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Analysis of Nerve Conduction Parameters in Post-Covid-19 Patients with Neuropathic symptoms

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ABSTRACT

Background: World is confronting various deleterious consequences of Covid-19. Neurological complications are of paramount importance amongst these. One of the uprooting neurological complications is of peripheral neuropathy. Nerve conduction study utilizes evaluation of conduction properties of nerves to diagnose and classify type of neuropathy.
Objective: The present study aims to identify the type of neuropathy in post-covid-19 patients with neuropathic symptoms.
Materials and Method: RMS SALUS software was used. Bilateral Median, Ulnar, Tibial and Common Peroneal motor nerves and Bilateral Median, Ulnar, Sural and Superficial peroneal sensory nerves were studied. Parameters included Compound muscle action potential (CMAP), Sensory nerve action potential (SNAP) and Nerve conduction velocity (NCV) measured in millivolt, microvolt and meter/second, respectively.
Result: Eighteen post-covid-19 patients with neuropathic symptoms underwent the procedure. Fourteen of them were electrodiagnostically proven cases of Guillain Barre Syndrome (GBS). Variants of GBS included seven cases of Acute inflammatory Demyelinating Polyneuropathy (AIDP), six of Acute motor sensory axonal neuropathy (AMSAN), one of Acute motor axonal neuropathy (AMAN). Out of the rest of four patients, two had normal nerve conduction findings in spite of having symptoms of muscular weakness and numbness. Other two had mononeuropathy.
Conclusion: While the neurological sequelae of Covid-19 are still underexplored, health care workers must be aware of the possible serious life threatening neurological complications as is GBS. Being an autoimmune disease, GBS can be triggered by Covid-19 infection. Nerve conduction study holds the mainstay for the diagnosis of neuropathy.
Write abstract/summary of your article here.

Keywords: Covid-19, SARS-CoV-2, Acute Inflammatory demyelinating Polyneuropathy, Guillain Barre Syndrome, Nerve conduction study.

INTRODUCTION

On March 11th 2020, WHO declared the SARS-Cov-2 pandemic. Common neurological symptoms reported were dizziness, headache, hypogeusia, hyposmia, muscle damage, ischemic and hemorrhagic stroke. [1] SARS-Cov-2 and its neurological complications have been reviewed, but are still underexplored. [2, 3]

Nerve conduction study holds the mainstay for the diagnosis of peripheral neuropathy. [4] Conduction properties of nerves are analyzed in terms of conduction velocity (in m/s), Compound muscle action potential

(CMAP) (in mV) and Sensory nerve action potential (SNAP) (in micro V).

Hence, in the light of above information, the present study aimed to develop a better understanding of the peripheral nerve function through nerve conduction test in patients with neuropathic symptoms in their post-covid- phase.

MATERIALS & METHODS

Study design: Cross sectional study

Study duration: August 2020 to May 2021

Type of participants: Post-covid-19 patients with neuropathic symptoms.

Type of material involved: RMS SALUS software was used.

Inclusion criteria: Both Male and female patients in Post-Covid-19 phase suffering with neuropathic symptoms of numbness and weakness.

Exclusion criteria: Non-Covid patients with Neuropathic symptoms,

Chronic Neuropathy,

Unco-operative patients,

Mentally unstable,

Patients who did not give consent for the study.

A written, informed consent was obtained from patients (or relatives) prior to data collection. Standard aseptic precautions were undertaken and the study was conducted at room temperature. Patients were positioned in Supine for all motor and sensory nerves study, while side lying position was being assumed for Sural nerve study.

Bilateral Median, Ulnar, Tibial and Common peroneal nerves were studied for motor nerves. Motor nerve conduction velocity (MNCV) and Compound muscle action potential (CMAP) amplitude were measured in m/s and mV respectively. Disc electrodes were used for motor nerve conduction recording. Recording electrode included Active and reference recording electrodes. Motor nerves were stimulated at proximal and distal sites and NCV was calculated based on distance between the two sites.

