OPEN ACCESS

Research Paper

Clinical Patterns of Guillain-Barré Syndrome Associated with the COVID-19 Pandemic

Ali Samir Yahya Al-Shakerji[1], Akram Mohammed Al-Mahdawi[2], Safaa Hussein Al Shammary[3]

ABSTRACT:

BACKGROUND:

Guillain Barré Syndrome is an autoimmune disease, with progressive weakness and areflexia, it can be triggered due to antigenic mimicry, and the association of COVID-19 and GBS cases throughout the pandemic has been reported worldwide.

OBJECTIVE:

To identify the clinical patterns of GBS associated with COVID-19 and its neurophysiological variants.

PATIENTS AND METHODS:

(51) Patients were collected during 2021 who were admitted to Baghdad Medical City and Neuroscience Hospital, and diagnosed with GBS according to the Asbury criteria, all of them had serological or radiological evidence of current or recent COVID-19 infection, the neurophysiological study was done for all of them and variants were identified.

RESULTS:

Males were (56.9%), half of GBS cases were presented in late spring after the peak of the second COVID-19 wave, the mean time interval between antecedent COVID-19 and GBS onset was 3.45 weeks, (82.4%) was ascending pattern, (5.9%) paraparetic, (5.9%) bilateral facial with distal paraesthesia, about (64.7%) had the demyelinating variant on Neurophysiological study, axonal in (29.4%) and equivocal in (5.9%).

CONCLUSION:

The classical ascending pattern is the most common clinical pattern associated with COVID-19 and demyelinating variant in neurophysiological studies.

KEYWORDS: Guillain Barré Syndrome, COVID-19, GBS variants, and Neurophysiological pattern.

[1] *FICMS Lecturer, Mosul Medical College, Nineveh, Iraq*

[2] *DM, CABM, MRCP, FRCP (London), FRCP (Edin), FACP, FAAN, Chairman of the Scientific Iraqi Council of Neurology, the Iraqi Board for Medical Specializations, Baghdad, Iraq*

[3] *M.Sc., Ph.D., American Board of Electrodiagnostic Medicine (ABEM), Assistant Professor, Al-Mustansiriyah Medical College, Baghdad, Iraq*

Iraqi Postgraduate Medical Journal, 2024; Vol. 23(4): 466-471

DOI: 10.52573/ipmj.2024.141037 *Received: July 25, 2023,* *Accepted: August 27, 2023*

INTRODUCTION:

Guillain-Barré syndrome (GBS) is an auto-reactive disease, that influences the nerve roots and peripheral nerves (polyradiculoneuropathy) that characterized by gradual weakness of the limbs and reduced or completely absent tendon reflexes (hyporeflexia or areflexia) [1], it is considered to be the most common and most serious acute demyelinating neuropathy, under this umbrella; there are several clinical variants with a characteristic pattern of presentation and pathological features [2]. It is usually triggered by a recent infection, vaccination, or surgery usually in the antecedent 1- 6 weeks. The body's immune system; in response to the antigenic mimicry, is turned on and the nerve roots and peripheral nerves are attacked [3]. Pathogenesis is still not fully understood, anti-gangliosides antibodies are found in the serum of some affected patients [4].

The incidence of GBS is 1- 4 in 100,000 per year and typically can increase during outbreaks of infectious agents that trigger the disease [5]. Not long ago, the epidemics of the Zika virus that occurred in French Polynesia and Latin America in the middle of the last decade were associated with an increase in cases being labelled as GBS [6, 7].

Patients with the common ascending variant present with distal numbness, along with or followed by a weakness that begins in the legs symmetrically and ascends to the upper limbs,

neck, and head musculatures. Reflexes are attenuated or completely lost symmetrically in most patients at disease onset [8, 9]. Patients' symptoms reach the peak within 4 weeks, and 20% to 30% of patients will need invasive mechanical ventilation [10]. Some patients present with variants of GBS that are distinct from the classic ascending pattern of sensory loss and weakness. These variants include (bilateral facial palsy with distal paraesthesia), (pharyngo–cervico–brachial weakness) or (paraparetic form); weakness without sensory symptoms (pure motor variant); and the Miller Fisher variant, which is characterized by ophthalmoplegia, areflexia, and ataxia. Broadly speaking, GBS variants are rarely 'in the pure form' and often overlap with the classic syndrome or display some characteristics of other variant forms [11].

