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Comparison of electrodiagnostic findings in patients with post-COVID-19 and non-COVID-19 Guillain-Barre syndrome

Recep Yevgi, Nuray Bilge
Atatürk University, Faculty of Medicine, Department of Neurology, Erzurum, Turkey

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ABSTRACT

Aim: The aim of this study is to compare the electrophysiological features of patients with Guillain-Barré syndrome (GBS) after Coronavirus disease–2019 (COVID-19) and the electrophysiological features of patients with non-COVID-19 GBS and to determine whether there is a difference between these two groups in terms of nerve dysfunction.

Material and Method: The electromyography results of the patients followed up with the diagnosis of GBS between December 2019 and December 2021 in the Neurology Department of Atatürk University Faculty of Medicine were retrospectively analyzed. Patients with a history of COVID-19 in the 6-week period before the occurrence of GBS were considered as the post-COVID-19 GBS group. Patients who did not have a history of COVID-19 but developed GBS were considered the non-COVID-19 GBS group. Electrodiagnostic findings of the patients were compared between two groups.

Results: Motor compound muscle action potential (CMAP) amplitude of the median nerve was detected as 1.94±1.43 mV in post-COVID-19 GBS group and 5.94±4.6 mV in non-COVID-19 GBS group ($p<0.05$). On the other hand, motor CMAP amplitude of ulnar nerve was 2.82±1.61 mV in post-COVID-19 GBS group and 6.28±4.2 mV in non-COVID-19 GBS group ($p<0.05$). Motor CMAP amplitude of the tibial nerve was detected as 1.3±1.06 mV in post-COVID-19 GBS group and 3.5±3.6 mV in non- COVID-19 GBS group ($p<0.05$). No significant difference was observed between the two groups in terms of other parameters.

Conclusion: Motor CMAP amplitudes of median, ulnar and tibial nerves were significantly low in post-COVID-19 GBS group when compared with non-COVID-19 GBS group. This result may indicate that the degree of axonal involvement and related nerve dysfunction in post-COVID-19 GBS patients in the acute period is higher than in non-COVID-19 GBS patients.

Keywords: Guillain Barre syndrome, COVID-19, EMG, CMAP, SNAP, distal latency, conduction velocity

INTRODUCTION

Guillain-Barré syndrome (GBS) is an acute immune-mediated inflammatory polyradiculoneuropathy. Progressive, symmetrical muscle weakness starting from the distal extremities and spreading to the proximal extremities, decreased, or lost deep tendon reflexes, cranial nerve palsy, bulbar symptoms, autonomic dysfunctions may be seen in GBS. The most common type of GBS is acute inflammatory demyelinating polyneuropathy (AIDP). However, there are also axonal forms such as acute motor axonal neuropathy (AMAN), acute motor and sensory axonal neuropathy (AMSAN).

The diagnosis of GBS is made by the patient's clinical history and examination findings. Cerebro spinal fluid (CSF) examination and electrodiagnostic investigations are other methods which can be used to support the GBS diagnosis. Observation of no cells in CSF examination despite of increased total protein concentration in GBS is named as albuminocytological dissociation. Electrodiagnostic findings in electromyography (EMG) include, slowing of nerve conduction velocity, prolongation of distal latencies, conduction block, temporal dispersion, A-waves, prolonged or absent F wave latency and reduction of compound muscle action potential (CMAP) amplitudes in axonal forms. EMG is beneficial in determining sub-types of GBS, differential diagnosis of GBS, determining the degree of nerve dysfunction, follow-up of patients and evaluating the prognosis.

Corresponding Author: Recep Yevgi, recep_yevgi@yahoo.com
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Coronavirus disease–2019 (COVID-19); is a disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 was first seen in December 2019 in Wuhan, caused pandemic all around the world and continues to be an important global health problem. Although COVID-19 mainly affects the respiratory system, increasing evidence shows that it may affect both the peripheral and central nervous systems (1-4).

GBS may occur between a few days to 6 weeks after Campylobacter jejuni, Cytomegalovirus, Influenza A and B, HIV and Zika virus infections. GBS cases developing after COVID-19 infection are also frequently reported (5-8). In addition to studies reporting that the clinical and prognostic features of GBS cases developing after COVID-19 are similar to non-COVID-19 GBS cases, there are also various studies showing the presence of certain differences (9,10).

The aim of this study is to compare the electrophysiological features of patients with GBS after COVID-19 and the electrophysiological features of patients with non-COVID-19 GBS and to determine whether there is a difference between these two groups in terms of nerve dysfunction.

