RESEARCH PAPER

Emerging axonal variants of Guillain Barré Syndrome "AMAN and AMSAN as a part of COVID-19 sequalae

Nareen H. Hasrat[1], Haithem J. Kadhum[2], Ali R. Hashim[3], Zaineb A. Yaqoob[4], Hassan A. Farid[5]

1. MBChB. MSc. Student (Neurophysiology), Department of Physiology, College of Medicine, University of Basrah, Iraq
2. MBChB. MSc. PhD. (Physiology), Department of Physiology, College of Medicine, University of Basrah, Iraq
3. MBChB. CABM. FRCP., (Medicine Neurology), Department of Medicine, College of Medicine, University of Basrah, Iraq
4. MBChB. FIBMS. (Clinical Neurophysiology), Department of Physiology, College of Medicine, University of Basrah, Iraq
5. MBChB. MSc. (Neurology), Institute of Medical and Biomedical Education, St. George's University of London, London, UK

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Abstract

Background: Guillain-Barré syndrome (GBS) is an immune-mediated peripheral nerve disease. Its frequency was noticed to have increased during the COVID-19 period. Based on electrophysiological studies, the most common type of this disease is the demyelinating type. However, axonal types have also been seen.

Methods: A large, analytical, cross-sectional study involving 2523 patients over a one-year period was conducted in Basrah, southern Iraq, to evaluate the neurophysiological changes for peripheral neuropathies following COVID-19 infection using nerve conduction studies and needle electromyography. The current study aims to evaluate the prevalence, clinical, and neurophysiological characteristics of patients with axonal variants of GBS.

Results and conclusions: The study found that the axonal variants of GBS represent about 10% of the total reported GBS in the governorate, and they are developed in about 1 in 1000 patients attending the neurology and neurophysiology clinics who had a history of COVID-19 infection.

Key words: Emerging axonal variants, Guillain Barré Syndrome, AMAN and AMSAN, COVID-19

Corresponding author: Nareen H. Hasrat, College of Medicine, University of Basrah

✉ **E-mail: nareenhaikaz@gmail.com**

Introduction

Guillain-Barré syndrome (GBS) is an immune-mediated peripheral nerve disease with a frequency of 1-2 occurrences per 100,000 individuals. When GBS is suspected, electrophysiological tests are required to confirm the diagnosis and rule out possible imitators. Other disorders linked with acute flaccid paralysis, such as myasthenic crises, acute presentation of the idiopathic inflammatory myopathies, and the atypical motor neuron disease patient presenting with abrupt respiratory failure are included in the differential diagnosis of pure motor syndrome. Associated clinical characteristics are frequently useful in differentiating these from GBS.[1] The electrodiagnostic study (EDX) is regarded as the

foundation for classifying the various subtypes of this syndrome. GBS has three primary subgroups based on electrophysiological results, including "acute inflammatory demyelinating polyneuropathy (AIDP)", "acute motor axonal neuropathy (AMAN)", and "acute motor sensory axonal neuropathy (AMSAN)".[2] Due to demyelination of the nerve roots, the early observations in AIDP included prolonged F-wave latencies or poor F-wave repeatability. This is followed by increased distal latencies (due to demyelination of the distal nerves) and temporal dispersion or conduction block. Slowing of nerve conduction velocities is less beneficial since it often occurs two to three weeks after initiation. However, depending on established criteria, the sensitivity of nerve conduction studies (NCS) may be as low as 22% in early AIDP and as high as 87% five weeks into the disease. In severe instances of AMAN, the motor nerve amplitudes are abolished or markedly reduced, and the distal latencies and conduction velocities are affected sparingly or minimally. In AMSAN, the sensory potentials are diminished in amplitude and frequently absent in addition to the reduction in motor potential amplitude.[3,4] The axonal variants of GBS are uncommon, and they are mainly reported in northern China, Japan, and the north of America, where they are mainly associated with *Campylobacter jejuni* infection.[2] According to the findings of Finsterer et al., peripheral neuropathy is remarkably prevalent among COVID-19 patients.[5] In 2021, Zuberbuhler, et al. did a literature study on the association between GBS and COVID-19 infection and discovered multiple case reports from various nations.[6] According to statistics, the number of GBS cases would increase by a factor of about five. Moreover, the frequency of GBS and chronic inflammatory demyelinating polyneuropathy (CIDP) is six times greater in the COVID-19 population than in the non-COVID-19 group, according to a recent cohort study from Basrah, southern Iraq.[7] This study brings to light an uncommon complication in a patient with a confirmed COVID-19 diagnosis, whose clinical and electrophysiological features imply axonal variations of GBS and estimates the frequency of such variants.