Electrodiagnostic studies are recommended to be done to confirm the diagnosis, especially in those with an unusual presentation, can also differentiate between the three electrophysiological subtypes of classical GBS: AIDP, AMAN, and AMSAN, and also helpful in giving a clue about the prognosis [12].

Nonetheless, electrophysiological evaluation could be within normal value if conducted too early in the disease process (within the 1st week) or done in initially mild disease, slowly progressive, proximal weakness, or clinical variants as in the Miller Fisher variant. So, those patients are labelled as 'equivocal' or 'unexcitable' [13, 14].

Treatment must be initiated, particularly for those with rapidly escalating disease processes or autonomic instability, or respiratory embarrassment. Studies have shown a favourable treatment response for intravenous immunoglobulin (IVIG) if given within 2 weeks of disease onset and for plasma exchange (PE) if given within 4 weeks [15]. The GBS disability scale is used for the estimation of functional disability and for documenting GBS disease progression [16].

Coronavirus 2019 (COVID-19):

The first reported state of pneumonia with an undetermined cause was announced in Wuhan City, PRC. The culprit was found to be a novel virus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS -CoV-2) [17]. Although COVID-19 typically presents with respiratory disease, there have been many records of remarkable neurological sequelae, as it can affect the entire neuroaxis [18].

The Association of GBS and COVID-19 Infection: The worldwide GBS incidence increases during pandemics as that seen in 2016 with the outbreaks of Zika virus, which mainly strike people of French Polynesia and Latin American states [7], GBS related to COVID-19 is now recorded worldwide, but the firmness and the mechanism of this relation and the clinical and electrophysiological patterns still hazy [19]. The Western world observed an excess of GBS cases during the last pandemic and demonstrated 80% of these are COVID-19 related [20].

PATIENT AND METHODS:

Study design:

This is a cross-sectional descriptive multicentre study conducted at Baghdad Medical City and Neuroscience hospital for the whole 2021 year. The study protocol was approved by the Scientific Council of Neurology /Iraqi Board for Medical Specializations in 2021. Verbal consent was taken from all patients in the study.

Subjects:

A total of 51 patients (29 males and 22 females) were diagnosed to have GBS according to Asbury criteria. All patients had evidence of current or prior (6 weeks ago) COVID-19 infection according to WHO case definition.

Exclusion criteria:

1. Patient with acute flaccid paralysis who doesn't match for Asbury criteria for diagnosis of GBS.
2. Paediatrics age group age less than 14 years.
3. Patients who didn't have evidence to meet the criteria of WHO COVID-19 case definition.
4. Patient with a history of taking COVID-19 vaccination.
5. Exclusion of other causes that can mimics GBS as HIV seroconversion, lymphoma, vasculitis and others.

RESULTS:

We collected 51 patients in the time period between January 2021 to December 2021, their mean age was 44.3 ± 18.1 years with a range between 14 and 80 years, most of them were males (56.9%). most cases admitted in the late spring (about 23 cases out of 51) in association with the second wave of COVID-19 pandemic with another less severe surge in the autumn, see chart (1).

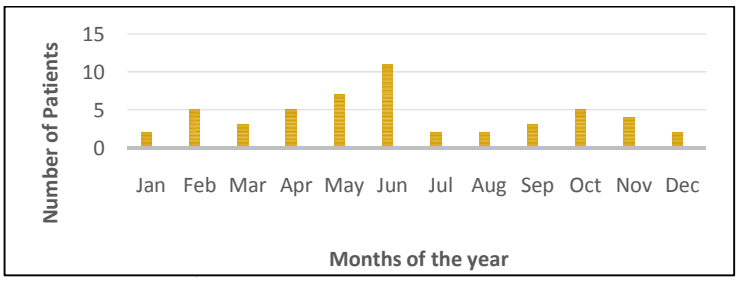

Chart (1), patient's distribution over months of the year.

