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Electrophysiological studies versus high-resolution nerve ultrasound in diagnosis of Guillain–Barré syndrome

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Abstract

Background Guillain–Barré syndrome (GBS) is polyneuropathy characterized by inflammation and immune-mediated processes that is classified into many subtypes based on electrophysiological and pathological criteria. The diagnosis of GBS can be confirmed using electrophysiological studies. However, electrophysiological studies may be normal when carried out early within 1 week in the course of the disease (Berciano et al. in J Neurol 264:221–236, 2017). One of the most useful imaging modalities for peripheral nerve diseases is ultrasonography (US). Nerve US in combination with electrophysiological studies provides an appropriate method in evaluating diseased peripheral nerves. This study aimed to enhance the reliability of early GBS diagnosis by correlating the findings of electrophysiological studies and nerve ultrasound. The nerve conduction studies (NCSs) in 37 GBS patients and 37 controls combined with cross-sectional area (CSA) assessment with US within the first 3 days of onset of symptoms and on day 14 after disease onset were evaluated.

Results At presentation, patients and controls did not differ significantly in NCS parameters ($p \geq 0.05$) except for a significantly longer F-wave minimum latency in the median, ulnar, and tibial nerves in patients ($p < 0.001$). While on day 14 all NCS parameters differed significantly in patients in comparison to controls ($p < 0.001$) with exception of the sural nerve parameters ($p \geq 0.05$). Except for the sural nerve ($p \geq 0.05$), all the examined nerves' CSAs were considerably higher in patients at presentation and on day 14 in comparison to the controls ($p < 0.001$). The subtypes of Guillain–Barré syndrome either demyelinating, axonal or mixed axonal and demyelinating did not significantly differ regarding the CSAs of all the examined nerves either at presentation or on day 14 ($p > 0.05$).

Conclusion Electrophysiological results in GBS are crucial in diagnosing the disease and understanding its pathophysiology, but serial NCSs are required. Ultrasound shows structural aspects of the nerve, so ultrasonography is a reliable tool which can be used in diagnosis and follow-up of early GBS. As a result, combining the two investigations has a complementary effect in the diagnosis and prognosis of GBS.

Keywords Guillain–Barré syndrome, Electrophysiological studies, Nerve ultrasonography

Introduction

Guillain–Barré syndrome (GBS) is polyneuropathy characterized by inflammation and immune-mediated processes with an abrupt onset that is classified into many subtypes based on electrophysiological and pathological criteria [1]. The diagnosis of GBS can be confirmed using electrophysiological studies, which can also provide

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some prognostic information. Furthermore, they can differentiate between the axonal and demyelinating subtype of GBS [2]. However, electrophysiological studies may be normal when carried out early within 1 week in the course of the disease, or in cases presented at early stages with proximal weakness, mild disease, slow development [3]. One of the most useful imaging modalities for peripheral nerve diseases is ultrasonography (US) because it is cheap, non-invasive, with great contrast resolution, and the ability to examine the whole course of the major peripheral nerves [4–6]. There has been an increase in research in recent years of peripheral nerve US in different neuropathies as GBS. Nerve US in combination with electrophysiological studies provides an appropriate method in evaluating diseased peripheral nerves. The cross-sectional area (CSA) changes, echogenicity, and surrounding epineurium are seen in the US of diseased nerves [7]. This study aimed to enhance the reliability of early GBS diagnosis by correlating the findings of electrophysiological studies and nerve ultrasound.

Methods

A case control study conducted in the Neurology and Diagnostic Radiology departments. The study took place from October 2017 to March 2021.

Thirty-seven adult patients of both genders, aged ≥ 18 years complaining of clinical manifestation suggestive of GBS as acute weakness in both upper and lower limbs, reduced or absent deep tendon reflexes, progression from days to four weeks with relative symmetry of clinical presentation, minor sensory symptoms, autonomic symptoms, or signs were involved.