MATERIAL AND METHOD

Ethics committee approval was obtained from the Atatürk University, Faculty of Medicine, Clinical Researches Ethics Committee (Date: 30.12.2021, Decision No: 9/17). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The EMG results of the patients followed up with the diagnosis of GBS between December 2019 and December 2021 in the Neurology Department of Atatürk University Faculty of Medicine were retrospectively analyzed. The clinical and demographic characteristics of the patients, their status of having COVID-19 disease, and EMG results were recorded. Patients under the age of 18, presence of polyneuropathy, diabetes mellitus, malignancy, rheumatological disease, pregnancy, alcoholism, toxic substances, patients with metal or drug exposure that can cause polyneuropathy, those with a history of hospitalization at the intensive care unit due to COVID-19, patients with excessive extremity edema, patients with a history of previous surgery, thromboembolic event, vaccination in the last 6 weeks were excluded from the study. Files of 57 GBS patients were reviewed. Among these patients, 5 patients due to previously known polyneuropathy, 3 patients due to diabetes mellitus, 1 patient due to pregnancy, 1 patient due to rheumatoid arthritis, 2 patients due to intensive care unit stay, 2 patients due to a history of vaccination were excluded. The study was continued with 43 GBS patients who met the inclusion criteria.

GBS was diagnosed according to National Institute of Neurological Disorders and Stroke (NINDS) criteria and was confirmed by CSF examination and EMG (11). Rajabally criteria were used for the electrophysiologic diagnosis of GBS (12). Disease severity was assessed according to the Hughes functional rating scale (0=normal to 6=dead) (13).

Patients with a history of COVID-19 in the 6-week period before the occurrence of GBS were considered as the post-COVID-19 GBS group. Patients who did not have a history of COVID-19 but developed GBS were considered the non-COVID-19 GBS group. COVID-19 infection was confirmed by SARS-CoV-2 real-time reverse transcriptase-polymerase chain reaction (RT-PCR). COVID-19-PCR or COVID-19 antibody in CSF in GBS patients was not studied for economic reasons.

CSF examination was performed within 7-15 days and EMG examination was performed within 4-10 days after the onset of GBS symptoms. EMG examination was performed by the same technician by using Dantec™ Keypoint® Focus brand device after providing optimal physical conditions in neurophysiology laboratory at Atatürk University Faculty of Medicine, Department of Neurology. Low and high pass filters are set to 2 kHz-20 kHz for motor studies and 20 Hz-2000 Hz for sensory studies. The sweep speed was 2 ms/section, and the stimulus duration was 0.05-0.1 ms. Right median, ulnar and sural nerves, and right peroneal and tibial nerves were evaluated in nerve conduction studies performed in EMG. Sensory nerve conduction studies were performed antidromically in all nerves.

Sensory nerve action potential (SNAP)'s of the median and ulnar nerves were recorded from II and V fingers respectively after stimulating the nerves from the wrist. Sural SNAP was recorded at 12 cm behind the lateral malleolus after stimulating the sural nerve from the edge of Achilles tendon. The median CMAP nerve was stimulated from the wrist and elbow and recorded from the abductor pollicis brevis muscle. The ulnar CMAP nerve was stimulated above the wrist and elbow and recorded from the abductor digiti minimi muscle. Peroneal CMAP was recorded from the extensor digitorum brevis muscle by stimulating the peroneal nerve above and below the caput fibulae. Tibial CMAP was recorded from the abductor hallucis muscle by stimulating the tibial nerve from the medial malleolus and popliteal fossa. Motor and sensory distal latencies, nerve conduction velocities and CMAP amplitudes of the nerves were recorded. The results were compared between the post-COVID-19 GBS group and non-COVID-19 GBS group.

Statistical Analysis

Summary statistics of all participants were obtained based on the means and standard deviations for normally distributed data and, medians and min-max for non-normal distributed data. The distribution of normality was assessed with the D'Agostino-Pearson test. Continuous variables with normal distribution belonging to two groups were compared using the student t-test whereas non-normal distributed data were compared using the Mann Whitney U test. Two tailed p -value < 0,05 was considered statistically significant. All statistical analyzes were performed using statistical package for the social sciences for windows (SPSS 20.0).

RESULTS

There were 13 patients in the post-COVID-19 GBS group and 30 patients in the non-COVID-19 GBS group. There were 7 female and 6 male patients in the post-COVID-19 GBS group and 15 female and 15 male patients in the non-COVID-19 GBS group. The mean age of the post-COVID-19 GBS group was 58.69±17.1 years, and the mean age of the non-COVID-19 GBS group was 52.5±19.7 years (p>0.05). There was no statistically significant difference between the two groups in terms of CSF findings (p>0.05). Demographic and clinical characteristics of the patients are given in **Table 1**.