Sensory nerve study included bilateral Median, Ulnar, Sural and superficial peroneal nerves. Sensory nerve conduct ion velocity (SNCV) and Sensory nerve action potential (SNAP) were studied in m/s and Microvolt, respectively. Ring electrodes were used for Sensory conduction recording in Median and Ulnar nerves, while disc electrodes were used for Sural and superficial peroneal nerve study. Sensory nerves were stimulated at single distal site. SNCV was calculated based on the distance measured from stimulation site to active recording electrode.

Ground electrode was positioned between stimulating and recording electrodes.

Cathode was placed distally

Patients were asked to keep the limbs in as relaxed position as possible to facilitate efficient stimulation and recording.

All the values obtained were analyzed and the type of neuropathy was classified. [5]

Standard protocol for Patient and Limb position and electrode placement were followed.[6] A total of 18 Post-Covid-19 referred patients with neuropathic symptoms underwent the procedure.

Statistical Analysis: Demographic data was analysed using Microsoft excel 2007.

RESULT

Eighteen post-covid-19 patients with neuropathic symptoms underwent the procedure of nerve conduction test.

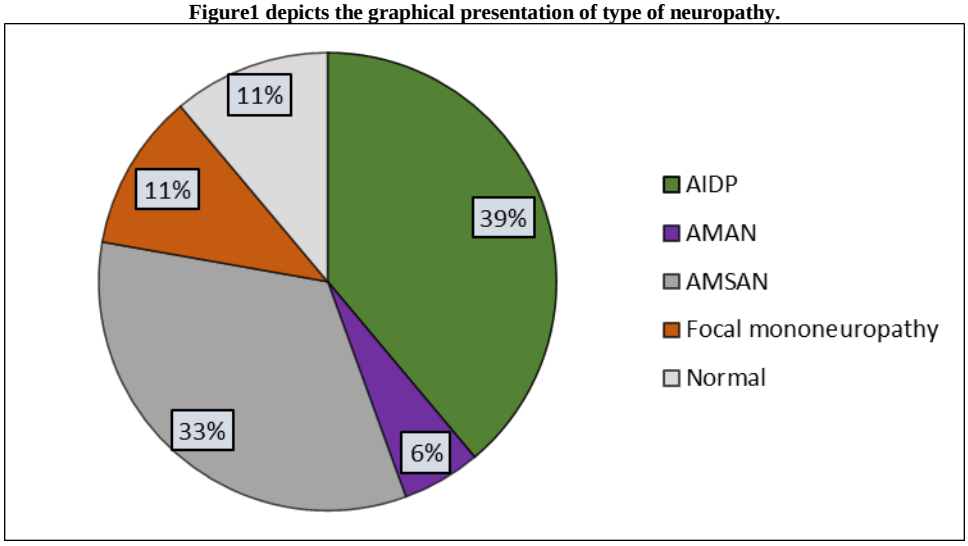
Table 1 shows the demographic data.

Variables	Mean+/- SD
Gender Male Female	 13 5
Age (in years)	52.944
Duration of onset of neuropathic symptoms after Covid-19 (in weeks)	6.277

Table2. Type and proportion of neuropathy

Type of neuropathy	Proportion
AIDP	7
AMAN	1
AMSAN	6
Focal mononeuropathy	2
Normal	2

Figure1 depicts the graphical presentation of type of neuropathy.



Out of 18 patients examined, 14 had electrodiagnostically proven Guillain barre syndrome (GBS). Variants of GBS included Acute inflammatory Demyelinating polyneuropathy (AIDP)-7, Acute motor axonal neuropathy (AMAN)-1, Acute motor sensory axonal neuropathy (AMSAN)-6 patients. Out of the rest of 4 patients, 2 had Normal Nerve conduction findings in spite of symptoms of muscle weakness, one patient had Right Peroneal nerve palsy and other patient had Left Lumbosacral plexopathy. Both of the later patients had a history of being comatose for a few days prior to the development of neuropathy.

All AIDP and AMSAN patients had bilateral lower limb weakness, difficulty in independent ambulation with intact sensations and bowel-bladder.