Patients with spinal nerve root compression, intracranial or spinal cord lesions, a history of GBS or chronic inflammatory demyelinating polyneuropathy (CIDP), medication-induced neuropathy, a hereditary neuromuscular disorder, any systemic disease affecting the peripheral nerves, such as diabetes mellitus, uremia, or chronic liver disease and critical care unit patients on mechanical ventilation were excluded. Another 37 healthy controls with similar age and sex were also included. All participants submitted informed written consent before participating in the study, which was authorized by the faculty of medicine ethical committee.

The following procedures were performed on all patients:

A complete history was taken, as well as a detailed general and neurological examination. Hughes-Score (HS) [8] at presentation and on day 14 was used to assess the functional status of patients. Lumbar puncture for cerebrospinal fluid (CSF) analysis for confirmation of GBS and findings are conclusive when CSF cell count less than 50/mL and CSF protein concentration higher than 60 mg/dL [9].

A clinical neurophysiologist with expertise in electrophysiology conducted a standardized electrophysiological study using a Neuropak Model MEB-2300k (Nihon Kohden Corporation, Tokyo, Japan, 2012) electromyography machine. All studies were performed by the same examiner. The study was performed as described by Preston and Shapiro [10]. It was carried out at presentation within 3 days of onset of symptoms and then repeated on day 14 from onset of disease. The subject was kept in a supine posture with a skin temperature greater than 32 °C for all recordings. The motor and sensory studies used filters with frequency ranges of 10 Hz to 5 kHz and 20 Hz to 2 kHz, respectively.

Median, ulnar, and tibial motor nerves were tested for distal motor latency (DML), compound muscle action potential (CMAP), and motor conduction velocity (MCV). The median, ulnar, and sural sensory nerves were tested for peak latency (PL), sensory nerve action potential (SNAP), and sensory conduction velocity (SCV) were evaluated. F-wave latencies (FL) were measured in the median, ulnar, and tibial nerves to assess the proximal nerve segments. All nerve conduction studies (NCSs) followed the standard protocol of supramaximal percutaneous stimulation with a constant-current stimulator and surface electrode recording. The electrophysiological criteria described by Preston and Shapiro [11] were applied for diagnosis of GBS. The Brighton criteria [9] were applied in GBS diagnosis.

Real-time high-resolution ultrasonography was carried out for the selected nerves with a linear probe (5–17 MHz) from a Philips IU22 machine (Philips Ultrasound 22,100 Bothell-Everett Highway; Philips Healthcare, Bothell, Washington, USA). It was carried out by a specialized Diagnostic Radiologist at presentation within 3 days of onset of symptoms and then repeated on day 14 from onset of disease. The clinical and electrophysiologic findings were kept hidden from the sonographer, and all scans were done by the same examiner.

The subjects were examined in supine positions. To see the nerve, the B mode was utilized, and the scanning depth remained constant at 3 cm (cm), but the focus was varied individually.

The probe was gently held over the skin to avoid nerve deformation, and the transducer was oriented perpendicular to the nerve to get the most clear and small CSA image. The color Doppler mode was utilized to distinguish arteries, veins, and nerve bundles. The CSA was then determined in square millimeters (mm^2) by direct tracing just inside the nerve's hyperechogenic rim in perpendicular planes with a tracing method measured. If more than one bundle was visible, the structures were

traced together with as little connective tissue as possible in between. The CSAs of the following nerves were measured at defined anatomical sites: the sural nerve was measured between the medial and lateral heads of the gastrocnemius muscle, the tibial nerve was measured at the popliteal fossa, the median nerve was measured at the upper arm, the forearm, and the wrist, and the ulnar nerve was measured at the upper arm and the wrist [12–14]. The controls were subjected to electrophysiological studies and nerve ultrasound.

Statistical analysis

We used IBM SPSS software version 20.0 to analyze the data after it was imported into the computer. Armonk, New York, IBM Corporation. To express categorical variables, numbers and percentages were applied. To analyze the association between category variables, the Chi-square test was applied. Continuous variables were verified for normality via the Shapiro–Wilk test. Statistics such as the mean, standard deviation, median, and range (minimum and maximum) were developed to represent distributed variables. Comparisons of normally distributed quantitative variables were made by means of the Student's t-test, and comparisons of the two time periods were made using the paired t-test. To compare the two time periods, we applied the Wilcoxon signed ranks test. For quantitative variables that did not follow a normal distribution, we applied the Mann–Whitney test to compare the two groups. At the 5% level, the results were considered significant.

