COVID-19 Associated Neuromuscular Disorders - An Electrodiagnostic Perspective

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ABSTRACT

This cross-sectional study aimed to describe electrodiagnostic (Edx) findings of neuromuscular disorders (NMD) associated with COVID-19 infection. Patients with history of COVID-19 infection and neuromuscular symptoms were included. After documenting the demographics, detailed examination and nerve conduction studies / electromyography (NCS / EMG) were performed. Descriptive statistics were determined. Polyneuropathy was the most common electrophysiological diagnosis (n = 22, 40%) and amongst these, Guillian Barre Syndrome (GBS) was the most common (n = 13, 23.6%). Patients with history of invasive ventilation had 2.5 times the risk of developing myopathic disorder [OR 2.5, 95% CI 0.6 – 9.9] and 2.6 times the risk of developing neuropathic disorder than those who did not require invasive ventilation [OR 2.6, 95% CI 0.8-8.5]. Polyneuropathy is the most common NMD associated with COVID-19 infection. Patients with history of invasive ventilation after COVID-19 are susceptible to develop neuropathic disorders. Further studies are needed to establish the causality of this correlation.

Key Words: *Polyneuropathy*, *Myopathy*, *Moneuritis multiplex*, *Facial nerve palsy*, *Critical illness polyneuropathy / myopathy*, *Neuromuscular junction disorders*, *Guillian barre syndrome*.

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COVID-19 infection was primarily thought to involve the respiratory system. However, it is now clear that *SARS-CoV-2* is a systemic disorder and may result in extrapulmonary organ injury including cardiovascular, endothelial, coagulation, renal, hepatobiliary, gastrointestinal, endocrinological, dermatological, and neurological involvement.[1] This may be the result of angiotensin converting enzyme 2 (ACE2) mediated direct tissue damage or likely indirect mechanisms including cytokine storm, endothelial cell damage, coagulopathy or renin–angiotensin-aldosterone system dysregulation.[1]

SARS-CoV-2 has affinity for neural tissue, and various COVID-19-related neurological and neuromuscular disorders (NMD) have been reported in the literature.[1] Electrodiagnostic (Edx) studies have an important diagnostic and prognostic role in the management of NMD. Globally, various studies describing Edx findings among patients with NMD due to COVID-19 infection have been reported. According to the authors' knowledge, Edx evaluation of NMD secondary to COVID-19 is understudied topic. This study aimed to describe the Edx features of neuromuscular diseases associated with COVID-19 in Pakistan.

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This prospective cross-sectional study took place in the Electrodiagnostic Department of the Armed Forces Institute of Rehabilitation Medicine, from February 2021 to October 2022. The primary source of data collection was medical history, examination, and records of patients. All patients referred to the electrodiagnostic clinic with neuromuscular symptoms and a prior history of COVID-19 infection in the past six months, confirmed by the reverse transcriptase polymerase chain reaction (RT-PCR) for *SARs-CoV-2* were included. Patients who either received vaccination of *SARs-CoV-2* in the past one month or had prior history of NMD, were excluded.

Demographic data, the severity of COVID-19 infection, history of invasive and non-invasive ventilation, comorbids, and detailed history of patients were taken. A physical medicine and rehabilitation (PM and R) specialist, who was trained and certified to perform nerve conduction studies / electromyography (NCS / EMG) planned and performed the test. EMG was performed using a disposable 28 gauge 40 mm concentric needle. Statistical Analysis was done using the Statistical Package of Social Sciences (SPSS) version 25. Frequencies and percentages were calculated for categorical variables. Mean and standard deviation were calculated for quantitative variables. Risk estimate (Relative Risk-RR) was calculated for the development of myopathic and neuropathic disorders among patients who received invasive or non-invasive ventilation. Chi-square test was used to compare with in-group differences. A p-value of <0.05 was considered significant.

Table I: Demographic data of patients.

Parameters		Total	Invasive ventilation	Non-invasive ventilation	No ventilation
No. of patients		55	18	22	15
Gender	Male n (%)	39 (71%)	15 (83%)	15 (68%)	9 (60%)
	Female n (%)	16 (29%)	3 (17%)	7 (32%)	6 (40%)
	p-value+		0.157	0.716	0.275
Severity of COVID-19 infection	Mild n (%)	11 (20%)	0 (0%)	0 (0%)	11 (73%)
	Moderate n (%)	4 (7%)	1 (6%)	0 (0%)	3 (20%)
	Severe n (%)	30 (54%)	7 (39%)	22 (100%)	1 (7%)
	Critical n (%)	10 (18%)	10 (56%)	0 (0%)	0 (0%)
	p-value+		0.000	0.000	0.000
Comorbidities	No comorbid n (%)	39 (71%)	10 (56%)	19 (86%)	10 (67%)
	Diabetes mellitus n (%)	6 (11%)	3 (17%)	1 (5%)	2 (13%)
	Ischaemic heart disease n (%)	4 (7%)	3 (17%)	0 (0%)	1 (7%)
	Deep vein thrombosis n (%)	2 (4%)	1 (6%)	0 (0%)	1 (7%)
	Hypertension n (%)	3 (5%)	1 (6%)	1 (5%)	1 (7%)
	Blood cancer n (%)	1 (2%)	0 (0%)	1 (5%)	0 (0%)
	p-value+		0.336	0.148	0.952

+*Chi-square test was used.*

Table II: Pathology of neuromuscular system in patients with COVID-19.

