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Myopathic Changes in Patients with Long-term Fatigue after COVID-19

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ABSTRACT

Background: Neurological symptoms during the acute infection include headache, disorientation, critical disease myopathy, stroke, abnormal cerebral perfusion, and leptomeningeal augmentation, as well as Guillain-Barre syndrome.
Objective: The aim of the current study was to look at the electrical activity of peripheral nerve and muscle in patients who had COVID-19-related continuing neuromuscular symptoms.
Patients and methods: This study was conducted in the period from Jan 2022 to June 2022. A total of 50 patients participated in the study. All patients were monitored at the Neurology Department of Alazhar University Hospital, New Damitta. In addition, 50 healthy controls matched for age and sex were recruited. All patients and healthy controls completed a thorough clinical assessment and neurological examination, which included force measurement, deep tendon reflex testing, and sensory evaluation, on the day of the neurophysiological assessment. The three average neuropathy ratings for each patient were also recorded; The Utah Early Neuropathy Score (UENS), the Michigan Neuropathy Screening Instrument (MNSI), and the Neuropathy Impairment Score (NIS).
Results: No statistical significant difference was found between the 2 studied groups regarding sex, age or BMI. The results of the studied groups' quantitative electromyography (qEMG), nerve conduction studies (NCS), Peroneal MCV (m/sec), Tibial MCV (m/sec), and Tibial minimum F-wave delay revealed extremely substantial difference between case and control groups. Sural SCV (m/sec), or Sural SNAP amplitude (mV), with the exception of Ulnar MCV (m/sec), Ulnar Palpitations, physical weariness, and myalgia all were significantly higher in the case group.
Conclusion: A typical finding in long-term COVID-19 is myopathic qEMG. We suggest that myopathy may play a significant role in these individuals' physical exhaustion.
Keywords: Myopathic changes, Long-term, Fatigue, COVID-19, Case control study, Alazhar University Hospital.

INTRODUCTION

The novel coronavirus illness COVID-19 is mostly caused by the severe acute respiratory syndrome 2 (SARS-CoV-2) virus, which has spread globally and is a serious health problem. Within the first year of the outbreak, millions more became sick, and more than 2.5 million people perished worldwide. In addition to having an impact on the nervous, cardiovascular, and renal systems, COVID-19 also affects the pulmonary system [(1)].

Among the neurological symptoms seen during the acute infection are headache, disorientation, Guillain-Barre syndrome, critical illness myopathy, stroke, aberrant cerebral perfusion, and leptomeningeal enhancement. There have been documented cases of COVID-19 with varying degrees of severity, from those with no symptoms to those requiring intensive care units (ICU) [(2)]. Numerous studies have demonstrated that COVID-19 can harm one's health in the long run, even in people who weren't admitted to the hospital. However, with those who are healing from severe COVID-19, especially those whom needed ICU care, we expect persistent issues [(3)].

It is currently unknown what causes COVID-19's persistent symptoms, what causes their underlying mechanisms, and how long they last. As a result, COVID-19's long-term neurological effects are still unknown [(4)]. The aim of the current study was to look at the electrical activity of peripheral nerve and muscle in patients who had COVID-19-related continuing neuromuscular symptoms.

PATIENTS AND METHODS

A case-control study was conducted at Alazhar University Hospital, New Damitta. The study was conducted on 50 patients with COVID-19 diseases from January 2022 to June 2022. All patients had evidence of prior SARS-CoV-2 infection through a polymerase chain reaction (PCR) test or antibodies. The Department of Infectious Diseases' Long-Term COVID-19 Clinic forwarded each patient with the suspicion that they had neuropathy. All patients were followed at the Neurology Department, Faculty of Medicine, Alazhar University, New Damitta. In addition, 50 healthy controls matched for age and sex were recruited. When COVID-19 patients with ongoing symptoms were sent for a neurophysiological test, the Long-Term COVID-19 Clinic assessed them. The patient's medical records were reviewed for persistent complaints.

Clinical Examination: All patients and controls got a thorough clinical examination as well as a neurological examination that included force estimation, profound ligament reflexes, and tactile testing when they arrived for the neurophysiological investigation. The three average neuropathy ratings for each patient were also recorded: the Utah Early Neuropathy Score (UENS), the Michigan Neuropathy Screening Instrument (MNSI), and the Neuropathy Impedance Score (NIS).
UENS is a solid predictor of early neuropathy due to its emphasis on tactile inclusion and division into subgroups that act on engine capability, little fibre

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reasonableness, enormous fibre feeling, and the Achilles reflex [5].