Results

This study included 74 people divided into two groups, each with 37 subjects. The first group included GBS patients, and the controls were the second group; the demographic and clinical data of both groups are displayed in Tables 1 and 2.

The results of electrophysiological studies and nerve ultrasonography of the right side were only presented.

At presentation, patients and controls did not differ significantly in NCS parameters ($p \geq 0.05$) except for a significantly longer F-wave minimum latency in the median, ulnar, and tibial nerves in patients ($p < 0.001$). While on day 14 all NCS parameters differed significantly in patients in comparison to controls ($p < 0.001$) with exception of the sural nerve parameters ($p \geq 0.05$) (Table 3).

Except for the sural nerve ($p \geq 0.05$), all the examined nerves' CSAs were considerably higher in patients at presentation and on day 14 in comparison to the controls ($p < 0.001$) (Table 4).

The subtypes of Guillain–Barré syndrome either demyelinating, axonal or mixed axonal and demyelinating did not significantly differ regarding the CSAs of all the examined nerves either at presentation or on day 14 ($p > 0.05$) (Tables 5, 6).

Table 1 Demographic data among patients and controls

	Control ($n = 37$)	Patients ($n = 37$)	Test of Sig.	*p*
Sex				
Male	21 (56.8%)	26 (70.3%)	$\chi^2 = 1.458$	0.227
Female	16 (43.2%)	11 (29.7%)		
Age (years)				
Mean ± SD	32.7 ± 7.99	34.4 ± 9.39	$t = 0.867$	0.389
Median (Min.–Max.)	33 (19–50)	35 (19–52)		
Weight (kilogram)				
Mean ± SD	85 ± 10.7	84.4 ± 11.3	$t = 0.265$	0.792
Median (Min.–Max.)	85 (66–109)	84 (68–110)		
Height (centimeter)				
Mean ± SD	170.9 ± 4.19	171.7 ± 4.66	$t = 0.787$	0.434
Median (Min.–Max.)	170 (160–183)	170 (162–185)		
Body mass index				
Mean ± SD	29.1 ± 3.26	28.6 ± 3.40	$t = 0.655$	0.515
Median (Min.–Max.)	28.7 (22.8–38.2)	28.4 (23.5–38.5)		

SD standard deviation, *Min.–Max* minimum–maximum, *t*: Student's *t*-test, χ^2 Chi-square test, *p p* value

Discussion

In this study, the NCSs in 37 GBS patients combined with US at 2 time-points: within the first 3 days of onset of symptoms and on day 14 after disease onset were evaluated.

In our study, males (70.3%) had a higher prevalence of GBS than females (29.7%). Our result agreed with Parmar and V Doshi [15] who showed male predominance (76%) compared to females (24%). Also Dash his colleagues [16] showed male predominance and in contrast to our study; Khan and his colleagues [17] found GBS to be equally frequent in men and women, which could be explained by variations in sample size and methodology.

The patients and controls did not significantly differ in terms of NCS parameters at time of onset of GBS, except for a prolonged F-wave minimum latency. This agreed with Alberti and colleagues [18] who found that F-wave examination is a preliminary examination in patients with GBS to establish the early diagnosis, and with Mizuguchi and colleagues [19] who demonstrated that abnormalities of nerve conduction examination in the first week will usually be found with abnormal F-waves. Other studies have found that the F-wave is either delayed or absent in 80–90% of AIDP patients due to the early affection of the proximal nerve segments and spinal roots [20, 21].