Materials and methods

Basrah-based multicentric analytical cross-sectional research was initiated to evaluate nerve conduction (NCS) and electromyographic (EMG) results in a patient with a history of COVID-19.[8] Cases of GBS axonal variants were identified during the evaluation of 2,532 patients who visited the neurology unit in Basrah teaching hospital and neurophysiology outpatient clinics in both Al-Sadr teaching hospital and Basrah Specialized Children's hospital over the course of one year, from July 1, 2021, to July 1, 2022. The participants were divided into two separate groups. The first group (1469 patients) consists of those who have had a confirmed COVID-19 infection in the previous year and were diagnosed using the European Center for Disease Control (eCDC) criteria, which include a positive polymerase chain reaction (PCR) and/or chest computed tomography (CT) demonstrating bilateral peripheral ground-glass opacities in the presence of strong clinical, serological, or epidemiological suspicion.[9] The second group of 1063 patients are comprised of individuals with a negative COVID-19 history. A consultant neurologist did a comprehensive history with medical and neurological tests, and a full evaluation of the patient's history and laboratory reports during his hospitalization for COVID-19 infection was undertaken. In the neurophysiology outpatient clinic at Basrah Specialized Children's Hospital, a specialised neurophysiologist utilises

the Neuropack X1 Neurodiagnostic System (a Nihon Kodhon product) to conduct a thorough electrodiagnostic exam consisting of nerve conduction studies and needle electromyography. Patients were classified as having either acute motor axonal neuropathy or acute motor and sensory axonal neuropathy if there was electromyographic evidence of axonal degeneration together with a reduction of more than 50 percent of the lower limit of the amplitudes of compound muscle action potentials or sensory nerve action potentials of the laboratory concerned in the presence of normal motor conduction velocities, distal motor latencies, and minimum F-wave latencies.[10] The clinical, laboratory, and electrophysiological parameters of patients were tabulated. The reference range for NCS parameters was derived from Preston and Shapiro's electromyography and neuromuscular diseases textbook on clinical neurophysiology, (2017).[11] The Statistical Package for Social Science (SPSS) version 26 software (Armonk, NY: IBM Corp.) was utilised to analyses the study's findings. The qualitative information was transcribed to a percentage and analyzed with Fisher's exact test. A p-value of 0.05 or less is considered statistically significant. Ethical permission was acquired by the Basrah Health Directorate (No. 911) and from the Basrah University College of Medicine's ethics committee (No. 7/9/6292) and an informed written consent was obtained from the patients who participated in this study.

Results

Only two patients from 1469 with a history of COVID-19 infection (0.13%) reported having an axonal variant of GBS; one was AMAN and the other was AMSAN. On the other hand, none of those who denied a history of COVID-19 infection reported having axonal GBS variants. The demyelinating GBS variant is significantly higher among those with COVID-19 infection compared to those with a negative history of COVID-19 (P-value = 0.002). Furthermore, the axonal variant was present in 2 of 19 patients with GBS (10.5%), (Table-1).

Table 1. Axonal and Demyelinating Variants of GBS

Diagnosis	History of COVID-19 No. (%)	No History of COVID-19 No. (%)	Total	P-value *
Axonal Variants (1st)	2 (0.13)	0 (0.00)	2	1.000 a 0.512 b 0.002 c
Demyelinating Variants (2nd)	16 (1.10)	1 (0.09)	17	
Not Developed GBS (3rd)	1451 (98.77)	1062 (99.91)	2513	
Total	1469	1063	2532	

* Fishers Exact Test
a, b, and c represent the difference between 1st and 2nd group, 1st and 3rd group, 2nd and 3rd group respectively.

Both cases of GBS axonal variants were young; one of them was male, and the other was female; none of them reported chronic medical illnesses (Table-2).

Table 2. Demographic Characteristics of the Two Patients

Demographic characteristics	AMAN	AMSAN
Age / Years	21	32
Gender	Male	Female
Height / cm	172	156
Residency	Urban	Urban
Chronic illnesses	None	None

AMAN: Acute motor axonal neuropathy, AMSAN: Acute motor sensory axonal neuropathy

The two patients reported a mild history of confirmed COVID-19 infection, which did not require hospitalization, and respiratory symptoms consistent with flu-like illness that did not persist longer than a week with normal oxygen saturation and laboratory investigations.

Furthermore, none of them received a COVID-19 vaccination. In addition, both patients denied any recent diarrheal illness (Table-3).

Table 3. The COVID-19 Characteristics of the Two Patients

COVID-19 characteristics	AMAN	AMSAN
The severity of COVID-19	Mild	Mild
The occurrence of cytokine storm	None	None
The history of hospitalization	None	None
Duration of respiratory illness	3 days	5 days
Oxygen saturation	98 %	99 %
Serum Ferritin	210	156
C-reactive protein (CRP)	3	7
Lactate dehydrogenase (LDH)	170	189
Neutrophil to Lymphocyte ratio (NLR)	2.2	1.9
PCR test	Positive	Positive
History of COVID-19 Vaccination	None	None
AMAN: Acute motor axonal neuropathy, AMSAN: Acute motor sensory axonal neuropathy, PCR: polymerase chain reaction		

The neurological illness developed within less than one month of the respiratory illness in both patients, and it is primarily affecting the lower limb and ascending, reaching a nadir of weakness within less than one month. A full basic metabolic workup, including a complete blood count, renal and liver function tests, blood glucose, electrolytes, B12 level, viral screen, inflammatory markers, anti-nuclear antibodies, and vasculitis panel, was done with normal inconclusive results. The details of the neurological examination, cerebrospinal fluid analysis and radiological images were summarised in (Table-4).