Parameters		Total	Invasive ventilation	Non-invasive ventilation	No ventilation
NCS / EMG Diagnosis	Unremarkable Study	17 (31%)	2 (11%)	8 (36%)	7 (47%)
	Neuropathy	26 (47%)	11 (61%)	8 (36%)	7 (47%)
	Myopathy	8 (14%)	4 (22%)	4 (18%)	0 (0%)
	Neuro-myopathy	2 (4%)	1 (6%)	1 (5%)	0 (0%)
	Neuromuscular junction pathology	2 (4%)	0 (0%)	1 (4.5%)	1 (7%)
	p-value+		0.147	0.777	0.204
Type of neuropathy (n = 28)	Axonal	22 (79%)	9 (53%)	8 (40%)	5 (33%)
	Demyelinating	6 (21%)	3 (17%)	1 (5%)	2 (13%)
	p-value+		0.242	0.328	0.812
Type of neuropathy based on the type of fibres involved (n = 28)	Sensory	1 (4%)	1 (6%)	0 (0%)	0 (0%)
	Motor	9 (32%)	4 (24%)	2 (10%)	3 (21%)
	Sensorimotor	18 (64%)	7 (41%)	7 (35%)	4 (29%)
	p-value+		0.247	0.484	0.829
Duration of neuropathy (n = 28)	Acute	15 (54%)	5 (29%)	5 (25%)	5 (33%)
	Sub-acute	11 (39%)	7 (41%)	2 (10%)	2 (13%)
	Chronic	2 (7%)	0 (0%)	2 (10%)	0 (0%)
	p-value+		0.063	0.120	0.614
Myopathy	Proximal	3 (30%)	1 (7%)	2 (10%)	0 (0%)
	Generalised	7 (70%)	4 (29%)	3 (15%)	0 (0%)
	p-value+		0.182	0.628	0.063

+*Chi-square test was used.*

Out of the 59 patients screened for inclusion, a total of 55 patients were included. Mean age of the patients was 48.9 ± 2.5 years. Mean interval between the start of COVID-19 symptoms and the appearance of neuromuscular symptoms was 33.5 ± 5.9 days. Out of the total patients, 2 (3.6%) patients died later. Thirty-nine (71%) patients were males and 16 (29%) were females. Neuromuscular symptoms reported by the participants were weakness of one or more limbs in 38 (69%), numbness of one or more limbs in 3 (5.5%), fatigue and body aches in 5 (9%) each, and burning sensation of hands and feet, facial weakness, drooping of eyelids, and low back pain in 1 (1.8%) each. Demographic data of patients are shown in Table I. Pathology of the neuromuscular system in patients with COVID-19 identified by NCS / EMG is shown in Table II. Specific electrophysiological diagnosis of the patients is as follows: Critical illness myopathy (CIM)-6 (11%), critical illness polyneuropathy / myopathy (CIPM)-2 (4%), normal study-17 (31%), acute motor polyneuropathy-3 (6%), sensorimotor polyneuropathy-5 (9%), mononeuritis multiplex-1 (2%), NMJ disorders-2 (4%), facial neuropathy (LMN)-1 (2%), median neuropathy at wrist B/L-2 (4%), AMSAN-8 (15%), AMAN-4 (7%), AIDP-1 (2%), upper-trunk plexopathy-1 (2%), and myopathy-2 (4%).

Patients with a history of invasive ventilation following COVID-19 infection had 2.5 times the risk of developing myopathic disorder than those who did not require invasive ventilation [RR: 2.5, 95% CI 0.6 – 9.9]. Patients who required non-invasive ventilation following COVID-19 infection were 1.6 times more likely to develop myopathic disorder than those who did not require ventilation [RR: 1.6, 95% CI 0.4-6.5]. Patients with a history of invasive ventilation

following COVID-19 infection were 2.6 times more likely to develop neuropathic disorder than those who did not require invasive ventilation [RR 2.6, 95% CI 0.8-8.5]. Patients who required invasive ventilation following COVID-19 infection were 2 times more likely to develop Guillian Barre Syndrome (GBS) than those who did not require ventilation [RR: 2, 95% CI 0.6-6.6].

The authors present a cohort of patients with COVID-19 who developed neuromuscular symptoms and reported to the NCS / EMG department for electrodiagnostic evaluation. Weakness of one or more limbs was the most common presentation of patients in this study. Polyneuropathy was the most common electrophysiological diagnosis in this study (n = 22, 40%). Amongst these, GBS was the most common polyneuropathy (n = 13, 23.6%).

