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Original article

Utility of Sequential Nerve Conduction Studies and Electromyography in Early Guillain-Barré Syndrome: A Clinical and Electrophysiological Study

Aya M. Elshebl[a], Khaled Sallam[a], Ayat Allah F. Hussein[b], Shaimaa M. Kasem[a]

[a] Department of Neuropsychiatry, Faculty of Medicine Benha University, Egypt. [b] Department of clinical Neuropsychiatry, Faculty of Medicine, Cairo University, Egypt.

Corresponding to: Aya M. Elshebl, Department of Neuropsychiatry, Faculty of Medicine, Benha University, Egypt.

Email:

aya.shebl@fmed.bu.edu.eg

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Abstract:

Background: Guillain-Barré syndrome (GBS) is the most common cause of acute flaccid paralysis. Nerve conduction studies (NCS) play an important role in GBS diagnosis and subtype classification but diagnosis of GBS in the very early stage may be challenging. The clinical presentation, course, the clinical recovery and outcome of GBS all are variable. **Aim of the work:** Our aim was to evaluate the clinical and neurophysiological findings of early Guillain-Barré syndrome and to identify factors that influence outcome. **Patient and Methods:** we prospectively recruited patients from clinical neurophysiology unit in Kasr Al –Ainy Hospitals and Benha University Hospitals, aimed to evaluate the clinical and neurophysiological findings of early GBS and to identify factors that influence outcome. The studied sample was 17 patients of GBS fulfilling its criteria**. Results:** majority of the patients were AIDP (76.5%), while (23.5 %) of patients were axonal (either AMAN or AMSAN)**.** Predictors of poor outcome were old age, cranial nerve dysfunction and respiratory muscle dysfunction. **Conclusion:** Electro-physiological studies play an important role in the early detection of GBS. Early diagnosis of GBS is essential as early treatment decreases the duration of GBS and its severity. Clinical presentation, course and outcome of GBS can be variable among patients.

Key Words: Early Guillain Barre Syndrome, conduction studies, outcome of Guillain Barre Syndrome

Abbreviation: Nerve conduction studies **(NCS),** Guillain-Barré Syndrome **(GBS),** acute inflammatory demyelinating polyneuropathy **(AIDP),** acute motor axonal neuropathy **(AMAN),** and acute motor sensory axonal neuropathy **(AMSAN)**

Introduction:

Guillain–Barré syndrome (GBS) is an acute polyradiculoneuropathy, characterized by a rapidly progressive, nearly symmetrical, flaccid weakness of the limbs. The clinical presentation, course, and the clinical recovery and outcome of GBS all are variable ***(1).***

GBS mortality ranges from 3% to 13%, and severe sequels might develop in 20% of the cases ***(2).*** It has been demonstrated that early diagnosis and proper treatment administered at a very early stage could shorten its course, reduce its severity, and decrease the possibility of mechanical ventilation ***(3).*** So, diagnosis of GBS requires medical history and physical examination results, assisted by specific electrophysiological examination and characteristic cytoalbuminologic dissociation in cerebrospinal fluid ***(4).*** GBS can be divided into demyelinating and axonal forms. The most frequent subtype of GBS is AIDP, while a few are the axonal form of GBS ***(5).***

The neurophysiological and pathological findings of AIDP indicate that demyelination of motor nerves is focal and patchy, so multiple segments of nerves need to be tested. The examination of multiple nerves and multiple segments of nerves could greatly improve diagnostic efficiency especially in the early stage. Many studies have begun to pay attention to the neurophysiological finding of GBS in the very early stage .Also, pathological hallmarks of AIDP and AMAN at early stage may be indistinguishable, and the observation of serial electrophysiological changes is important to accurately delineate and define the electrophysiological pattern and the GBS subtype ***(6).***

This study was conducted to examine the clinical presentation and functional outcomes in early GBS.

Patients and Methods

This study was a prospective cohort study, conducted at clinical neurophysiology unit in Kasr Al –Ainy Hospital and Benha University Hospitals, aimed to evaluate the clinical and neurophysiological findings of early GBS and to identify factors that influence outcome. The studied sample was 17 patients of GBS fulfilling its criteria ***(7).***

Inclusion criteria:

- Patients were recruited and diagnosed according to criteria of the National Institute of Neurological Disorders and Stroke (NINDS) (revised form 1990) ***(8)*** and the Brighton Collaboration in 2014 ***(7)*** during the period from November 2021 till March 2023.

Exclusion criteria:

- All patients not fulfilling the criteria of GBS.
- Patients with metabolic or electrolyte disturbance as diabetes mellitus, chronic kidney disease.