Table 4. The Neurological Characteristics of the Two Patients

Neurological characteristics	AMAN	AMSAN
Time of onset of neurological complain in relation to COVID-19	21 days	15 days
Limb weakness	Proximal initially then Distal ascending lower and upper	Start distally and ascending up mainly lower limb
Paraesthesia and numbness	None	In the lower limbs and hands
Neuropathic burning pain	None	In the lower limbs
Low back pain	Yes	Yes
Unsteady gait (ataxia)	Unable to walk	Sensory ataxia with positive Romberg's test
Sphincter dysfunction	None	None
Dysphagia / Dysarthria	None	None
Dyspnoea	None	None
Facial asymmetry	None	None
Bulbar signs	None	None
Muscle wasting	None	None
Muscle fasciculation	None	None
Tone	Hypotonia	Hypotonia
Power	Upper limb grade 3 and lower limb grade 2	Upper limb grade 5 and lower limb grade 3
Reflexes	Upper limb preserved and lower limb hyporeflexia	Upper limb preserved and lower limb hyporeflexia
Coordination	Unable to assess	Impaired mainly with eye closure
Sensation	Normal	Decrease pin prick and touch in gloves and stock distribution with impaired vibration up to the malleolus and impaired proprioception up to the ankle and preserved vibration and proprioception in upper limbs
Lumbosacral MRI	Normal	Normal
CSF analysis	Not done due to patient refusal	High protein with no cell
AMAN: Acute motor axonal neuropathy, AMSAN: Acute motor sensory axonal neuropathy, MRI: Magnetic resonance image, CSF: Cerebrospinal fluid		

Regarding the motor nerve conduction study of the first patient (AMAN) at day 7, the distal latencies and the nerve conduction velocities of all the studied nerves were within normal range, but the amplitudes were all affected and below the lower limit of normal. Both sided peroneal nerves and the right sided tibial nerve were not recordable. The late responses in the form of F-wave minimal latency recorded from the bilateral ulnar nerves and left tibial nerve were normal, and the H-reflex from the left side was also normal. At Day 42, distal latencies and nerve conduction velocities were still within normal limits, and the amplitude of the median and ulnar nerves on both sides had improved. The right sided peroneal nerve was recordable with very small amplitude. However, no responses could be gained form left peroneal nerve and right sided tibial nerve. No significant changes were recorded for the ulnar and left sided tibial nerves' F wave minimal latencies or from the left sided H-reflex. The sensory nerve conduction studies for the median nerve recorded from digit II, the ulnar nerve recorded from digit V, and the sural nerve in the lower limb were all normal in their amplitude and nerve conduction time bilaterally at both day 7 and day 42 (Table-5).