Out of the 10 (18%) patients who had myopathy, 6 (11%) patients had CIM and 2 (4%) patients had CIPM. However, myopathy was more common (12 out of 18 patients) in a single-centre study conducted by Hameed *et al*.[2] The increased proportion of patients with myopathy reported by Hameed *et al*. can be because the majority of the patients in their study were intubated (11 out total 18) and had received steroid (n = 15, 83%).[2] Multiple factors are responsible for the development of myopathy after COVID-19 infection which include erroneous excitation-contraction coupling, electrolyte imbalances, use of high-dose steroids, neuromuscular blocking agents, and direct invasion of muscle tissue by a virus.[3]

Out of the 13 (23.6%) patients with GBS, 8 patients had AMSAN and 4 had AMAN. These variants of GBS after COVID-19 infection resembled those of the classic GBS.[4] In contrast to the present study, Abu-Rumeileh *et al*. concluded that acute inflammatory demyelinating polyneuropathy (77.4%) was the most common GBS variant after COVID-19 infection.[4] It may be because the majority of the participants of the studies included in the systematic review were from Western countries where demyelinating variants of GBS are common as compared to the Asian countries.[4]

Because of the limited data, the authors could not accurately comment on whether the patients developed GBS before, during or after the start of COVID-19 infection. COVID-19 infection can progress sub-clinically or the patients can develop symptoms of GBS in the absence of respiratory symptoms of COVID-19 infection and it can go unnoticed until significant weakness occurs.[5] In this study, patients who required invasive ventilation following COVID-19 infection were 2 times more likely to develop GBS. However, this may be clinically not significant because of the small sample size. Similar to other viral illnesses, *SARs-CoV-2* has been linked to GBS, however, clear association has not been documented.[6] These associations assume that molecular mimicry between viral proteins and gangliosides containing sialic acid residues of peripheral nerves result in damage to myelin and axons of peripheral nerves.[6]

The authors have reported detailed electrophysiological features of NMD in patients after COVID-19 infection in Pakistan. However, this study is not without limitations. The functional status of the patients was not evaluated. Because of the limited data and a small sample size, the authors cannot comment on the temporal relationship of these disorders with COVID-19 infection.

In conclusion, polyneuropathy is the most common NMD associated with COVID-19 infection. Patients with history of invasive ventilation secondary to COVID-19 may be susceptible to develop neuropathic disorders, however, further studies are needed to establish the causality of this correlation.

ETHICAL APPROVAL:
This study was approved by the Ethical Review Committee of the Hospital (Approval No. 2021/09/trg). The study was conducted in accordance with the principles of the Declaration of Helsinki.

PATIENT'S CONSENT:
Written informed consent was obtained from all participants and in cases where patients themselves were unable to give consent, written informed consent was obtained from their next of kin.

COMPETING INTEREST:
The authors declared no conflicts of interest.

AUTHORS' CONTRIBUTION:
MTK, UA, UY: Conceptualisation.
MTK: Data curation and formal analysis.
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REFERENCES

1. Ning Q, Wu D, Wang X, Xi D, Chen T, Chen G, *et al*. The mechanism underlying extrapulmonary complications of the coronavirus disease 2019 and its therapeutic implication. *Signal Transduct Target Ther* 2022; **7(1)**:57. doi: 10.1038/s41392-022-00907-1.
2. Hameed S, Khan AF, Khan S. Electrodiagnostic findings in COVID-19 patients: A single center experience. *Clin Neurophysiol* 2021; **132(12)**:3019-24. doi: 10.1016/j.clinph.2021.10.001.
3. Bagnato S, Boccagni C, Marino G, Prestandrea C, D'Agostino T, Rubino F. Critical illness myopathy after COVID-19. *Int J Infect Dis* 2020; **99**:276-8. doi: 10. 1016/j.ijid.2020.07.072.
4. Abu-Rumeileh S, Abdelhak A, Foschi M, Tumani H, Otto M. Guillain-Barre syndrome spectrum associated with COVID-19: An up-to-date systematic review of 73 cases. *J Neurol* 2021; **268(4)**:1133-70. doi: 10.1007/s00415-02010124-x.

5. Bracaglia M, Naldi I, Govoni A, Ventura DB, De Massis P. Acute inflammatory demyelinating polyneuritis in association with an asymptomatic infection by SARS-CoV-2. *J Neurol* 2020; **267(11)**:3166-8. doi: 10.1007/s00415-020-10014-2.

6. Sriwastava S, Kataria S, Tandon M, Patel J, Patel R, Jowkar A, *et al*. Guillain Barre Syndrome and its variants as a manifestation of COVID-19: A systematic review of case reports and case series. *J Neurol Sci* 2021; **420**:117263. doi: 10.1016/j.jns.2020.117263.