The mean MRC sum was (30.9 ± 15.6 out of 60) with a range from (4 to 60), the facial nerve is the most commonly affected cranial nerve (56.8%) followed by the bulbar nerves (39.2%) and ocular nerves (5.9%), sensory symptoms including numbness and paraesthesia were found in (84.4%) whereas pure ataxia was evident in only (3.9%) related to patients with the miller fisher variant, autonomic involvement including labile blood pressure was found in about one-third of patients (35.3%) which was nearly similar to the percentage of patients who require RCU admission and invasive ventilation (29.4%).

The classification of cases according to the clinical pattern of the presentation showed that nearly most cases (82.4%) were ascending in presentation with few cases presented as other minor variety as paraparetic (5.9%), bilateral facial with distal paraesthesia (5.9%), Miller Fisher (2.9%) and pharyngeal-cervical-brachial pattern only (1.9%), see table (2).

Table 2: Patient's demographic and detailed muscular involvement.

Age	Mean age 44.3 ± 18.1 years			
Gender	Male 56.9%		Female 43.1%	
Residency	Urban 62.7%		Rural 37.3%	
Time interval between COVID-19 and GBS onset.	Mean 3.45 weeks ± 1.5 SD			
MRC Sum (0-60)	Mean 30.9 ± 15.6 SD range (4 – 60)			
Cranial Nerve involvement	72.5%	Ocular Nerves	3/51	5.9%
		Facial Nerve	29/51	56.8%
		Bulbar nerve	20/51	39.2%
Limbs & neck involvement	94.1%	Neck	19/51	56.8%
		Upper limbs	40/51	78.4%
		Lower limbs	46/51	90.1%
Sensory symptoms	84.4%			
Autonomic involvement	35.3%			
Need for invasive ventilation	29.4% (15 cases out of 51)			

The classification of cases according to the clinical pattern of the presentation showed that nearly most cases (82.4%) were ascending in presentation with few cases presented as other minor variety as paraparetic (5.9%), bilateral facial with distal paraesthesia (5.9%), Miller Fisher (2.9%) and pharyngeal-cervical-brachial pattern only (1.9%), see table (3).

The obtained neurophysiological patterns were classified into demyelinating type (AIDP) which was the most common (64.7%), the axonal type was (29.4%) and (5.9%) were patients with equivocal or non-excitable study, so we depend on other criteria (like CSF albumino-cytological dissociation) for diagnosis of GBS.

Table 3: GBS clinical variants & Neurophysiological Pattern.

Clinical Pattern		No. of Cases	Percentage %	
Ascending		42	82.4%	
Paraparetic		3	5.9%	
Miller Fisher		2	2.9%	
Pharyngeal–cervical–brachial		1	1.9%	
Bilateral Facial		3	5.9%	
Pure sensory		0	0.0%	
Pure Autonomic		0	0.0%	
Neurophysiological Pattern				
AIDP		33/51	64.7%	
Axonal	AMAN	6/51	11.7%	29.4%
	AMSAN	9/51	17.7%	
Equivocal or non-excitable		3/51	5.9%	

The outcome of patients studied on discharge was expressed using the GBS disability scale [16], of them only (19.6%) has minimal symptoms who was able to return to their usual life while (80.4%) had severe walking difficulties or being bed-bound, see table (4).

Table 4: Outcome by GBS disability scale (out of 6).

Grade 1	4 cases	19.6%	Mean 3.5 ± 1.8 SD
Grade 2	6 cases		
Grade 3	16 cases	≥3 scale = 80.4%	
Grade 4	18 cases		
Grade 5	0 case		
Grade 6	7 cases		

DISCUSSION:

The time interval from emergence of COVID-19 features and GBS symptoms was 3.45 ±1.5 weeks (the time interval was approximated by weeks as it was hard to precisely determine the onset of prodromal infection) which was very close to what found by Filosto M. et al study [20] in Italia 24.2 ± 11.6 days, whereas in Caress MD et al study [21] & Luijten LW et al study [22] the time interval were 11 days & 13 days; respectively, This variation in time interval may be related to the silent non-specific prodromal symptoms of infection which when asked about retrospectively; difficult to be estimated precisely.