Table 1. Clinical and demographic characteristics of the patients

Characteristic	Post-COVID-19	Non-COVID-19	p
Age (mean±SD)	58.6±17.1	52.5±19.7	
Patient number (n)	13	30	
Gender (n, %)			
Female	7 (53.8)	15 (50)	
Male	6 (46.2)	15 (50)	
GBS Type (n, %)			
AIDP	7 (53.8)	17 (56.7)	
AMSAN	4 (30.8)	8 (26.7)	
AMAN	2 (15.4)	4 (13.3)	
MFS	-	1 (3.3)	
HFGSS (median, min-max)	3 (2-5)	2 (1-5)	
Treatment (n, %)			
IVIG	9 (69.2)	26 (86.6)	
Plasmapheresis	4 (30.8)	3 (13.4)	
CFS findings			
Protein (mg/dL) (median, min-max)	56.5 (42-161)	52.5 (35-198)	0.89
Glucose (mg/dL) (median, min-max)	67 (51-105)	64 (48-110)	0.25
Chloride (mmol/L) (median, min-max)	123 (119-128)	124 (117-127)	0.91

n:number, AIDP: Acute inflammatory demyelinating polyneuropathy; AMAN: Acute motor axonal neuropathy; AMSAN: Acute motor-sensory axonal neuropathy; MFS: Miller Fisher syndrome, HFGSS: Hughes functional grading scale score, IVIG: Intravenous immunoglobulin, CSF: Cerebrospinal fluid

In nerve conduction studies, motor CMAP amplitude of the median nerve was detected as 1.94±1.43 mV in post-COVID-19 GBS group and 5.94±4.6 mV in non-COVID-19 GBS group (p<0.05) (**Table 2**). On the other hand, motor CMAP amplitude of ulnar nerve was 2.82±1.61 mV in post-COVID-19 GBS group and 6.28±4.2 mV in non-COVID-19 GBS group (p<0.05) (**Table 2**).

Table 2. Motor Nerve Conduction Studies (Right)

Motor nerve conduction studies	Post-COVID-19	Non-COVID-19	p
Median CMAP Amp. (mV)	1.94±1.43	5.94±4.6	<0.001*
Median CMAP Distal Latency (ms)	5.1 (2.6-13.3)	4.22 (0-28.2)	0.64
Median NCV (m/s)	40.8 (19.8-63.9)	43.8 (0-64.1)	0.93
Ulnar CMAP Amp. (mV)	2.82±1.61	6.28±4.2	0.007*
Ulnar CMAP Distal Latency (ms)	3.9 (1.1-8.9)	3.6 (2.1-11.3)	0.8
Ulnar NCV (m/s)	47.3 (25.2-67.3)	44.9 (14.6-69.4)	0.95
Peroneal CMAP Amp. (mV)	0.8 (0-4.46)	1.4 (0-12.9)	0.13
Peroneal CMAP Distal Latency (ms)	6.3±7.1	5.5±3.1	0.6
Peroneal NCV (m/s)	32.3 (0-50)	37,4 (0-52)	0.18
Tibial CMAP Amp. (mV)	1.3±1.06	3.5±3.6	0.04*
Tibial CMAP Distal Latency (ms)	6.7±4.7	5.2±3	0.2
Tibial NCV (m/s)	37.3 (0-44.4)	36.5 (0-56.4)	0.6
Tibial F-Wave Latency (ms)	44.5 (38.2–62.5)	46.4 (32.2-65.1)	0.8

CMAP: Compound muscle action potential, NCV: Nerve conduction velocity, Amp: Amplitude, * Statistical significance

Motor CMAP amplitude of the tibial nerve was detected as 1.3±1.06 mV in post-COVID-19 GBS group and 3.5±3.6 mV in non- COVID-19 GBS group (p<0.05) (**Table 2**). Motor CMAP amplitudes of median, ulnar and tibial nerves were significantly low in post-COVID-19 GBS group when compared with non-COVID-19 GBS group. There was no statistically significant difference between the post-COVID-19 GBS and non-COVID-19 GBS groups in terms of the motor distal latencies and nerve conduction velocities of the median, ulnar, peroneal, and tibial nerves (**Table 2**). There was no statistically significant difference between the post-COVID-19 GBS and non-COVID-19 GBS groups in terms of tibial F wave latencies. In sensory nerve conduction studies, no statistically significant difference was found between the two groups in terms of SNAP amplitudes, distal latency and nerve conduction velocities of the median, ulnar and sural nerves (**Table 3**).