The UENS score ranges from 0 to 42, and the greatest score for little fibre capability is 26.

MNSI, a test for detecting diabetic polyneuropathy, contains 15 items describing decreased touch sensitivity.

NIS is a test for estimating profound ligament reflexes, upper and lower limit muscle strength, and tactile discernment. It has been utilised as a result measure in clinical preliminary exams and has values that range from 0 to 280. All patients were subjected to the following inquiries: whether they had muscle issues, myalgia, or a summed-up feeling of actual exhaustion.

Electrophysiological examinations: NCS and EMG procedures were carried out using Key Points, utilising both conventional methods and Net EMG technology [6,7]. Skin temperature was maintained at or above 32 degrees Celsius using a heating lamp.

Nerve conduction studies (NCS):

The recording region of the expendable pre-gelled surface anodes (Ag/AgCl) for NCS went from 15 mm to 20 mm.

On the healthy controls, just ulnar NCS was performed; on patients, the middle and ulnar nerves were evaluated. Peroneal, tibial, sural, and dorsal sural cutaneous tactile NCS were acted on in the two patients and solid controls, however, on the prevailing sideural cutaneous tactile NCS were acted on in the two patients and solid controls, however, on the prevailing side. In situations where the side effects were hilter-kilter or more articulated in the farthest points, two-sided middle and ulnar tangible and engineered NCS were acted.Furthermore, in patients with side effects related to these nerves, tangible and engineered NCS were acted on in the relevant nerves.For the middle tangible NCS, digit II, and for ulnar nerve feeling, digit 5, antidromic tactile nerve activity possibilities (SNAP) were recorded. The compound muscle activity potential (CMAP) of the abductor pollicis brevis was estimated while middle-engine NCS was applied to the wrist and elbow. During ulnar engine NCS, the nerve was animated at the wrist, beneath the elbow, or more. The abductor digiti minimi was then used to record CMAP. After peroneal nerve feeling at the lower leg, the flexor digitorum brevis CMAP and capitulum fibulae were both recorded.

The tibial nerve was recorded by the abductor hallucis muscle, which also stimulated the common malleolus and the fossa poplitea. Running parallel to the edge of the Achilles ligament, the sura was used to stimulate the sural nerve, which is 13 cm distant from the horizontal malleolus. For the dorsal sural cutaneous NCS, measurements were made from the centre of the fifth metatarsal bone, exactly across from the extensor digitorum longus ligament of the fifth toe [7,8]. Around 12 cm away, behind the sidelong malleolus, was where the sensation first appeared. Distal engine deferral, engine and tangible conduction speed (CV), CMAP and SNAP abundance, and least F-wave inertness were the estimated engine NCS properties. Base-to-top plentifulness estimates were acquired for the middle and ulnar tactile NCS; however, top-to-top SNAP measurements, CMAP amplitudes, and the sural and dorsal sural cutaneous nerves were all obtained.

Quantitative electromyography (qEMG):

All healthy controls underwent qEMG on their biceps brachii, vastus medialis, and front tibial muscles, whereas patients had their biceps brachii, vastus medialis, and first tibial muscles examined. Additionally, qEMG of various muscles was used in patients with pertinent side effects. Utilizing the office's typical channel settings of 20 Hz–10 kHz, gain (100 mV/division), and clear speed (ten milliseconds/division), a qEMG was conducted using a concentric 35 mm Dantec needle terminal.

Ten different sites were checked for the existence of unrestrained activity (possibilities of fibrillation, positive sharp waves, and fasciculations), and irregularity was anticipated where unrestrained action would occur frequently [7].

By putting about 20 engine unit potentials (MUPs) through a powerless, purposeful restriction, the quantitative engine unit potential (MUP) investigation was completed. We evaluated the sufficiency, level, and mean span of polyphasic possibilities. A MUP has been described as polyphasic if the number of stages is greater than five.For the simple possibilities, the mean MUP term was calculated. A mean MUP term deemed myopathic was one that was below the 95% certainty timespan controls.

Laboratory tests: All patients went through routine blood tests for *thyroid*-stimulating hormone (TSH), HbA1c, and vitamin B12. In addition, most patients' drawn-out Coronavirus period levels of myoglobin, lactic dehydrogenases (LDH), creatinine kinases (CK), and erythrocyte sedimentation rate (ESR) were measured.

