtype according to Hughes criteria noted in our study at admission was AIDP and Inexcitable nerves which were seen in 19 out of 64 patients each. Normal initial NCS study was seen in 14/64 patients probably due to very early study. The other subtypes noted were AMAN and AMSAN in 9/64 patients and 3/64 patients respectively. A study from the neighbouring country of Pakistan showed that of 175 cases, 46% were demyelinating, 31% axonal, and the rest unclassifiable.¹⁵ Initial studies from Northern China¹⁶ showed a predominance of AMAN cases. Later studies from northwest China¹⁷ and Hong Kong¹⁸ reported that the demyelinating pattern was the major electrophysiological subtype there.

Electrophysiological changes in Guillain Barre syndrome are dynamic and can change with time (eg. Secondary axonal changes in AIDP or development of critical illness neuropathy in a patient with GBS)⁹. In our study, it was seen that the initial NCS study showed a higher AIDP and Inexcitable subtypes. Out of the 19 patients with AIDP, there was a shift in the diagnosis in 4 patients, with 3 patients showing Inexcitable nerves at one month and 1 showing AMAN. This change could be considered as secondary axonal damage in AIDP which may be a delayed feature in these cases. Our findings align with those of Kuwabara et al., who described nerve conduction studies (NCS) in typical acute inflammatory demyelinating polyneuropathy (AIDP) patients. They observed a progressive prolongation in distal motor latencies during the 8 weeks following the onset of the disease, likely reflecting the slow-conducting remyelinating fibers of distal nerve segments. In a previous retrospective study, the authors found that GBS patients with positive anti-ganglioside antibodies had normalization or near-normalization of their serial distal motor latencies at 5 weeks whereas antibody-negative patients had progressive demyelination up to 5 weeks²⁰. Also, the recovery of motor CMAP is considered to be delayed as compared to improvement in the

Distal Latencies and Conduction velocities which occur early giving electrophysiological impression of axonal subtype on repeat NCS²⁶. Another explanation for this change in diagnosis is the relatively low sensitivity of the diagnostic criteria, estimated to be 20-30%²⁵.

All cases that were initially normal electrophysiologically showed a change in subtype, highlighting the importance of repeat NCS studies in patients suspected of having Guillain-Barré syndrome. Among the 14 initially normal cases, 2 shifted to AIDP (14.23%), 7 to AMAN (50%), 2 to AMSAN (14.23%), 2 became inexcitable (14.23%) and 1 patient succumbed due to severe illness (7.2%) by the end of one month. This finding aligns with previous studies that indicated electrophysiological tests conducted within the first five days of symptom onset may be normal or inconclusive, with changes often becoming evident after one week^{21,22,23}.

In our study, the total AMAN diagnosed at admission was 9. At the end of one month out of these 9 patients, 3 patients died and the electrophysiological tests of the rest of the cases showed that 3 remained AMAN, 1 shifted to AMSAN, one to AIDP, and one to inexcitable. The progression of AMAN to AMSAN and AMAN to inexcitable could be explained by the hypothesis put forward by Albers et al., which suggests that sensory and motor conduction abnormalities are dynamic and evolve progressively after the onset of the illness. They also noted that changes in sensory nerves tend to occur later than those in motor nerves²⁴. The shift from AMAN to AIDP could be attributed to an initial misdiagnosis, likely due to the lower sensitivity of the diagnostic criteria for axonal subtypes in the early stages of the illness²⁵.

Out of the 3 AMSAN cases diagnosed initially, 2 remained AMSAN at one month and one had Inexcitable subtype at one month. This shift in the subtype was attributed to the dynamic changes in the nerve conduction abnormalities which resulted in inexcitable nerves at the end of one month (Albers et al.,)²⁴. In our study, a total of 19 patients had inexcitable subtype at admission out of which 13 remained the same at one month, one turned out to be AIDP, 1 became AMSAN and 4 died. The Initial diagnosis of Inexcitable nerves was attributed to either severe demyelination or severe axonal injury resulting in inexcitable nerves. Shift in the diagnosis from Inexcitable to AIDP and AMSAN was considered due to partial improvement in the nerves at one month.

CONCLUSION:

This study highlights the dynamic nature of electrophysiological changes in Guillain-Barré Syndrome, emphasizing the need for repeat nerve conduction studies to accurately diagnose subtypes over time, which further helps in better prognostication of the patients.