Table 3. Sensory Nerve Conduction Studies (Right)

Sensory Nerve Conduction Studies	Post-COVID-19	Non-COVID-19	p
Median SNAP Amp. (mV)	5,6 (0-20)	3,5 (0-23,1)	0.4
Median SNAP Distal Latency (ms)	3.04±2,2	2,15±1.96	0.2
Median NCV (m/s)	31 (0-62,5)	36,3 (0-64,5)	0.9
Ulnar SNAP Amp. (mV)	7,5±8,5	6,8±8,4	0.8
Ulnar SNAP Distal Latency (ms)	2.4±2.4	1.7±1.8	0.2
Ulnar NCV (m/s)	31 (0-62,5)	36,3 (0-64,5)	0.9
Sural SNAP Amp. (mV)	5.2±7	7.1±7.7	0.4
Sural SNAP Distal Latency (ms)	1.5±1.7	1.7±1.8	0.6
Sural NCV (m/s)	35 (0-75.7)	32.2 (0-75.8)	0.7

SNAP: Sensory nerve action potential, NCV: Nerve conduction velocity, Amp: Amplitude

DISCUSSION

In our study, the CMAP amplitudes of the median, ulnar and tibial nerves were significantly lower in post-COVID-19 GBS patients compared to the non-COVID-19 GBS group. Our study results may show that motor nerve dysfunction is significantly higher in the acute period, especially in post-COVID-19 GBS patients.

In a study comparing the electrophysiological characteristics of 24 GBS patients associated with SARS-CoV-2 with control GBS patients; there was no significant difference between the two groups in median, ulnar, peroneal, and tibial nerve CMAP amplitudes (14). In the same study; ulnar, peroneal, and tibial nerve distal motor latencies were found to be prolonged in the control GBS group when compared with the SARS-CoV-2 associated GBS group. In our study, no significant difference was found between two groups. In various studies evaluating GBS cases which has developed after COVID-19, it has been reported that the AIDP form of GBS is seen most frequently, followed by AMSAN and AMAN forms, respectively (15,16). While our study was conducted on all forms of GBS, the fact that this study was conducted only on the AIDP form of GBS and not including AMAN and AMSAN forms in the study may have caused different results for CMAP and SNAP amplitude values of nerves between two studies. Likewise, in the aforementioned study, ulnar, peroneal, and tibial nerve motor distal latencies were found to be prolonged in the control group, whereas in our study there was no difference between the two groups. This difference between studies may be related to the fact that SARS-CoV-2-associated GBS was less demyelinating and non-demyelinating forms were not included in this study.

In a case series presenting the electrophysiological features of 3 patients who developed GBS after COVID-19, CMAP amplitudes of some nerves were low, while SNAPs of many nerves could not be obtained (17). Electrophysiological data of the cases reported in this study confirmed axonal involvement in COVID-19-associated GBS and were consistent with our results.

In a study in which patients with post-COVID-19 fatigue symptoms were evaluated electrophysiologically; no difference was found for the motor conduction velocities and CMAP amplitudes of the ulnar, peroneal, and tibial nerves between groups (18). In the same study, there was no difference between the groups in terms of ulnar and sural nerve sensory conduction velocities and SNAPs. In this study, electrophysiological studies were performed 77-255 days after the onset of acute COVID-19 symptoms, and it was shown that there was no significant nerve dysfunction in COVID-19 patients without GBS. In line with these data, it can be deduced that COVID-19 does not normally cause nerve dysfunction, but a significant nerve dysfunction due to axonal neuropathy occurs in post-COVID-19 GBS patients, and the degree of this dysfunction is higher when compared with non-COVID-19 GBS patients.

CONCLUSION

Our study has limitations such as the fact that it was conducted on a small number of patients, and it did not include control EMG examinations of the patients and data on clinical prognosis. According to our research, our study is the first to show that the degree of axonal involvement and related nerve dysfunction in post-COVID-19 GBS patients in the acute period is electrophysiologically higher than in non-COVID-19 GBS patients. We believe that more comprehensive multicenter studies on this subject will be beneficial.

ETHICAL DECLARATIONS

Ethics Committee Approval: Ethics committee approval was obtained from the Atatürk University, Faculty of Medicine, Clinical Researches Ethics Committee (Date: 30.12.2021, Decision No: 9/17).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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