Table 2 Clinical data among patients ($n=37$)

Clinical data	No. (%)
Preceding infection	
No	11 (29.7%)
Gastrointestinal	10 (27.0%)
Respiratory	16 (43.2%)
Clinical presentation	
Motor	10 (27%)
Motor and sensory	27 (73%)
Cranial nerve	
No	17 (45.9%)
Facial	7 (18.9%)
Bulbar	5 (13.5%)
Facial and bulbar	8 (21.6%)
Autonomic symptoms	
No	29 (78.4%)
Yes	8 (21.6%)
Hughes-Score (HS) at presentation and (on day 14)	
	HS 0 $n=0$ ($n=0$) HS 1 $n=2$ ($n=1$) HS 2 $n=4$ ($n=2$) HS 3 $n=10$ ($n=14$) HS 4 $n=21$ ($n=20$)
Guillain–Barré syndrome subtype	
Demyelinating	22 (59.5%)
Axonal	4 (10.8%)
Mixed axonal and demyelinating	11 (29.7%)
Treatment	
Intravenous immunoglobulins	37 (100%)
Plasmapheresis	0 (0%)

Regarding the ultrasound, our study showed that all sensorimotor nerve CSAs in patients were considerably larger at disease onset when compared to controls, however, the structure of the sural nerve which is totally sensory nerve did not change considerably, which could be the ultrasonography equivalent of the sural sparing finding in NCSs [22].

In acute GBS the cause of the focal enlargement of the nerves is unknown, however it could be the ultrasonography association of swelling of the nerve sheath due to focal inflammatory edema of demyelination, as evidenced by histopathology [14, 23].

This study showed that swelling of the nerves occurred in places other than the typical entrapment locations, such as the ulnar nerve in the upper arm, the popliteal nerve in the popliteal fossa, and the median nerve in the middle of the arm. These results were consistent with those of other studies [23, 24].

On day 14 from onset of disease, our result showed the patients had marked reduction of CMAP, prolonged DML, reduction of motor CV and prolonged F-wave in upper and lower limb studded nerves except for the sural nerve parameters in comparison to controls. This agreed with Preston and Shapiro [11] who shown that, while more than ninety percent of patients will experience motor NCS abnormalities within the first weeks, considerably smaller number will experience sensory NCS abnormalities. Typically, sensory studies are intact in the early stages of GBS. But after one or two weeks they reveal sural sparing that is sensory response of the sural nerve is intact, while sensory responses of median and ulnar nerves are diminished or absent. These findings also agreed with previous studies which showed prolonged F-wave latency in early GBS especially in median and ulnar nerves but when we repeated NCS after 2 weeks there were significant changes in DML, CMAP and MCV of different nerves [3, 25].

In our study, we noticed that CSAs of examined nerves still enlarged when measured on day 14 in both distal and proximal portions of nerves. This finding agreed with Sugimoto and colleagues [26] who showed that the CSAs of the proximal and distal segments were almost identical. [14, 23] discovered that the median and ulnar nerves CSAs were significantly reduced between the first eight weeks and after 12 weeks, but if we follow our patients longer maybe we yield these results.

We found no statistical difference between subtypes of Guillain–Barré syndrome at onset or on day 14. In contrast to a prior study, the authors discovered that axonal subtypes exhibited lower CSAs at certain nerve locations than demyelinating subtypes [27]. Also [28, 29] found that nerve enlargement detected by US is much more pronounced in demyelinating than in axonal polyneuropathies.

Wallerian degeneration caused axonal affection of the peripheral nerves corresponding to reduction of CMAP amplitude in our study could be another cause of nerve hypertrophy. Axonopathy may result in hypertrophy of nerve fascicles, a remodeling cascade as previously explored in sarcoid neuropathy [30], which, in addition to remyelination, could be another cause of nerve hypertrophy [31], and beside edema and inflammation [13, 14].

From the above finding, we noticed that nerve ultrasound was highly positive in comparison to electrophysiological studies in early GBS manifested by enlarged CSAs in almost all studied nerves in contrast to electrophysiological studies which manifested by prolonged F-wave latency only which also could be normal so we