Table 5. Nerve conduction Study Parameters of AMAN Patient

Nerve	Site	Distal latency (ms)	Amplitude (mv)	Conduction velocity (m/s)	Nerve	Site	Distal latency (ms)	Amplitude (mv)	Conduction velocity (m/s)
Median (APB)	Lt	3.4 (≤ 4.4)	2.2 (≥ 4)	55.3 (≥ 49)	Median (APB)	Lt	3.4	6.4 (≥ 4)	61.3 (≥ 49)
	Rt	3.5 (≤ 4.4)	3.1 (≥ 4)	53.2 (≥ 49)		Rt	3.4	7.9 (≥ 4)	59.1 (≥ 49)
Ulnar (ADM)	Lt	2.9 (≤ 3.3)	2.4 (≥ 6)	55.8 (≥ 49)	Ulnar (ADM)	Lt	2.7 (≤ 3.3)	7.1 (≥ 6)	63.4 (≥ 49)
	Rt	2.7 (≤ 3.3)	1.3 (≥ 6)	58.0 (≥ 49)		Rt	3.0 (≤ 3.3)	5.1 (≥ 6)	66.3| (≥ 49)
Peroneal (EDB)	Lt	NR	NR	NR	Peroneal (EDB)	Lt	NR	NR	NR
	Rt	NR	NR	NR		Rt	5.0 (≤ 6.6)	0.3 (≥ 2)	58.5 (≥ 44)
Tibial (AHB)	Lt	4.5 (≤ 5.8)	1.3 (≥ 4)	49.9 (≥ 41)	Tibial (AHB)	Lt	4.7 (≤ 5.8)	2.5 (≥ 4)	51.5 (≥ 41)
	Rt	NR	NR	NR		Rt	NR	NR	NR
Late responses									
Ulnar F wave minimal latency	Lt	31.0 (≤ 32)			Ulnar F wave minimal latency	Lt	31.2 (≤ 32)		
	Rt	30.6 (≤ 32)				Rt	30.7 (≤ 32)		
Tibial F wave minimal latency	Lt	53.2 (≤ 56)			Tibial F wave minimal latency	Lt	54.6 (≤ 56)		
	Rt	NR				Rt	NR		
H reflex minimal latency (Ankle)	Lt	30.3 (≤ 32)			H reflex minimal latency (Ankle)	Lt	30.2 (≤ 32)		
	Rt	NR				Rt	NR		
Sensory nerve conduction study (Antidromic study)									
Nerve	Site	Latency (ms)	Amplitude (mv)	Conduction velocity (m/s)	Nerve	Site	Distal latency (ms)	Amplitude (mv)	Conduction velocity (m/s)
Median (Digit II)	Lt	2.4 (≤ 3.5)	67.3 (≥ 20)	50.0 (≥ 50)	Median (Digit II)	Lt	2.4 (≤ 3.5)	54.5 (≥ 20)	50.0 (≥ 50)
	Rt	2.3 (≤ 3.5)	56.8 (≥ 20)	52.2 (≥ 50)		Rt	2.3 (≤ 3.5)	43.5 (≥ 20)	52.0 (≥ 50)
Ulnar (Digit V)	Lt	2.2 (≤ 3.1)	40.2 (≥ 17)	50.4 (≥ 50)	Ulnar	Lt	2.1 (≤ 3.1)	45.0 (≥ 17)	50.4 (≥ 50)
	Rt	2.2 (≤ 3.1)	35.7 (≥ 17)	50.4 (≥ 50)		Rt	2.2 (≤ 3.1)	44.9 (≥ 17)	55.6 (≥ 50)
Sural	Lt	2.5 (≤ 4.4)	14.5 (≥ 6.0)	48.0 (≥ 40)	Sural	Lt	2.5 (≤ 4.4)	17.4 (≥ 6.0)	48.0 (≥ 40)
	Rt	2.4 (≤ 4.4)	16.4 (≥ 6.0)	50.2 (≥ 40)		Rt	2.5 (≤ 4.4)	15.2 (≥ 6.0)	48.0 (≥ 40)

Lt: Left, Rt: Right, NR: No response, APB: Abductor pollicis brevis, ADM: Abductor digiti minimi, EDB: Extensor digitorum brevis, AHB: Abductor hallucis brevis

The needle EMG of the AMAN patient at day 10, while examining the right sided deltoid muscle, first dorsal interosseous muscle (FDI), vastus medialis muscle (VM), tibialis anterior muscle (TA), and extensor hallucis longus muscle (EHL), showed reduced recruitment in the VM, TA, and EHL muscles with normal morphology MUAPs in all of the studied nerves, and no spontaneous activity was detected. During the follow up of the patient at day 60, features of both active denervation and reinnervation were reported, which include spontaneous activities in the form of fibrillations (Fibs) and positive sharp waves (PSWs) that were recorded from FDI and TA muscles. The MUAPs of all the studied muscles were of long duration, high amplitude, and polyphasic except in the deltoid (Table-6).

Table 6. Needle EMG Parameters of AMAN Patient

Needle electromyography										
Day 7						Day 42				
Findings	**Deltoid**	**FDI**	**VM**	**TA**	**EHL**	**Deltoid**	**FDI**	**VM**	**TA**	**EHL**
Spontaneous activity	Nill	Nill	Nill	Nill	Nill	Nill	Fibs / PSWs	Fibs / PSWs	Fibs / PSWs	Fibs / PSWs
MUAP Duration	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Long	Long	Long
MUAP Amplitude	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Large	Large	Large
Recruitment	Normal	Normal	Normal	Reduced	Reduced	Normal	Reduced	Reduced	Reduced	Reduced
Number of phases	Normal	Normal	Normal	Normal	Normal	Occasional polyphasia	Normal	Polyphasic	Polyphasic	Polyphasic

FDI: First dorsal interosseous muscle, VM: Vastus medialis muscle, TA: Tibialis anterior muscle, EHL: Extensor hallucis longus muscle, Fibs: Fibrillations, PSWs: Positive sharp waves, MUAP: Motor unit action potential

For the motor nerve conduction study of the second patient (AMSAN) at day 10, the distal latencies and the nerve conduction velocities of the right and left median, ulnar, and tibial nerves were within normal range, but the amplitudes were all affected and below the lower limit of normal. Peroneal nerves on both sides were not recordable. The late responses in the form of F-wave minimal latency recorded from bilateral ulnar and tibial nerves and H-reflex latency from both sides were normal. At day 60, distal latencies and nerve conduction velocities were still within normal limits, and improvement was noticed in the amplitude of the right and left median nerves, although no significant changes were noticed in the ulnar and tibial nerves on either side. Peroneal nerves on both sides had been recorded with very small amplitudes. No significant changes were recorded for the ulnar and tibial nerves' F wave minimal latencies or for H-reflex bilaterally. The sensory nerve conduction studies for the median nerve recorded from digit II, the ulnar nerve recorded from digit V, and the sural nerve in the lower limb showed normal conduction times. Regarding the amplitude, all were significantly affected on both sides, with the findings worsening at day 60 of examination in comparison to day 7, (Table-7).