1 patient of AMAN had sudden, severe (Grade-2, Oxford MMT scale) weakness of all four limbs along with ventilator support.

DISCUSSION

The present article showed that the nerve conduction parameters are altered in post-covid-19 patients having neuropathic symptoms.

GBS is defined as an acute immune mediated disease of the peripheral nerves and nerve roots (Polyradiculoneuropathy) that is usually elicited by various infections. [7] Pathologically, the nerves undergo segmental demyelination. The common clinical manifestations are of distal paresthesia, symmetric weakness of limbs, and cranial muscles, and distal areflexia. The extra-ocular and sphincter muscles are usually spared. [5]

Several case reports have been published which suggest a link between GBS and COVID-19. Many of these had a post infectious course of GBS, as in this study. The duration of onset of symptoms varied from 2 -3 weeks. [21-23]

All of the patients in the present study had a Post-infectious course with duration of onset of symptoms ranging from 2-6 weeks.

On the other hand, para infectious GBS has also been discovered in many case reports. Patients developed quadriparesis with or without ventilator requirement during their Covid phase in hospital.[24-26]

The major variants commonly confronted are AIDP, AMAN, AMSAN and Miller

Fisher syndrome.[27] The later was not encountered in the present study.

Asia confronted an epidemic of SARS which arose from SAR-Cov in February 2003.[8] while myalgia and fever were common features, neurological manifestations were observed in 30% of patients.[9] MERS CoV outbreak occurred in Saudi Arabia in June 2012 [10] Neurlogical studies have confirmed the diagnosis of Acute Polyneuropathy in post infectious phase of MERS and SARS. [11-15] Zika virus have also been found to be associated with GBS. [16]

Corona virus possess neuroinvasive and neurotropic potential which increases its affinity towards human nervous system.

1. ACE-2 receptor mechanism

ACE-2 receptors are widely expressed in human nervous tissues along with the respiratory endothelium. Direct cytotoxic effect of the virus through ACE-2 receptors has been postulated and is also the supposed mechanism for GBS in viral infections by Zika, SARS and MERS.[17] This mechanism leads to rapid evolution of Acute polyneuropathy after the onset of COVID-19 symptoms, that is in the parainfectious phase.

2. Immune mediated mechanism

It has been postulated that the Glycoconjugates present in human nervous tissues resemble the glycoproteins on the surface of Corona virus. Hence, when the immune system is activated against the virus, it also harms the Glycoconjugates on human nervous tissue, thus causing damage to the myelin sheath or Schwann cells. This mechanism of nerve injury is popularly termed as "Molecular Mimicry". [18] Also, SARS-CoV-2 virus comprise of 2 hexapeptides which are akin to Human Heat shock proteins 60 and 90. These proteins have immunogenic potential associated with the occurrence of Acute and Chronic demyelinating polyneuropathy.[19] This is an indirect mechanism that leads to development of Acute Polyneuropathy which is apparent only after a few days or weeks or even months following the acute infectious phase, that is in the post infectious phase. Neurological complications occur as a result of activation of immune mechanism against one's own tissues. "Cytokine storm" has been described by [20]

Hence, the possible mechanism of GBS in the present study is supposed to be due to auto-immune insult caused by Covid-19 virus.

Two of the patients having focal mononeuropathy and plexopathy could be due to improper positioning during the comatose phase. And the other two subjects having Normal NCS in spite of having muscle weakness was due to Rhabdomyolysis (one of the post covid complications) in their post-covid-phase.

CONCLUSION

Hence, in the light of above findings, it could be concluded that SARS-CoV-2 can affect the peripheral nervous system and could cause serious life-threatening neurological complications like GBS. So, it requires an alert upgradation for all the health care workers and have a high index of suspicion in case of neuropathic symptoms in Post Covid-19 phase so as to diagnose and provide timely treatment.

Nerve conduction study holds the mainstay for the diagnosis of peripheral neuropathy.

Further Recommendations

Study on large scale is required to explore many other neurological complications which could dehisce once the pandemic resolves.

Also a follow up study of the above patients will assist in determining the course of neuropathy.

Including EMG study will be more informative.

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