Ethical Approval:

This study was ethically approved by the Institutional Review Board of the Faculty of Medicine, Al-Azhar University (New Damitta, Egypt). Written informed consent was obtained from all participants. This study was executed according to the code of ethics of the World Medical Association (Declaration of Helsinki) for studies on humans.

Statistical Analysis

The collected data were introduced and statistically analyzed by utilizing the Statistical Package for Social

Sciences (SPSS) version 24 for Windows. Qualitative data were defined as numbers and percentages. Chi-Square test/Fisher's exact test was used for comparison between categorical variables as appropriate. Quantitative data were tested for normality by the Kolmogorov-Smirnov test. The Normal distribution of variables was described as mean and standard deviation (SD), and an independent sample t-test was used for comparison between groups. P value ≤0.05 was considered to be statistically significant.

RESULTS

Table 1 demonstrates the demographic characteristics of the two studied groups. No statistical significant difference was found between the two studied groups regarding sex, age or BMI.

Table (1): Demographic characteristics of the studied groups.

Variable		Cases Group (n = 50)		Control Group (n = 50)		P-value
		N	%	N	%	
Sex	**Male**	27	54%	28	56%	0.84
	Female	23	46%	22	44%	
Age		54.34 ± 6.3		55.8 ± 5.17		0.17
Weight		78.5 ± 4.5		77.5 ± 4.1		0.51
BMI (kg/m^2)		29.8 ± 3.73		29.76 ± 3.01		0.13

BMI: Body mass index, P value <0.05 is significant, P value <0.01 is highly significant, SD: Standard deviation.

Table **2** demonstrates the findings of NCS and qEMG on the groups under investigation. The results of the studied groups' qEMG, NCS, Peroneal MCV (m/sec), Tibial MCV (m/sec), and Tibial minimum F-wave delay revealed extremely substantial difference between case and control groups. Sural SCV (m/sec), or Sural SNAP amplitude (mV), with the exception of Ulnar MCV (m/sec), Ulnar Palpitations, physical weariness, and myalgia all were significantly higher in the case group.

Table (2): Results from nerve conduction studies (NCS) and quantitative electromyography (qEMG) among the studied groups.

Variable	Cases Group (n = 50)	Control Group (n = 50)	P-value
MUP duration (ms) (BB)	10.2 ± 0.2	11.7 ± 0.4	<0.001
MUP amplitude (µV) (BB)	212.1 ± 10.1	262.5 ± 15.1	<0.001
MUP duration (ms) (VM)	10.2 ± 0.4	12.6 ± 0.2	<0.001
MUP amplitude (µV) (VM)	261.5 ± 10.4	300.2 ± 17.8	<0.001
MUP duration (ms) (TA)	11.4 ± 0.32	13.1 ± 0.21	0.003
MUP amplitude (µV) (TA)	322.0 ± 9.04	357.6 ± 19.8	<0.001
Ulnar SCV (m/sec)	59.2 ± 1.27	59.4 ± 0.9	0.01
Ulnar SNAP amplitude (µV)	21.3 ± 2.31	24.7 ± 3.2	0.024
Ulnar MCV (m/sec)	62.1 ± 1.0	62.9 ± 1.19	0.22
Ulnar CMAP amplitude (mV)	13.1 ± 1.28	13.7 ± 1.0	0.087
Ulnar minimum F-wave latency (ms)	25.6 ± 1.95	25.2 ± 1.87	0.77
Peroneal MCV (m/sec)	44.85 ± 0.85	46.8 ± 0.97	0.35
Peroneal CMAP amplitude (mV)	6.98 ± 0.52	7.92 ± 0.75	0.001
Peroneal minimum F-wave latency (ms)	49.3 ± 3.7	46.1 ± 2.49	0.001
Tibial MCV (m/sec)	49.1 ± 0.99	51.1 ± 1.18	0.22
Tibial CMAP amplitude (mV)	21.7 ± 1.91	20.16 ± 1.30	0.008
Tibial minimum F-wave latency (ms)	48.52 ± 3.8	47.05 ± 3.57	0.66
Sural SCV (m/sec)	54.9 ± 1.35	57.3 ± 1.07	0.10
Sural SNAP amplitude (µV)	16.6 ± 2.0	14.2 ± 1.8	0.46

P value< 0.05 is significant, P value< 0.01 is highly significant, SD: Standard deviation

Table 3 shows Long term symptoms of patients with and without myopathic electromyography (EMG). There was significant increase in Palpitations, Physical fatigue and Myalgia in cases group.