Table 7. Nerve conduction Study Parameters of AMSAN Patient

Motor nerve conduction study									
Day 10					Day 60				
Nerve	**Site**	**Distal latency (ms)**	**Amplitude (mv)**	**Conduction velocity (m/s)**	**Nerve**	**Site**	**Distal latency (ms)**	**Amplitude (mv)**	**Conduction velocity (m/s)**
Median (APB)	Lt	3.2 (≤ 4.4)	2.2 (≥ 4)	50.3 (≥ 49)	**Median (APB)**	Lt	3.3 (≤ 4.4)	3.6 (≥ 4)	55.2 (≥ 49)
	Rt	3.4 (≤ 4.4)	1.5 (≥ 4)	54.5 (≥ 49)		Rt	3.4 (≤ 4.4)	4.1 (≥ 4)	56.4 (≥ 49)
Ulnar (ADM)	Lt	2.4 (≤ 3.3)	3.9 (≥ 6)	53.2 (≥ 49)	**Ulnar (ADM)**	Lt	2.6 (≤ 3.3)	3.5 (≥ 6)	57.3 (≥ 49)
	Rt	2.5 (≤ 3.3)	2.7 (≥ 6)	54.2 (≥ 49)		Rt	2.7 (≤ 3.3)	3.0 (≥ 6)	58.7 (≥ 49)
Peroneal (EDB)	Lt	NR	NR	NR	**Peroneal (EDB)**	Lt	5.2 (≤ 6.6)	0.3 (≥ 2)	49.6 (≥ 44)
	Rt	NR	NR	NR		Rt	5.4 (≤ 6.6)	0.7 (≥ 2)	47.5 (≥ 44)
Tibial (AHB)	Lt	4.7 (≤ 5.8)	2.1 (≥ 4)	50.2 (≥ 41)	**Tibial (AHB)**	Lt	4.7 (≤ 5.8)	2.5 (≥ 4)	51.5 (≥ 41)
	Rt	4.3 (≤ 5.8)	1.4 (≥ 4)	51.6 (≥ 41)		Rt	4.6 (≤ 5.8)	1.1 (≥ 4)	47.2 (≥ 41)
Late responses									
Ulnar F wave minimal latency	Lt	29.1 (≤ 32)			**Ulnar F wave minimal latency**	Lt	28.8 (≤ 32)		
	Rt	30.2 (≤ 32)				Rt	30.9 (≤ 32)		
Tibial F wave minimal latency	Lt	51.5 (≤ 56)			**Tibial F wave minimal latency**	Lt	52.1 (≤ 56)		
	Rt	51.0 (≤ 56)				Rt	52.2 (≤ 56)		
H reflex minimal latency (Ankle)	Lt	30.1 (≤ 32)			**H reflex minimal latency (Ankle)**	Lt	30.4 (≤ 32)		
	Rt	30.0 (≤ 32)				Rt	30.2 (≤ 32)		
Sensory nerve conduction study (Antidromic study)									
Nerve	**Site**	**Latency (ms)**	**Amplitude (mv)**	**Conduction velocity (m/s)**	**Nerve**	**Site**	**Distal latency (ms)**	**Amplitude (mv)**	**Conduction velocity (m/s)**
Median (Digit II)	Lt	2.3 (≤ 3.5)	9.9 (≥ 20)	52.0 (≥ 50)	**Median (Digit II)**	Lt	2.2 (≤ 3.5)	11.0 (≥ 20)	54.5 (≥ 50)
	Rt	2.3 (≤ 3.5)	11.2 (≥ 20)	52.0 (≥ 50)		Rt	2.3 (≤ 3.5)	7.5 (≥ 20)	52.0 (≥ 50)
Ulnar (Digit V)	Lt	2.1 (≤ 3.1)	7.2 (≥ 17)	52.3 (≥ 50)	**Ulnar**	Lt	2.0 (≤ 3.1)	10.2 (≥ 17)	55.0 (≥ 50)
	Rt	2.2 (≤ 3.1)	13.1 (≥ 17)	50.0 (≥ 50)		Rt	2.2 (≤ 3.1)	8.9 (≥ 17)	50.0 (≥ 50)
Sural	Lt	2.3 (≤ 4.4)	4.5 (≥ 6.0)	43,4 (≥ 40)	**Sural**	Lt	2.2 (≤ 4.4)	3.4 (≥ 6.0)	45.4 (≥ 40)
	Rt	2.4 (≤ 4.4)	5.9 (≥ 6.0)	41.6 (≥ 40)		Rt	2.3 (≤ 4.4)	3.2 (≥ 6.0)	43.0 (≥ 40)