- Previous history of any neurological disorder of lower motor neuron nature.
- Previous history of any medications that affect result of EMG and NCS as statins**.**

Ethical consideration:

The protocol of the study was approved by the Research Ethics Committee of Faculty of Medicine, Benha University. Informed written consent was obtained from all patients or their relatives.

All patients were subjected to: (1) General data including:

- Demographic data and detailed neurological history.
- Special interest was given to measurement of the blood pressure and pulse rate for any autonomic dysfunction as well as the temperature for exclusion of any infection.

(2) Neurological Examination:

- With special attention on cranial nerves examination, the degree of affection of the motor and sensory systems as well as the deep tendon reflexes.

I. Motor system examination: The muscle power was graded according to the Medical Research Council scale (MRC) ***(9).*** Grade 5 (Normal): complete range of motion against gravity and full resistance. Grade 4 (Good): complete range of motion against gravity with some resistance. Grade 3 (Fair): complete range of motion against gravity. Grade 2 (Poor): complete range of motion with gravity eliminated. Grade 1 (Trace): slight muscle contraction, no joint motion. Grade 0 (Zero): no evidence of contraction.

II. Hughes functional grading scale (HFGS) which provides a measure of disability and to rate clinical performance ***(10).*** Motor function deficits were scored on the HFGS scale, ranging from 0 to 6, with higher numbers indicating more severe disability. it was done for all the patients at 2 time (before and after treatment) and the HFGS score was defined as follows***(10):***

Hughes score	**Clinical performance**
0	healthy state
1	minor symptoms and capable of running
2	Able to walk 5 meters or more without assistance but unable to run
3	able to walk 5 m across an open space with help
4	bedridden or chair-bound
5	require assisted ventilation for at least a part of the day
6	dead

- Presence of respiratory muscle dysfunction.
- Presence of bowel or bladder dysfunction.

(3) Electrophysiological studies: It was carried out by using Viking Natus machine. Those studies were carried out to the patients within 48–72 h of admission and after 3 weeks of treatment.

- NCS and electromyography were performed in the four limbs. Studied nerves were selected on the basis of clinical data:
  - Motor NCS were routinely estimated in median, ulnar, tibial and peroneal nerves .They included: the distal motor latency, conduction velocity, the compound muscle action potential (CMAP) and the proximal nerve conduction studies (F-wave latency).
  - The sensory conduction studies were done for the median, ulnar and sural and superficial peroneal nerves. They included the distal sensory latency, conduction velocity and amplitude of sensory nerve action potential.
- Patients were classified into the AIDP or AMAN group according to the electrodiagnostic criteria described by Uncini et al ***(11) & (12).***

(B)EMG:

Electromyography, using concentric needle electrodes, done for abductor digiti minimi (ADM), biceps brachii muscles and Tibialis anterior for each patient for visual assessment of:

- The insertional activity
- Spontaneous activity,
- Motor unit action potential (MUAP) analysis (i.e., duration and amplitude).
- Spatial recruitment of MUAPs (i.e., normal, reduced, or early interference pattern).

(4) Follow up:

Evaluation was done after 3weeks for:

- Electrophysiological studies were performed in the four limbs (the same nerves and muscles) previously mentioned.
- Motor disability by using HFGS:

Patients with HFGS > 3 (unable to walk) at follow up were considered to have a poor early prognosis and those with HFGS ≤ 3(able to walk with or without assistance) had good early prognosis.

Statistical methods:

The collected data was revised, coded, and tabulated using Statistical package for Social Science (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). Data were presented and suitable analysis was done according to the type of data obtained for each parameter.

Numerical data was summarized as means and standard deviations. Categorical data was summarized as numbers and percentages.

Comparisons between two groups were done using Mann Whitney U test for numerical data. Categorical data was compared using Chi-square test or Fisher's exact test if appropriate.