The MRC sum; which can give a clue about the severity of muscles involvement on presentation found to be 30.9 ± 15.6 in this study, whereas it was 26.3±18.3 in Filosto M. et al study in Italy [20] and was 33.1 ± 17.8 in Lopez-Hernandez JC et al study in Mexico [23]. Filosto M. et al; stated that patients with COVID-19 when developing GBS, showed lower MRC sum scores when compared with those with negative evidence of COVID-19 (26.3±18.3 vs 41.4±14.8, p=0.006) & more frequent admission to the ICU (50% vs 17.6%, p=0.03) [20].

The clinical variants found by Lopez-Hernandez JC et al [23] in Mexico, showed that ascending variant was the most common type (71.4%) and the Miller Fisher variant was about (11.4%) which is comparable to the results of this study (82.4% and 2.9% respectively), in Filosto M. et al study in Italia [20]; the ascending variant was (90%) while the Pharyngeal–cervical–brachial variant, facial diplegia, and pure sensory form was (3.3%) for each.

In Elshebawy et al study [24] in Egypt, the neurophysiological pattern showed that AIDP was found in (59.5%) whereas AMSAN in (19%), this is going with our results of (AIDP 64.7%, AMSAN 17.7% & AMAN 11.7%). The equivocal or non-excitable neurophysiological study was found in 5.9% in this study which may be related to the timing of study as it was too early in the disease course or related to severe non-excitable nerves, this percentage is comparable to what was demonstrated by Lopez-Hernandez JC et al [23] which was (3.6%).

Finally, coming to the outcome of our patients, we found that (80.4%) had Hughes disability scale of ≥3, Mean 3.5 ± 1.8, with 7 patients died because of GBS and its complication, comparing these results with Lopez-Hernandez JC et al in Mexico [23] in which ≥3 Hughes scale was (71.4%) of patients and in Filosto M. et al in Italia, the mean Hughes scale was 4.18±1.3 with zero death.

CONCLUSION:

Interestingly the ascending clinical pattern was the most frequently seen in this study, with an array of other minor variants coming to light because of a high incidence of cases, also high tendency to affect cranial nerves and cause sensory symptoms. The demyelinating electrodiagnostic characteristics were found to be mostly seen in this study during the COVID-19 pandemic. The presented cases tend to have more severe muscles weakness at presentation with high percentages becoming dependent and needing extensive physiotherapy & rehabilitation along with a relatively high mortality rate.

REFERENCES:

1. Guillain G, Barré JA, Strohl A. Radiculoneuritis syndrome with hyperalbuminosis of cerebrospinal fluid without cellular reaction. Notes on clinical features and graphs of tendon reflexes. 1916. InAnnales de medecine interne 1999;150:24-32.
2. Willison HJ, Jacobs BC, van Doorn PA. Guillain-barre syndrome. The Lancet. 2016 ;388:717-27.
3. Nobuhiro Y, Hartung HP. Guillain-Barré syndrome. N Engl J Med. 2012;366:2294-304.
4. Yuki N. Infectious origins of, and molecular mimicry in, Guillain-Barré and Fisher syndromes. The Lancet infectious diseases. 2001;1:29-37.
5. Jacobs BC, Rothbarth PH, Van der Meché FG, Herbrink P, Schmitz PI, De Klerk MA, Van Doorn PA. The spectrum of antecedent infections in Guillain-Barré syndrome: a case-control study. Neurology. 1998;51:1110-15.
6. Defabio AC, Scott TR, Stenberg RT, Simon EL. Guillain-Barré syndrome in a patient previously diagnosed with COVID-19. The American journal of emergency medicine. 2021;45:154-55.
7. Cao-Lormeau VM, Blake A, Mons S, Lastère S, Roche C, Vanhomwegen J, Dub T, Baudouin L, Teissier A, Larre P, Vial AL. Guillain-Barré Syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study. The Lancet. 2016;387:1531-39.
8. Leonhard SE, Mandarakas MR, Gondim FA, Bateman K, Ferreira ML, Cornblath DR, van Doorn PA, Dourado ME, Hughes RA, Islam B, Kusunoki S. Diagnosis and management of Guillain–Barré syndrome in ten steps. Nature Reviews Neurology. 2019;15:671-83.
9. Van den Berg B, Walgaard C, Drenthen J, Fokke C, Jacobs BC, Van Doorn PA. Guillain–Barré syndrome: pathogenesis, diagnosis, treatment and prognosis. Nature Reviews Neurology. 2014 ;10:469-82.
10. Sejvar JJ, Baughman AL, Wise M, Morgan OW. Population incidence of Guillain-Barré syndrome: a systematic review and meta-analysis. Neuroepidemiology. 2011;36:123-33.
11. Willison HJ, Jacobs BC, van Doorn PA. Guillain-barre syndrome. The Lancet. 2016 ;388:717-27.
12. Vucic S, Cairns KD, Black KR, Chong PS, Cros D. Neurophysiologic findings in early acute inflammatory demyelinating polyradiculoneuropathy. Clinical neurophysiology. 2004;115:2329-35.
13. Meulstee J, Van der Meche FG. Electrodiagnostic criteria for polyneuropathy and demyelination: application in 135 patients with Guillain-Barré syndrome. Dutch Guillain-Barré Study Group. Journal of Neurology, Neurosurgery & Psychiatry. 1995;59:482-86.
14. Rajabally YA, Durand MC, Mitchell J, Orlikowski D, Nicolas G. Electrophysiological diagnosis of Guillain–Barré syndrome subtype: could a single study suffice?. Journal of Neurology, Neurosurgery & Psychiatry. 2015;86:115-19.
15. Raphaël JC, Chevret S, Hughes RA, Annane D. Plasma exchange for Guillain-Barré syndrome. Cochrane Database of Systematic Reviews. 2012.
16. van Koningsveld R, Steyerberg EW, Hughes RA, Swan AV, van Doorn PA, Jacobs BC. A clinical prognostic scoring system for Guillain-Barré syndrome. The Lancet Neurology. 2007;6:589-94.
17. Li JY, You Z, Wang Q, Zhou ZJ, Qiu Y, Luo R, Ge XY. The epidemic of 2019-novel-coronavirus (2019-nCoV) pneumonia and insights for emerging infectious diseases in the future. Microbes and infection. 2020;22:80-85.
18. Wu Y, Xu X, Chen Z, Duan J, Hashimoto K, Yang L, Liu C, Yang C. Nervous system involvement after infection with COVID-19 and other coronaviruses. Brain, behavior, and immunity. 2020 ;87:18-22.
19. Caress JB, Castoro RJ, Simmons Z, Scelsa SN, Lewis RA, Ahlawat A, Narayanaswami P. COVID-19–associated Guillain-Barré syndrome: The early pandemic experience. Muscle & nerve. 2020 ;62:485-91.

20. Filosto M, Piccinelli SC, Gazzina S, Foresti C, Frigeni B, Servalli MC, Sessa M, Cosentino G, Marchioni E, Ravaglia S, Briani C. Guillain-Barré syndrome and COVID-19: an observational multicentre study from two Italian hotspot regions. Journal of Neurology, Neurosurgery & Psychiatry. 2021;92:751-56.

21. Caress JB, Castoro RJ, Simmons Z, Scelsa SN, Lewis RA, Ahlawat A, Narayanaswami P. COVID-19–associated Guillain-Barré syndrome: The early pandemic experience. Muscle & nerve. 2020 ;62:485-91.

22. Luijten LW, Leonhard SE, van der Eijk AA, Doets AY, Appeltshauser L, Arends S, Attarian S, Benedetti L, Briani C, Casasnovas C, Castellani F. Guillain-Barré syndrome after SARS-CoV-2 infection in an international prospective cohort study. Brain. 2021;144:3392-404.

23. Briseño-Godínez ME, Arauz A, López-Hernández JC, de Saráchaga AJ, Pérez-Valdez EY, May-Más RN, López-Hernández G, Bazán-Rodriguez L, Galnares-Olalde JA, León-Manríquez E, Vargas-Cañas ES. Prognostic Factors in Elderly Patients With Guillain-Barré Syndrome: Does Age Matter?. The Neurohospitalist. 2021;11:303-9.

24. Elshebawy H, Ezzeldin MY, Elzamarany EH. Characteristics of COVID and post COVID polyneuropathies in adults and pediatrics: an Egyptian sample. The Egyptian Journal of Neurology, Psychiatry and Neurosurgery. 2021;57:1-7.