Table (3): Long term symptoms of patients with and without myopathic electromyography (EMG).

Variable	Cases Group (n = 50)	Control Group (n = 50)	P-value
Duration between acute COVID-19 and EMG [Median (IQR)]	205 (108-238)	215 (168-248)	0.763
Headaches	18 (36%)	28 (56%)	0.04481
Difficulties in concentrating	30 (60%)	28 (56%)	0.68532
Memory problems	28 (56%)	22 (44%)	0.23014
Dyspnea	46 (92%)	45 (90%)	0.72677
Chest pain	36 (72%)	28 (56%)	0.09558
Palpitations	18 (36%)	7 (14%)	0.01107
Physical fatigue	48 (96%)	17 (34%)	<0.001
Myalgia	37 (74%)	0 (0%)	<0.001

DISCUSSION

The connected nerves of all patients with focused symptoms were thoroughly examined, including a side-by-side NCS comparison and, if necessary, an EMG.
In a recent case report, symptoms and electrodiagnostic testing identified a lateral antebrachial cutaneous nerve disorder called pure sensory neuralgic myotrophy [(9)]. Although it is possible that the wedged people had a form with only tactile or bodily function contributions, we were unable to confirm the wedged people's mono-neuropathic limb or lumbosacral rubor using NCS or myogram, attributable to the speculation that contaminations trigger a resistant interceded pathophysiologic element for amyotrophic horizontal pathology; it might be that none of the patients had extreme uneasiness before fostering their condition, which might propose pain wasting away.

Paraesthesia and overwhelming sensations were consequently discovered by patients with distal, bilaterally symmetric tactile problems, which could highlight very little fibre pathology. A lot of testing occurs in this manner, together with quantitative tangible evaluations and skin biopsies. Be that as it may, the poor clinical outcomes do not show an obvious very small or large fibre polyneuropathy. It is believed that some of the side effects were mental in nature and cannot be completely ruled out. Similar results were recorded by**Agergaard *et al.*** [(3)].
Myopathy has been reported to develop in severe Coronavirus patients who required intensive care unit care [(10)]; however, this is not usually distinguishable from a basic sickness pathology of various aetiologies [(11)].Patients who were admitted to intensive care units were excluded from our study. We discovered that moderate to severe Coronavirus was followed by a significantly higher prevalence of pathology qEMG, and half of the patients were not even closely monitored by the medical clinic. Most patients elaborated on their actual sluggishness and pain after learning about muscle complaints, despite the fact that they were excluded from a neuroscience evaluation because they had tangible irregularities as persistent side effects.

Because exhaustion has been identified as a common side effect of both intense [(12)] and end-of-day Coronavirus, we believe our findings are extremely significant as a possible explanation [(13, 14)]. Over the course of 40 days of Coronavirus openness, the pathologic assessment of the hearts of 40 hospitalised Coronavirus casualties uncovered microthrombi, immunoactive C5b-9 markers, and a provocative reaction that planned mitochondrial stress [(15)]. In Walk 2003, Leung *et al*. [(16)] reported that the skeletal muscles of eight consecutive severe acute respiratory syndrome patients had safe interceded confined myofiber putrefaction. In an exceedingly new case report [(17)], a patient with SARS-CoV-2 sickness with pathology was found to possess muscle diagnostic test proof of infection, prompting kind I interferonopathy. The high predominance of pain displayed before examinations upholds this thought [(14)]. Furthermore, rhabdomyolysis during severe illness has been linked to unfortunate outcomes in a variety of partners [(18)]. Another translation of our discoveries is that the patients' idleness might need to be created for them since inertia has been shown to regulate MUP signals on their own.

CONCLUSION

In patients with light or direct SARS-CoV-2 sickness, pathology qEMG has been undeniable to be a continual chase down in end of the day Coronavirus contamination. It is suggested that the particular drowsiness of those patients may be altogether due to pathology. Exploration may aid clinical professionals in the discovery of novel therapeutic targets for Coronavirus medical care. Such medicines might diminish the grimness experienced by a good number of SARS-CoV-2-beset people and also the mammoth monetary weight of the infection.

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