Results:

- Mean age was 37 years with standard deviation of 12 years ranging from 19-65years. The majority were males (58.8%) while females were (41.2%). **(Table1)**
- Majority of patients had quadriparesis (94.1%) while (5.9 %) had paraparesis; Twelve (70.6%) out of 17 patients had sensory symptoms mainly numbness or paresthesia; Fifteen (88.2%) out of 17 patients had absent deep tendon reflexes ; Cranial nerve dysfunction was seen in (23.6%), with the facial nerve affection in (11.8%) and (11.8%) had more than one nerve affection, autonomic dysfunction was seen (23.5%), while absent in (76.5%) of patients; Respiratory muscle affection was seen in (17.6%) of patient ; and(88.2%) of patients received plasma exchange and (11.8%) received plasma exchange and IVIG. **(Table2)**
- Mean of GBS disability scale was significantly lower in patients at recovery stage (2.71) compared to the patients at acute stage (3.94) denoting improvement of functional status. **(Table 3)**
- Mean age of patients with poor prognosis (49) was significantly higher than patients with good prognosis (33.17); there is significant correlation between presence of cranial nerve dysfunction, respiratory muscle affection and poor prognosis **(Table 4)**
- Improvement of conduction studies was observed in (70.6%) of patients while it was not improved in (29.4%) of patients according to changes of conduction studies in parallel to clinical improvement**(Table 5)**
- Majority of the patients were AIDP (76.5%), while (23.5 %) of patients were axonal (either AMAN or AMSAN) **(Figure 1).**
- Twelve patients (70.6%) patients had good prognosis. Nine of them were demyelinating (52.9%) while three (17.7%) were axonal in nature. Five patients (29.4%) had bad prognosis .Four of them (23.5%0 were demyelinating while one patient (5.9%) was axonal in nature **(Table 6)**

Table 1: Demographic data among patients with Guillain Barre Syndrome:

	Patients n = 17	
	No.	***%***
Gender		
Male	10	58.8
Female	7	41.2
Age (years)		
Mean ± SD.	37.94 ± 12.87	
Median (Min. – Max.)	36.0 (19.0 – 65.0)	

Table 2: Clinical symptoms among patients with Guillain Barre Syndrome:

Pattern of limb weakness	Patients n = 17	
	No.	***%***
Pattern of limb weakness (1)		
• **Quadriparesis**	16	94.1
- **Ascending**	12	70.6
- **Simultaneous**	4	23.5
• **Paraparesis**	1	5.9
Sensory symptoms		
Absent	5	29.4
Present	12	70.6
Deep tendon reflexes		
Absent	15	88.2
Diminished	2	11.8
Cranial nerve dysfunction		
Absent	13	76.4
Facial palsy	2	11.8
Bulbar and facial palsy	2	11.8
Autonomic dysfunction		
Absent	13	76.5
Present	4	23.5
Bladder/bowel involvement		
Absent	15	88.2
Present	2	11.8
Respiratory muscle affection		
No	14	82.4
Yes	3	17.6
Type of treatment		
Plasma exchange	15	88.2
Plasma exchange and IVIG	2	11.8

Table (3): Comparison between patients at acute (baseline) and recovery (follow up) stages regarding Hughes functional grading scale (HFGS):

	Baseline (acute stage) N = 17	Follow up (recovery stage) N = 17	Change Mean ±SE.	Test	P
Hughes functional grading scale (HFGS)					
Mean ± SD.	3.94 ± 0.43	2.71 ± 0.92	↓ 1.24 ± 0.20	t= 6.126	<0.001*
Median (Min. – Max.)	4.0 (3.0 – 5.0)	2.0 (2.0 – 4.0)			

SD: Standard deviation, Min.: Minimum, Max.: Maximum**. t:** Paired t test**.P:** Comparing baseline and follow up**, *: Significant when p<0.05.**

Table (4): Demographic, clinical data and final prognosis of studied patients

	Final prognosis				Test	P
	Good N = 12		**Poor N = 5**			
	No.	***%***	***No.***	***%***		
Sex						
Male	9	75.0	1	20.0	X^2= 4.408	FE 0.101
Female	3	25.0	4	80.0		
Age (years)						
Mean ± SD.	33.17 ± 12.26		49.40 ± 4.04		t= 2.849	0.012*
Median (Min. – Max.)	32.0 (19.0 – 65.0)		48.0 (45.0 – 55.0)			
Pattern of limb weakness						
Quadriparesis	11	91.7	5	100.0	X^2= 0.443	FE 1.000
Paraparesis	1	8.3	0	0.0		
Sensory symptoms						
Absent	4	33.3	1	20.0	X^2= 0.302	FE 1.000
Present	8	66.7	4	80.0		
Deep tendon reflexes						
Absent	10	83.3	5	100.0	X^2= 0.944	FE 1.000
Diminished	2	16.7	0	0.0		
Cranial nerve dysfunction						
Absent	12	100.0	1	20.0	X^2= 12.554	FE 0.002*
Present	0	0.0	4	80.0		
Autonomic dysfunction						
Absent	11	91.7	2	40.0	X^2= 5.236	FE 0.053
Present	1	8.3	3	60.0		
Bladder/bowel involvement						
Absent	12	100.0	3	60.0	X^2= 5.440	FE 0.074
Present	0	0.0	2	40.0		
Respiratory muscle affection						
No	12	100.0	2	40.0	X^2= 8.743	FE 0.015*
Yes	0	0.0	3	60.0		

X2: Chi–Square, FE: Fisher exact,
P: Comparing good and poor outcome, *: Significant when p<0.05.