Table 3 Nerve conduction study parameters among patients and controls

	Control ($n=37$)	Patients		P_1	P_2	P_3
		At presentation ($n=37$)	On day 14 ($n=37$)			
	Mean ± SD	Mean ± SD	Mean ± SD			
Median						
DML (ms)	3.77 ± 0.25	3.82 ± 0.25	6.10 ± 1.79	$^{U}p_1 = 0.376$	$^{U}p_2 < 0.001^{*}$	$^{Z}p_3 < 0.001^{*}$
CMAP (mV)	9.40 ± 3.09	8.97 ± 2.74	4.46 ± 2.01	$^{U}p_1 = 0.642$	$^{U}p_2 < 0.001^{*}$	$^{Z}p_3 < 0.001^{*}$
MCV(m/s)	58.2 ± 6.20	56.9 ± 6.24	36.6 ± 11	$^{U}p_1 = 0.341$	$^{U}p_2 < 0.001^{*}$	$^{Z}p_3 < 0.001^{*}$
F-wave latency (ms)	27.5 ± 1.89	36.7 ± 3.78	38.3 ± 4.22	$^{U}p_1 < 0.001^{*}$	$^{U}p_2 < 0.001^{*}$	$^{Z}p_3 = 0.003^{*}$
PL (ms)	2.94 ± 0.31	3.02 ± 0.32	4.59 ± 1.37	$^{U}p_1 = 0.242$	$^{U}p_2 < 0.001^{*}$	$^{Z}p_3 < 0.001^{*}$
SNAP (μV)	32 ± 4.65	30.9 ± 4.51	16.4 ± 5.06	$^{U}p_1 = 0.393$	$^{U}p_2 < 0.001^{*}$	$^{Z}p_3 < 0.001^{*}$
SCV(m/s)	59 ± 7.91	57.1 ± 7.38	35.9 ± 7.67	$^{U}p_1 = 0.239,$	$^{U}p_2 < 0.001^{*}$	$^{Z}p_3 < 0.001^{*}$
Ulnar						
DML (ms)	2.78 ± 0.27	2.89 ± 0.24	5.32 ± 2.12	$^{U}p_1 = 0.090$	$^{U}p_2 < 0.001^{*}$	$^{Z}p_3 < 0.001^{*}$
CMAP (mV)	9.76 ± 2.43	8.95 ± 1.51	5.51 ± 1.59	$^{U}p_1 = 0.258$	$^{U}p_2 < 0.001^{*}$	$^{Z}p_3 < 0.001^{*}$
MCV (m/s)	57.5 ± 5.81	55.9 ± 5.67	36.4 ± 10.8	$^{U}p_1 = 0.211$	$^{U}p_2 < 0.001^{*}$	$^{Z}p_3 < 0.001^{*}$
F-wave latency (ms)	28.0 ± 1.93	36.5 ± 3.47	38.9 ± 4.38	$^{U}p_1 < 0.001^{*}$	$^{U}p_2 < 0.001^{*}$	$^{Z}p_3 < 0.001^{*}$
PL (ms)	2.69 ± 0.23	2.83 ± 0.35	4.32 ± 1.15	$^{U}p_1 = 0.126$	$^{U}p_2 < 0.001^{*}$	$^{Z}p_3 < 0.001^{*}$
SNAP (μV)	32.9 ± 6.41	32.7 ± 6.08	15.8 ± 5.65	$^{U}p_1 = 0.880$	$^{U}p_2 < 0.001^{*}$	$^{Z}p_3 < 0.001^{*}$
SCV (m/s)	58.2 ± 7.14	56.2 ± 4.57	36 ± 7.29	$^{U}p_1 = 0.214$	$^{U}p_2 < 0.001^{*}$	$^{Z}p_3 < 0.001^{*}$
Tibial						
DML (ms)	4.40 ± 0.58	4.56 ± 0.55	7.09 ± 1.62	$^{U}p_1 = 0.147$	$^{U}p_2 < 0.001^{*}$	$^{Z}p_3 < 0.001^{*}$
CMAP (mV)	9.64 ± 5.35	8.58 ± 4.07	4.31 ± 1.45	$^{t}p_1 = 0.343$	$^{t}p_2 < 0.001^{*}$	$^{t1}p_3 < 0.001^{*}$
MCV(m/s)	48.8 ± 3.22	47.2 ± 3.75	32.97 ± 7.98	$^{U}p_1 = 0.030^{*}$	$^{U}p_2 < 0.001^{*}$	$^{Z}p_3 < 0.001^{*}$
F-wave latency (ms)	48.5 ± 2.95	58.3 ± 3.79	59.6 ± 4.11	$^{U}p_1 < 0.001^{*}$	$^{U}p_2 < 0.001^{*}$	$^{Z}p_3 = 0.070$
Sural						
PL (ms)	3.57 ± 0.35	3.66 ± 0.36	3.71 ± 0.34	$^{U}p_1 = 0.255$	$^{U}p_2 = 0.07$	$^{Z}p_3 = 0.43$
SNAP (μV)	12.3 ± 4.21	11.7 ± 3.59	11.35 ± 2.9	$^{U}p_1 = 0.614$	$^{U}p_2 = 0.268$	$^{Z}p_3 = 0.626$
SCV(m/s)	53.4 ± 5.46	52.6 ± 4.93	51.8 ± 4.74	$^{U}p_1 = 0.473$	$^{U}p_2 = 0.151$	$^{Z}p_3 = 0.083$