Lt: Left, Rt: Right, NR: No response, APB: Abductor pollicis brevis, ADM: Abductor digiti minimi, EDB: Extensor digitorum brevis, AHB: Abductor hallucis brevis

The needle EMG of the AMSAN patient at day 10, while examining the right sided deltoid muscle, first dorsal interosseous muscle (FDI), vastus medialis muscle (VM), tibialis anterior muscle (TA), and extensor hallucis longus muscle (EHL), showed reduced recruitment in the VM, TA, and EHL muscles with normal morphology MUAPs in all of the studied nerves, and no spontaneous activity was detected. During the follow up of the patient at day 60, features of both active denervation and reinnervation were reported, which include spontaneous activities in the form of fibrillations (Fibs) and positive sharp waves (PSWs) that were recorded from FDI and TA muscles. The MUAPs of all the studied muscles were of long duration, high amplitude, and polyphasic except in the deltoid (Table-8).

Table 8. Needle EMG Parameters of AMSAN Patient

Needle electromyography										
Day 10						Day 60				
Findings	Deltoid	FDI	VM	TA	EHL	Deltoid	FDI	VM	TA	EHL
Spontaneous activity	Nill	Nill	Nill	Fibs +	Nill	Nill	Fibs / PSWs	Nill	Fibs / PSWs	Nill
MUAP Duration	Normal	Normal	Normal	Normal	Normal	Normal	Long	Long	Long	Normal
MUAP Amplitude	Normal	Normal	Normal	Normal	Normal	Normal	High	High	High	Normal
Recruitment	Normal	Normal	Reduced	Reduced	Reduced	Normal	Reduced	Reduced	Reduced	Reduced
Number of phases	Normal	Normal	Normal	Normal	Normal	Normal	polyphasic	Polyphasic MUAPs	Polyphasic MUAPs	Polyphasic MUAPs
FDI: First dorsal interosseous muscle, VM: Vastus medialis muscle, TA: Tibialis anterior muscle, EHL: Extensor hallucis longus muscle, Fibs: Fibrillations, PSWs: Positive sharp waves, MUAP: Motor unit action potential										

Discussion

It became increasingly evident that GBS is one of the neurological sequelae of COVID-19 as a part of the long COVID-19 syndrome, and many case reports were published at the beginning of the outbreak, followed by more evidence-based studies that confirmed the relationship between COVID-19 and immune-related peripheral neuropathies.[7,12,13] Furthermore, many reports indicate the occurrence of GBS following the COVID-19 vaccination.[14-16] Between this and that, most literature talked about the demyelinating variants of GBS, which is the quite common subtype of GBS that was formerly known as acute demyelinating polyneuropathy (AIDP). However, as previously stated, there are other rare variants of GBS that affect the nerve's axon rather than the myelinated sheet, resulting in axonal degeneration of either motor nerves only (known as acute motor axonal neuropathy, or AMAN) or both motor and sensory fibers of the peripheral nerves (known as acute motor sensory axonal neuropathy, or AMSAN).[17] The most widely acknowledged mechanism of GBS caused by COVID-19 is the development of antibodies against the pathogen's surface glycoproteins, which may harm peripheral neurons due to a similar native protein structure (molecular mimicry).[18] Other hypotheses include hyperinflammation as a result of a cytokine storm in COVID-19-infected individuals.[19] In the present study, the majority of GBS cases (16 of 18; 88.9%) were demyelinating; however, a description of this type is outside the scope of this paper. The macrophages often penetrate the gap between the Schwann cell and axon, leaving the myelin sheath relatively intact in AMAN and