Table (5): Conduction studies outcome:

Conduction studies outcome		
Improved	12	70.6
Not improved	5	29.4

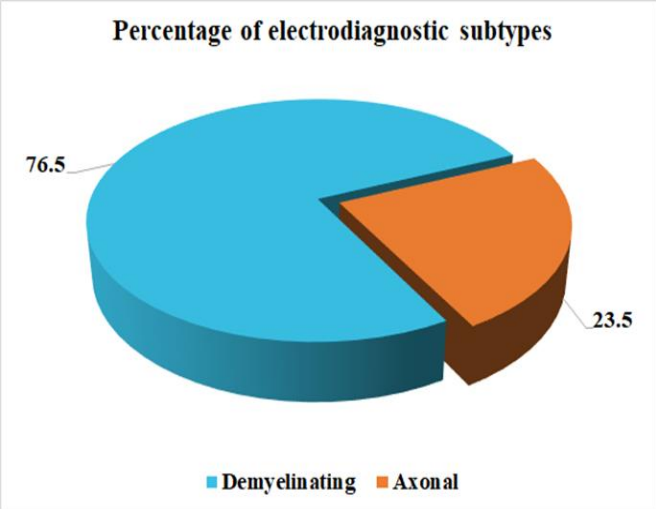

Figure (1): Pie chart for electrodiagnostic subtypes shows that majority of the patients were AIDP (76.5%), while (23.5 %) of patients were axonal (either AMAN or AMSAN).

Table (6): Final prognosis of patients (according to Hughes functional grading scale (HFGS) :

	Patients n = 17	
	No.	***%***
Final prognosis		
Good	12	70.6
• **Demyelinating**	9	52.9
• **Axonal**	3	17.7
Poor	5	29.4
• **Demyelinating**	4	23.5
• **Axonal**	1	5.9

Discussion:

In early stages of GBS, atypical clinical symptoms and signs may lead to a delayed diagnosis ***(13).*** But early diagnosis of GBS is essential as early treatment decreases the duration of GBS and its severity. It would also help in reducing GBS patients that would require mechanical ventilation. Confirmation of diagnosis of GBS depends on NCS. It along with EMG is used in diagnosis, and different neurophysiological diagnostic criteria have been proposed ***(14).***Also, prediction of prognosis is important in GBS because the clinical course is variable and prediction would enable clinicians to give proper treatment and supportive care from the beginning of the disease ***(15).***The present study was a prospective cohort study recruited from patients of GBS at early stage from clinical neurophysiology unit in Kasr Al –Ainy Hospitals and Benha University Hospitals, aimed to evaluate the clinical and neurophysiological findings of early GBS and to identify factors that influence outcome. NCS were performed in the four limbs during acute and recovery stage; motor

NCS were routinely estimated in median, ulnar, tibial and peroneal nerves, and sensory NCS in median, ulnar, sural and superficial peroneal nerves. Studied nerves were selected on the basis of clinical data.

All patients had a Hughes Functional Grading Scale score ***(10)*** at admission and after 3 weeks at recovery stage. A significant difference was observed ($P<0.05$) between them. Motor function deficits were scored at follow up according to Hughes functional grading scale (HFGS). Patients with HFGS >3 (unable to walk) at follow up were considered to have a poor early prognosis and those with HFGS ≤ 3(able to walk with or without assistance) had good early prognosis.

According to the International Study on GBS, the disease is prevalent in all age categories. The incidence rate increases with age, and shows bimodal distribution with peaks for young (15–34 years) and older (>60 years) adults ***(8).*** In this study the mean age of the studied sample was (37.94 ± 12.87) ranging between 19 and 65 years old, a finding similar to previous study ***(16).*** Also, our study revealed that older age was associated with poor outcome as reported in several previous studies ***(16) & (17).***

Males were the dominant gender reported in our study, with 10 cases (58.8%). This finding is supported by several previous studies showing a male predominance ***(14) & (18).*** But, there was no influence of sex on outcome of patients.