SD standard deviation, *U* Mann–Whitney test, *Z* Wilcoxon signed ranks test, p_1 p value for comparing between the patients at presentation and controls, p_2 p value for comparing between the patients on day 14 and controls, p_3 p value for comparing between the patients at presentation and on day 14, *DML* distal motor latency, *CMAP* compound muscle action potential, *MCV* motor conduction velocity, *PL* peak latency, *SNAP* sensory nerve action potential, *SCV* sensory conduction velocity, *ms* millisecond, *mV* millivolt, *m/s* meter per second, *μV* microvolt

* Statistically significant at $p \leq 0.05$

concluded that nerve ultrasound could be an alternative reliable diagnostic tool in early GBS.

This study has some limitations; only four individuals with GBS axonal variant were included, making a reliable comparison with demyelinating variant impossible. Another limitation was the short observation period; so, we cannot expect if ultrasound improvement in the enlarged verves happens before clinical improvement or vice versa based on our data. Finally, this study could not have included any individuals admitted to ICU who had a poor recovery, as a result, the findings must be cautiously interpreted. Consequently, to investigate the progression of nerve hypertrophy in GBS, large multicenter trials with short observation periods are required.

Conclusion

Electrophysiological results in GBS are crucial not only in diagnosing the disease, but also in understanding its pathophysiology and assessing the nerve function but serial NCSs are required since the outcomes of the condition alter significantly over time. Ultrasound shows structural aspects of the nerve such as the nerve fascicles, echogenicity, and vascularity, so ultrasonography is a reliable tool which can be used in diagnosis and follow-up of early GBS. As a result, combining the two investigations has a complementary effect in the diagnosis and prognosis of GBS.