AMSAN.[20,21] Attachment of the SARS-CoV-2 virus to cell surfaces, mediated by the spike (S) protein, which binds to gangliosides with sialic acid residues, has been postulated as a likely mechanism in a similar fashion to the demyelinating variant.[22] Alternately, T-cell activation followed by the production of inflammatory mediators by macrophages may be a viable mechanism, supported by a multisystem inflammatory state that leads to para-infectious GBS.[23] The current study reported two cases of the axonal variant of GBS, one being AMAN and the other being AMSAN, with a percentage of about 5% for each variant, which is actually much lower than what was reported by Chakraborty & Chandra (2021), who describe a percentage of around 37% for AMAN and 25% for AMSAN from the total reported GBS cases.[24] However, our results are more in line with Sriwastava et al.'s (2021) systematic review. They looked at 50 cases of GBS and found that 12% of them had AMSAN and 2% had AMAN.[25] Oure reported two patients actually were of young age with a history of mild and trivial COVID-19, but both cases were reported within a very short period from the diagnosis of COVID-19, suggesting a possibility of para-infectious phenomena rather than post-infectious phenomena, and this is consistent with the findings of Chakraborty & Chandra (2021); Cares et al. (2020); and Zhao et al. (2020).[24,26,27] Even though none of our cases have a COVID-19 PCR test from the CSF, the literature suggests that the usual CSF COVID-19 PCR in the reported GBS cases is negative, which makes it more likely that the disease is caused by immune system dysregulation.[24] Antiganglioside IgG autoantibodies are usually identified in about fifty percent of GBS patients, and their presence confirms the diagnosis. The AMAN subtype is more significantly associated with antiganglioside antibodies than the AIDP subtype. Despite the fact that anti-ganglioside antibody testing might possibly assist researchers in understanding SARS-CoV-2-associated neurological symptoms better,[28] anti-GM1 antibodies were negative in the majority of COVID-19-associated GBS cases, and none of the five axonal variant cases described by Chakraborty and Chandra (2021) included a positive antibody.[24] In our study, neither the AMAN nor the AMSAN patients were tested for these antibody types, but more solid axonal damage evidence was confirmed by the electrophysiological testing that demonstrated a significant decline in the amplitude of the nerve fibers. In addition, a follow-up electrodiagnostic test was done for the two patients, confirming the evidence of Wallerian degeneration and re-enervation by the needle EMG. The main limitation of this study is the limited number of patients with axonal variants, making the statistical analysis of no significant relevance. Moreover, the absence of antibody testing however this will add nothing for diagnosis and patient care.

In conclusions, GBS is a developing and significant neurological illness in people with COVID-19. As an uncommon axonal variation linked with COVID-19, physicians should be mindful of its occurrence. To avoid serious consequences, all patients with sensory or motor neurological impairments should be evaluated for GBS clinically and electrophysiologically and treated as soon as feasible.

Conflicts of interest

The authors declare no conflict of interest in this study.

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References

1. Nguyen TP, Taylor RS. Guillain Barre Syndrome. In: StatPearls [Internet]. StatPearls Publishing; 2022.
2. Dimachkie MM, Barohn RJ. Guillain-Barré syndrome and variants. Neurol Clin 2013; 31(2):491-510.
3. Yadegari S, Nafissi S, Kazemi N. Comparison of electrophysiological findings in axonal and demyelinating Guillain-Barre syndrome. Iran J Neurol 2014; 13(3):138-143.
4. Rath J, Schober B, Zulehner G, et al. Nerve conduction studies in Guillain-Barré syndrome: Influence of timing and value of repeated measurements. J Neurol Sci 2021; 420: 117267.
5. Finsterer J, Scorza FA, Scorza CA, Fiorini AC. Peripheral neuropathy in COVID-19 is due to immune-mechanisms, pre-existing risk factors, anti-viral drugs, or bedding in the Intensive Care Unit. Arq Neuropsiquiatr 2021;79(10): 924-928.
6. Zuberbühler P, Conti ME, León-Cejas L, et al. Guillain-Barre syndrome associated to COVID-19 infection: a review of published case reports. Síndrome de Guillain-Barré asociado a infección por COVID-19: revisión de casos publicados. Rev Neurol 2021; 72(6): 203-212.
7. Hasrat NH, Kadhum HJ, Hashim AR, Yakob ZA, Kadhim LA, Farid HA. Neurographic Evidence of Inflammatory Polyneuropathies in Peri-COVID-19 Circumstances and Their Relationship with Acute Disease Severity and Inflammatory Storm. Cureus 2022; 14(3): e23517.
8. Hasrat NH, Kadhum HJ, Hashim AR, Yakob ZA, Kadhim LA, Farid HA. Neurophysiological changes by nerve conduction study and electromyography in acute and long-term COVID-19 circumstances: a comparative study protocol and review. J Xi'an Shiyou Univ 2022; 18: 241-249.
9. Case definition for coronavirus disease 2019 (COVID-19), as of 3 December 2020 [Internet]. European Centre for Disease Prevention and Control. [cited 2022 Nov 26].
10. Rees JH, Soudain SE, Gregson NA, Hughes RA. Campylobacter jejuni infection and Guillain-Barré syndrome. N Engl J Med 1995; 333(21): 1374-1379.
11. Preston DC, Shapiro BE. Electromyography and neuromuscular disorders: clinical-electrophysiologic correlations. Elsevier Inc., Amsterdam, Netherlands; 2017.
12. Abu-Rumeileh S, Abdelhak A, Foschi M, Tumani H, Otto M. Guillain-Barré syndrome spectrum associated with COVID-19: an up-to-date systematic review of 73 cases. J Neurol 2021; 268(4): 1133-1170.
13. Aladawi M, Elfil M, Abu-Esheh B, et al. Guillain Barre Syndrome as a Complication of COVID-19: A Systematic Review. Can J Neurol Sci 2022; 49(1): 38-48.
14. McKean N, Chircop C. Guillain-Barré syndrome after COVID-19 vaccination. BMJ Case Rep 2021; 14(7): e244125.
15. Kim JE, Min YG, Shin JY, et al. Guillain-Barré Syndrome and Variants Following COVID-19 Vaccination: Report of 13 Cases. Front Neurol 2022; 12: 820723.
16. Shao SC, Wang CH, Chang KC, Hung MJ, Chen HY, Liao SC. Guillain-Barré Syndrome Associated with COVID-19 Vaccination. Emerg Infect Dis 2021; 27(12): 3175-3178.
17. Hughes RA, Cornblath DR. Guillain-Barré syndrome. Lancet 2005; 366(9497): 1653-1666.