Patients with GBS differ from each other regarding the degree as well as distribution of motor and sensory symptoms plus the presence of cranial nerve deficits and autonomic dysfunction. Regarding the clinical presentation, we found that all patients (100%) had motor symptoms. The extent of weakness was estimated by calculating the sum of MRC grades ***(9)*** at admission and after 3weeks. This is consistent with previous studies that reported that motor weakness was the most frequent symptom (73.8–100%) then sensory symptoms that were represented in (52.7%)of patients ***(7)&(18).***

In our study, 12 patients (70.6%) had sensory affection either superficial or deep but there was no influence on outcome.

Involvement of cranial nerves was observed in 4 patients (23.6%) with either unilateral or bilateral facial palsy, bulbar palsy or both. And, it was correlated with poor outcome. This is consistent with previous studies that found that involvement of cranial nerves was more common in severe forms of GBS and was associated with poor prognosis ***(17) & (19).***

Also, in our study two patients (11.8%) had diminished deep tendon reflexes in upper and lower limbs, while absent in 15 patients (88.2%).

In this study, we found autonomic dysfunction in 4 patients (23.5%) but there was no influence of it on outcome. In contrast, *Puyuan et al in 2021* considered dysautonomia as a risk factor for severity with a significant difference in outcome in the severe GBS and non-severe GBS groups ***(17).*** Also, Islam and colleagues in 2019 identified autonomic involvement as an important risk factor for mechanical ventilation and poor outcome ***(20).***

Malaga and colleagues found that the frequency of respiratory failure in GBS was 14% ***(21);*** while in our study 3 patients (17.6%) had respiratory muscles affection but only one (5.8%) patient of them needed mechanical ventilator during course of disease. Respiratory muscles affection was correlated with poor outcome. This is consistent with finding reported by Khedr EM and Shehab MM in 2023. As they found that respiratory insufficiency was correlated with poor outcomes ***(22).***

NCS was taken as golden standard for diagnosis. 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***(23).***

Regarding conduction studies in both upper and lower limbs, there was a significant improvement of conduction velocity, latencies and amplitude the studied nerves (motor and sensory) after 3weeks of treatment when compared to those at initial assessment.

Also, there was a significant improvement of F wave latencies, ratio between pCMAP and dCMAP (either duration or amplitude) after treatment when compared to those at initial assessment. Improvement of conduction studies was observed in 12 patients (70.6%) while not improved in 5 patients (29.4%) according to changes of conduction studies in parallel to clinical improvement.

In our study, patients were classified into the AIDP or AMAN group according to the electrodiagnostic criteria described by Uncini et al ***(11) & (12).*** We found that AIDP was the most common type in 13 of patients (76.5%) followed by axonal subtype either (AMAN or ASMAN) in 4 of patients (23.5%).

According to epidemiological studies from Western Europe and North America AIDP constitutes 80%–90% of GBS ***(24).*** While most studies have reported that AIDP to be the most common subtype ***(25) & (26),*** one study reported predominance of axonal subtypes ***(27).***

In our study, all patients received immunotherapy either plasmapheresis or IVIG which available at time of treatment in addition to conventional supportive care and physiotherapy. The efficacy of IVIg and plasma exchange in the treatment of GBS has been validated by previous study ***(28).*** Because treatment with PE and IVIg are equally effective, the choice between them is dictated by treatment availability, facility expertise, and patient comorbidities or contraindications ***(29).***

Most of patients in our study 15 (88.2%) were treated by plasma exchange and (11.7%) of patients needed plasma exchange and IVIG. None of patients were received steroids.

The reason why some patients continue to deteriorate and may be paralytic for months despite starting treatment early is not known. These patients might have a severe or prolonged immune attack causing severe axonal degeneration or treatment might act insufficiently in these individuals. This often raises the question

whether these patients may have chronic inflammatory demyelinating polyneuropathy with acute onset (A-CIDP). So, longer follow-up duration is needed to further delineate electromyographic changes in the onset and recovery of GBS.

Therefore, it is important to identify patients with severe GBS at the early stage of disease and assign them with intensive care units to reduce the occurrence of residual sequel and mortality.

Conclusion

Clinical presentation, course and outcome of GBS can be variable among patients. So, recognizing the risk factors that may result in severe disability in the early stages of GBS can guide clinicians in devising an effective treatment plan. This study consistently highlights the negative impact of older age, cranial nerve involvement, and respiratory muscle involvement on the development of severe disability in early GBS.

Limitation of the study

Our sample size is very small; additional electromyographic studies involving a larger patient population with longer follow-up duration are needed to further delineate electromyographic changes in the onset and recovery of GBS.

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