Table 4 Nerve cross-sectional area among patients and control

Cross-sectional area (mm^2)	Controls ($n=37$)	Patients		P_1	P_2	P_3
		At presentation ($n=37$)	On day 14 ($n=37$)			
	Mean ± SD Median (Min.–Max.)	Mean ± SD Median (Min.–Max.)	Mean ± SD Median (Min.–Max.)			
Median nerve						
Wrist	4.74 ± 0.54 4.90 (4.0–5.90)	5.92 ± 0.90 6 (4.50–8.50)	6.02 ± 0.94 6 (4.50–8.50)	$^{U}p_1 < 0.001^{*}$	$^{U}p_2 < 0.001^{*}$	$^{Z}p_3 = 0.102$
Forearm	6.17 ± 1.27 5.90 (4–9.30)	8.04 ± 0.96 7.90 (6.70–10.70)	8.40 ± 1.11 8.10 (6.70–10.7)	$^{t}p_1 < 0.001^{*}$	$^{t}p_2 < 0.001^{*}$	$^{t1}p_3 = 0.010^{*}$
Upper arm	6.58 ± 0.84 6.40 (5.50–8.50)	8.85 ± 0.55 9 (7.90–9.80)	8.74 ± 0.53 8.80 (7.90–9.80)	$^{U}p_1 < 0.001^{*}$	$^{U}p_2 < 0.001^{*}$	$^{Z}p_3 = 0.046^{*}$
Ulnar nerve						
Wrist	3.54 ± 0.59 3.60 (2.90–5)	5.26 ± 0.99 4.90 (3.80–7.80)	5.50 ± 0.86 5.50 (4.50–7.80)	$^{U}p_1 < 0.001^{*}$	$^{U}p_2 < 0.001^{*}$	$^{Z}p_3 = 0.034^{*}$
Upper arm	5.16 ± 0.67 5 (4–6.50)	7.05 ± 1.99 6.10 (4.90–11)	7.70 ± 2.01 7.90 (4.90–11)	$^{U}p_1 < 0.001^{*}$	$^{U}p_2 < 0.001^{*}$	$^{Z}p_3 = 0.015^{*}$
Tibial nerve at popliteal fossa	20.9 ± 2.31 21.1 (16.8–25.2)	27.4 ± 4.20 25.8 (20.9–30.9)	28 ± 2.37 28.8 (22.7–33.5)	$^{U}p_1 = 0.001^{*}$	$^{U}p_2 < 0.001^{*}$	$^{Z}p_3 < 0.001^{*}$
Sural nerve at calf	2.24 ± 0.40 2.30 (1.60–3)	2.32 ± 0.37 2.4(1.8– 3.2)	2.40 ± 0.38 2.3 (1.9–3.5)	$^{U}p_1 < 0.32$	$^{U}p_2 < 0.62$	$^{Z}p_3 = 0.35$

SD standard deviation, *t* Student's *t*-test, t_1 paired *t*-test, *U* Mann–Whitney test, *Z* Wilcoxon signed ranks test, p_1 *p* value for comparing between the patients at presentation and controls, p_2 *p* value for comparing between the patients on day 14 and controls, p_3 p value for comparing between the patients at presentation and on day14, mm^2 *square* millimeter

* Statistically significant at $p \leq 0.05$

Table 5 Relation between Guillain–Barré syndrome subtype and nerve cross-sectional area at presentation among patients (n = 37)

Cross-sectional area (mm^2)	Guillain–Barré syndrome subtype			Test of sig.	*p*
	Demyelinating ($n=22$)	Axonal ($n=4$)	Mixed ($n=11$)		
	Mean ± SD Median (Min.–Max.)	Mean ± SD Median (Min.–Max.)	Mean ± SD Median (Min.–Max.)		
Median nerve					
Wrist	5.9 ± 0.9 6.0 (4.5–8.5)	6.1 ± 1.1 6.1 (4.7–7.5)	5.9 ± 0.8 5.9 (4.9–7.5)	$H=0.306$	0.858
Forearm	8.2 ± 1.0 8.0 (7.0–10.7)	7.6 ± 0.8 7.6 (6.9–8.5)	7.8 ± 0.8 7.9 (6.7–9.8)	$F=1.063$	0.357
Upper arm	8.8 ± 0.5 9.0 (7.9–9.8)	8.9 ± 0.1 8.9 (8.7–9.0)	8.9 ± 0.7 9.0 (8.0–9.8)	$H=0.301$	0.860
Ulnar nerve					
Wrist	5.4 ± 1.1 5.5 (3.8–7.8)	4.8 ± 0.5 4.6 (4.5–5.6)	5.1 ± 0.8 4.9 (3.9–6.8)	$H=1.439$	0.487
Upper arm	7.1 ± 1.9 6.1 (5.0–10.6)	5.7 ± 0.6 5.9 (4.9–6.2)	7.4 ± 2.3 6.2 (5.0–11.0)	$H=2.495$	0.287
Tibial nerve at popliteal fossa	28.14 ± 4.1 26.4 (20.9–33.9)	25.07 ± 2.59 24.15 (23–28.9)	26.8 ± 4.7 23.9 (21.9–33.6)	$F=1.07$	0.353
Sural nerve at calf	2.31 ± 0.36 2.35 (1.8–3.2)	2.27 ± 0.37 2.3 (1.8–2.7)	2.37 ± 0.42 2.3 (1.8–3)	$F=0.128$	0.88

SD standard deviation, *p* p value, mm^2 *square* millimeter, *F* F for one-way ANOVA test, *H* H for Kruskal–Wallis test