18. Kajumba MM, Kolls BJ, Koltai DC, Kaddumukasa M, Kaddumukasa M, Laskowitz DT. COVID-19-Associated Guillain-Barre Syndrome: Atypical Para-infectious Profile, Symptom Overlap, and Increased Risk of Severe Neurological Complications. SN Compr Clin Med 2020; 2(12): 2702-2714.
19. Teuwen LA, Geldhof V, Pasut A, Carmeliet P. COVID-19: the vasculature unleashed [published correction appears in Nat Rev Immunol. 2020 Jun 4:]. Nat Rev Immunol 2020; 20(7): 389-391.
20. Vucic S, Kiernan MC, Cornblath DR. Guillain-Barré syndrome: an update. J Clin Neurosci 2009; 16(6):733-741.
21. Yuki N, Kuwabara S, Koga M, Hirata K. Acute motor axonal neuropathy and acute motor-sensory axonal neuropathy share a common immunological profile. J Neurol Sci 1999; 168(2): 121-126.
22. Dalakas MC. Guillain-Barré syndrome: The first documented COVID-19-triggered autoimmune neurologic disease: More to come with myositis in the offing. Neurol Neuroimmunol Neuroinflamm 2020; 7(5): e781.
23. Toscano G, Palmerini F, Ravaglia S, et al. Guillain-Barré Syndrome Associated with SARS-CoV-2. N Engl J Med 2020; 382(26): 2574-2576.
24. Chakraborty U, Hati A, Chandra A. Covid-19 associated Guillain-Barré syndrome: A series of a relatively uncommon neurological complication. Diabetes Metab Syndr 2021; 15(6): 102326.
25. Sriwastava S, Kataria S, Tandon M, et al. Guillain Barré 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.
26. Caress JB, Castoro RJ, Simmons Z, et al. COVID-19-associated Guillain-Barré syndrome: The early pandemic experience. Muscle Nerve 2020; 62(4): 485-491.
27. Zhao H, Shen D, Zhou H, Liu J, Chen S. Guillain-Barré syndrome associated with SARS-CoV-2 infection: causality or coincidence? Lancet Neurol 2020; 19(5): 383-384.
28. Cutillo G, Saariaho AH, Meri S. Physiology of gangliosides and the role of antiganglioside antibodies in human diseases. Cell Mol Immunol 2020; 17(4): 313-322.

الاعتلال العصبي المحوري المحيطي الحاد (AMAN & AMSAN) وعلاقته بالفايروس التاجي المستجد

المقدمة : تعتبر متلازمة الاعتلال العصبي المحيطي الحاد هي أحد الامراض المناعية اللي تصيب الجهاز العصبي المحيطي وقد لوحظ في الآونة الأخيرة زيادة بهذا النوع من المرض مع انتشار الفايروس التاجي المستجد. بالاعتماد على دراسة تخطيط الاعصاب والعضلات فأن النوع الأشهر هو النوع المزيل لغشاء المايلين المحيط بالأعصاب لكن لوحظ في الوقت الحالي انتشار النوع المؤثر على محور الخلية العصبية أيضا.

المنهجية البحث والاهداف : تم اجراء دراسة تحليلية لـ ٢٥٢٣ مريض خلال سنه واحدة في محافظة البصرة في جنوب العراق لغرض دراسة التغيرات الفسيولوجية العصبية في الاعصاب المحيطية بعد الإصابة بالفايروس التاجي المستجد باستخدام تخطيط الاعصاب والعضلات. كانت الدراسة تهدف لحساب مدى انتشار الاعتلال العصبي المحوري المحيطي الحاد ودراسة خصائصه السريرية والفسيولوجية.

النتائج والاستنتاجات : وجدت الدراسة بأن النوع المحوري من اعتلال الاعصاب المحيطية الحاد يشكل ١٠٪ من العدد الكلي لحالات اعتلال الاعصاب المحيطية في محافظة البصرة ويحصل بمعدل ١ لكل ١٠٠٠ مريض يراجع استشارية الجملة العصبية والفسلجة العصبية ممن كان لديهم أصابه سابقة بالفايروس التاجي المستجد

الكلمات المفتاحية: المتغيرات المحورية الناشئة ، متلازمة Guillain Barré، AMAN ، AMSAN، كوفيد ١٩.