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Conflict Of Interest - Nil

Figure 1 showing electrophysiological subtypes at admission

Figure 2 Showing electrophysiological subtypes at one month

REFERENCES

- McGrogan A, Madle GC, Seaman HE, et al. The epidemiology of Guillain-Barré syndrome worldwide. *Neuroepidemiology* 2009;32:150-63.
- Sejvar JJ, Baughman AL, Wise M, Morgan OW. Population incidence of Guillain-Barré syndrome: A systematic review and meta-analysis. *Neuroepidemiology* 2011;36:123-33.
- van den Berg B, Walgaard C, Drenthen J, Fokke C, Jacobs BC, van Doorn PA. Guillain-Barré syndrome: pathogenesis, diagnosis, treatment and prognosis. *Nat Rev Neurol*. 2014 Aug;10(8):469-82
- Alsheklee A, Hussain Z, Sultan B, Katirji B. Guillain-Barré syndrome: incidence and mortality rates in US hospitals. *Neurology*. 2008 Apr 29;70(18):1608-13
- Jacobs, B.C.; Rothbarth, P.H.; van der Meché, F.; Herbrink, P.; Schmitz, P.I.; de Klerk, M.A.; van Doorn, P.A. The spectrum of antecedent infections in Guillain-Barré syndrome. *Neurology* 1998, 51, 1110-1115.
- Tosun A, Dursun Ş, Akyıldız UO, Oktay S, Tataroğlu C. Acute motor-sensory axonal neuropathy with hyperreflexia in Guillain-Barré syndrome. *J Child Neurol*. 2015 Apr;30(5):637-40
- Fokke C, van den Berg B, Drenthen J, Walgaard C, van Doorn PA, Jacobs BC. Diagnosis of Guillain-Barré syndrome and validation of Brighton criteria. *Brain*. 2014 Jan;137(Pt 1):33-43
- Yuki N, Hartung H-P. Guillain-Barré syndrome. *N Engl J Med* 2012;366:2294-304
- Ibrahim J, Grapperon AM, Manfredonia F, van den Bergh PY, Attarian S, Rajabally YA. Serial electrophysiology in Guillain-Barré syndrome: A retrospective cohort and case-by-case multicentre analysis. *Acta Neurol Scand*. 2018 Mar;137(3):335-340. doi: 10.1111/ane.12872. Epub 2017 Nov 21. PMID: 29164611.
- Antonino Uncini, Satoshi Kuwabara, Electrodiagnostic criteria for Guillain-Barré syndrome: A critical revision and the need for an update, *Clinical Neurophysiology*, Volume 123, Issue 8, 2012, Pages 1487-1495, ISSN 1388-2457, doi.org/10.1016/j.clinph.2012.01.025.

- Guémy C, Durand M-C, Brisset M, Nicolas G. Changes in electrophysiological findings suggestive of demyelination following Guillain-Barré syndrome: A retrospective study. *Muscle & Nerve*. 2023;67(5):394-400. doi:10.1002/mus.27803
- Berciano J, Orizaola P, Gallardo E, Pelayo-Negro AL, Sánchez-Juan P, Infante J, Sedano MJ. Very early Guillain-Barré syndrome: A clinical-electrophysiological and ultrasonographic study. *Clin Neurophysiol Pract*. 2019 Nov 30;5:1-9. doi: 10.1016/j.cnp.2019.11.003. PMID: 31886449; PMCID: PMC6923288.
- Böyükbaşı F, Ersen G, Gündüz A, Karaali-Savrun F, Yazici S, Uzun N, Akalin MA, Kiziltan ME. Guillain-Barré Syndrome and Its Variants: Clinical Course and Prognostic Factors. *Noro Psikiyatir Ars*. 2019 Mar;56(1):71-74. doi: 10.5152/npa.2017.18091. Epub 2018 Jul 5. PMID: 30911241; PMCID: PMC6427085.
- Verma, R., Sharma, P., & Garg, R. K. (2011). *Clinical profile and outcome of Guillain-Barré syndrome in a tertiary care hospital in India*. *Journal of Clinical Neuroscience*, 18(3), 348-352. doi:10.1016/j.jocn.2011
- Shafiqat S, Khealani BA, Awan F, et al. Guillain-Barré syndrome in Pakistan: similarity of demyelinating and axonal variants. *Eur J Neurol*. 2006;13:662-665. (Pakistan study)
- Pieter A van Doorn, Liselotte Ruts, Bart C Jacobs, Clinical features, pathogenesis, and treatment of Guillain-Barré syndrome, *The Lancet Neurology*, Volume 7, Issue 10, 2008
- Jiang W, Wang HD, Huang YG, et al. Guillain-Barré syndrome in northwestern China. *Electromyogr Clin (china variants) Neurophysiol*. 2001;41:387-391.
- Hui AC, Chow KM, Tang AS, et al. Electrophysiological, clinical and epidemiological study of Guillain-Barré syndrome in Hong Kong Chinese. *J Clin Neurosci*. 2005;12:134-136.
- N. Shahrizaila, K.J. Goh, S. Abdullah, R. Kuppusamy, N. Yuki, Two sets of nerve conduction studies may suffice in reaching a reliable electrodiagnosis in Guillain-Barré syndrome, *Clin. Neurophysiol*. 124 (2013) 1456-1459
- Kuwabara S, Ogawara K, Misawa S, Koga M, Mori M, Hiraga A, et al. Does Campylobacter jejuni infection elicit "demyelinating" Guillain-Barré syndrome? *Neurology* 2004;63:529-33.
- Gordon P.H., Wilbourn A.J. Early electrodiagnostic findings in Guillain-Barré syndrome. *Arch. Neurol*. 2001;58:913-917. [PubMed] [Google Scholar]
- Griffin J.W., Li C.Y., Ho T.W., Tian M., Gao C.Y., Xue P. Pathology of the motor-sensory axonal Guillain-Barré syndrome. *Ann. Neurol*. 1996;39:17-28. [PubMed] [Google Scholar]
- Grimm A., Décard B.F., Axer H. Ultrasonography of the peripheral nervous system in the early stage of Guillain-Barré syndrome. *J. Peripher. Nerv. Syst*. 2014;19:234-241. [PubMed] [Google Scholar]
- Albers JW, Donofrio PD, McGonagle TK. Sequential electrodiagnostic abnormalities in acute inflammatory demyelinating polyradiculoneuropathy. *Muscle Nerve*. 1985 Jul-Aug;8(6):528-39. doi: 10.1002/mus.880080609. PMID: 16758578.
- Ibrahim J, Grapperon A-M, Manfredonia F, van den Bergh PY, Attarian S, Rajabally YA. Serial electrophysiology in Guillain-Barré syndrome: A retrospective cohort and case-by-case multicentre analysis. *Acta Neurol Scand*. 2017;00:1-6.
- Nortina Shahrizaila et al., Two sets of nerve conduction studies may suffice in reaching a reliable electrodiagnosis in Guillain-Barré syndrome *Clinical Neurophysiology* 124 (2013) 1456-1459.