Table 6 Relation between Guillain–Barré syndrome subtype and nerve cross-sectional area on day 14 among patients ($n=37$)

Cross-sectional area (mm^2)	Guillain–Barré syndrome subtype			Test of sig.	*p*
	Demyelinating ($n=22$)	Axonal ($n=4$)	Mixed ($n=11$)		
	Mean ± SD Median (Min.–Max.)	Mean ± SD Median (Min.–Max.)	Mean ± SD Median (Min.–Max.)		
Median nerve					
Wrist	6.0 ± 1.0 6.0 (4.5–8.5)	6.1 ± 1.1 6.1 (4.7–7.5)	6.0 ± 0.9 5.9 (4.9–7.5)	$H=0.153$	0.927
Forearm	8.6 ± 1.1 8.1 (7.5–10.7)	8.4 ± 1.3 8.3 (6.9–10.0)	8.0 ± 1.0 7.9 (6.7–10.0)	$F=1.025$	0.370
Upper arm	8.7 ± 0.5 8.8 (7.9–9.8)	8.9 ± 0.1 8.9 (8.7–9.0)	8.8 ± 0.6 8.8 (8.0–9.8)	$H=0.308$	0.857
Ulnar nerve					
Wrist	5.7 ± 0.9 5.8 (4.5–7.8)	4.8 ± 0.5 4.6 (4.5–5.6)	5.3 ± 0.7 5.2 (4.5–6.8)	$H=4.350$	0.114
Upper arm	7.5 ± 2.0 6.4 (5.0–10.6)	6.5 ± 1.8 6.0 (4.9–9.0)	8.6 ± 1.9 9.0 (5.0–11.0)	$H=4.379$	0.112
Tibial nerve at popliteal fossa	28.3 ± 2.4 28.9 (22.7–33.5)	28.0 ± 2.1 29.0 (24.9–29.2)	27.5 ± 2.5 26.9 (24.7–31.5)	$H=0.306$	0.858
Sural nerve at calf	2.3 ± 0.38 2.3 (1.9–3.5)	2.2 ± 0.21 2.2 (1.9–2.4)	2.5 ± 0.37 2.5(1.9–3)	$F=1.05$	0.361

SD standard deviation, *p* p value, *mm^2 square* millimeter, *F* F for one-way ANOVA test, *H* H for Kruskal–Wallis test

Abbreviations

CIDP	Chronic inflammatory demyelinating polyneuropathy
CMAP	Compound muscle action potential
CSA	Cross-sectional area
CSF	Cerebrospinal fluid
CV	Conduction velocity
DML	Distal motor latency
EMG	Electromyography
GBS	Guillain–Barré syndrome
Hz	Hertz
kHz	Kilohertz
MHz	Megahertz
mm^2	Millimeter square
ms	Millisecond
mV	Millivolt
m/s	Meter per second
mg/dL	Milligram per deciliter
mL	Milliliter
MCV	Motor conduction velocity
NCS	Nerve conduction studies
PL	Peak latency
SCV	Sensory conduction velocity
SNAP	Sensory nerve action potential
US	Ultrasonography

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Author contributions
AA carried out the design and conception of the study, the analysis and interpretation of data and helped to draft the manuscript. NM carried out the design and conception of the study, participated in the sequence alignment, data collection, interpretation of data and drafting of manuscript. ES carried out the design and conception of the study, participated in the sequence alignment, data collection, interpretation of data and drafting of manuscript. SO carried out the study conception and design, participated by acquisition of data and performed the statistical analysis and drafted the manuscript. MW carried out the design and conception of the study, the analysis and interpretation of data and helped to draft the manuscript. AR carried out the study conception and design, participated in its design, and drafted the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
Availability of data and materials: the data are publicly available at the Faculty of Medicine, Suez Canal University.

Declarations

Ethics approval and consent to participate
The study was approved by the Ethics committee of Suez Canal Faculty of medicine on October 18, 2017. Committee Number: 3249. An informed written consent was taken from all the participants in the study.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests (financial or non-financial).

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