Available online on 15.11.2021 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Full Text Article

Review Article

A Review on Gullian Barre Syndrome and its Association with COVID 19

Subin Sam[1], R. Sambath Kumar[2]*, N. Venkateswaramurthy[3]

[1] *Post Graduate Student, Department of Pharmacy Practice, J.K.K. Nattraja College of Pharmacy, Namakkal (Dt), Kumarapalayam- 638 183, Tamil Nadu, India.*

[2] *Professor and Head, Department of Pharmaceutics, J.K.K. Nattraja College of Pharmacy, Namakkal (Dt), Kumarapalayam- 638 183, Tamil Nadu, India.*

[3] *Professor and Head, Department of Pharmacy Practice, J.K.K. Nattraja College of Pharmacy, Namakkal (Dt), Kumarapalayam- 638 183, Tamil Nadu, India.*

Article Info:

Article History:

Received 21 September 2021
Reviewed 14 October 2021
Accepted 18 October 2021
Published 15 November 2021

Cite this article as:

Sam S, Sambath Kumar R, Venkateswaramurthy N, A Review on Gullian Barre Syndrome and its Association with COVID 19, Journal of Drug Delivery and Therapeutics. 2021; 11(6):188-193

DOI: http://dx.doi.org/10.22270/jddt.v11i6.5115

Abstract

Guillain-Barré syndrome (GBS) is an immune-mediated disease that affects peripheral nerves and can lead to life-threatening consequences. It affects around 10000 people per year worldwide. Since the outbreak of acute respiratory syndrome coronavirus-2 (sar-cov-2) the incidence of GBS has been increased with a fatality rate of 4-7%. The exact association between the Sar-cov-2 and GBS is still unknown. GBS commonly presents after viral infections such as influenza virus, campylobacter jejuni, and zika virus. Clinical recognition of SC2-GBS is required in order to administer appropriate treatment on time and enhance the overall output of the infection. In most of the conditions patient was treated with intravenous immunoglobulins and outcome was seen within eight weeks of treatment. less outcome was seen in older age in line with previous findings for both GBS and COVID-19. Studies should be conducted to compare patients associated with GBS to those with concurrent non-COVID-19 GBS to see if the incidence of GBS is higher in those with COVID-19.

Keywords: Guillian-Barre syndrome, COVID-19, SAR-COV2

*Address for Correspondence:

Dr. R. Sambath Kumar, Professor and Head, Department of pharmaceutics, J.K.K. Nattraja College of Pharmacy, Kumarapalayam-638183, Tamil Nadu, India.

ORCID ID: *https://orcid.org/0000-0003-1454-9582*

INTRODUCTION

Coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory distress syndrome coronavirus 2(SARS-CoV-2) and was declared as a pandemic by world health organisation in march 2020. [1,2] Coronaviruses can cause a variety of systemic infections, the most significant of which are respiratory complications, which are similar to severe acute respiratory syndrome coronavirus (SARS-CoV). Fever, cough, dyspnoea, myalgia, headache, and diarrhoea are the most common symptoms at the onset of disease after an incubation period of approximately 5.2 days and the symptoms of COVID-19 are dependent on the age and the patient's underlying medical illness and also the condition of the immune system. [3,4]

During the covid pandemic neurological complications has been established in those patient who were having severe infections. Gullian Barre Syndrome emerged as potentially serious complication among them and some other complications that include Bell's palsy, seizures, meningoencephalitis, cerebrovascular accidents, acute flaccid myelitis). [5] Around 70% of patients with GBS had an illness before developing GBS. Infectious agents such as Campylobacter jejuni, Influenza virus, Cytomegalovirus and more recently Zika virus have been shown to trigger GBS in laboratory tests. [6-9]

GBS is an intense immune-mediated illness affecting the peripheral nerves and nerve roots and is typically accompanied by a lung or gastrointestinal infection. It causes ascending symmetrical limb weakness and paresthesia, as well as areflexia or hyporeflexia and diminished or absent deep tendon reflexes, with or without involvement of the ventilatory and cranial nerves. are the hallmark clinical signs of GBS, which can last anywhere from a few days to several weeks. [10,11] Majority of the patients report air duct or gastrointestinal infection are mainly reported within 2-4 week before the inception of GBS neurological symptoms. [12]. GBS is usually caused by a viral or bacterial infection. Because of the antigen's structural similarities to axons and myelin, it stimulates the immune system and causes injury to the nerve roots and peripheral nerves. [13] GBS has a number of subtypes such as the basic type (acute inflammatory demyelinating neuropathy, or AIDP) and the subtypes AMAN (acute motor and axonal neuropathy) and AMSAN (acute motor and sensory axonal neuropathy), Miller-Fisher syndrome (MFS), polyneuritis cranialis (PNC), and the Pharyngeal-cervical-brachial (PCB) variant (Bickerstaff encephalitis) (BFE). GBS is typically diagnosed using the

criterion of Brighton If there is symmetrical, progressive, flaccid lower > upper limb Para paresis, if tendon reflexes in weak limbs are decreased, if the disease course is monophasic and the interval between onset and nadir spans from 12 h to 28 days, and if cerebrospinal fluid (CSF) studies demonstrate a cell count, of 50 cells/L, if CSF protein is elevated (disease), and if nerve conduction studies show a demyelinating lesion of motor nerves acute inflammatory demyelinating neuropathy (AIDP) or an axonal lesion of motor nerves (AMAN), or an axonal lesion of motor and sensory nerves (AMSAN) [14]. All GBS variants are associated with a previous viral or bacterial infection. The subtype and clinical features of GBS are primarily determined by the type of infections that came before it. [15] The association between COVID-19 and Guillain-Barre syndrome is now frequently reported, although the degree and mechanism of the link, as well as the clinical and electro diagnostic patterns, are still unknown. [13]

METHODS:

COVID-19-associated Guillain-Barré syndrome was studied in all categories of published studys. Individual case reports and some case series, as well as cohort studies, were found through a search of PubMed and Google Scholar databases, as well as individual case reports and some case series. Google Scholar and PubMed were used to find full-text articles. RT PCR (reverse transcriptase polymerase chain reaction), blood tests, chest X rays were performed and for the detection of GBS, CSF, electromyography and immunological studies that were performed.

EPIDEMIOLOGY OF GBS:

GBS has a recorded incidence rate of 1 to 2 cases per 100,000 individuals and 0.4 to 1.4 cases for every 100,000 children each year. Age-related increases in Guillain-Barre syndrome (0.06 per 100,000 children and 0.27 per 100,000 elderly people above the age of 80) and the disease is slightly more common in men than in women. [16] The prevalence of GBS did not rise between March 2020 and May 2020 in a UK study of 47 Sars-cov-2 associated Gullian-Barre syndrome (SC2-GBS) patients compared to the years 2016–2019. In contrast, a retrospective, multi-centre investigation of 34 SC2-GBS patients from northern Italy found that the anticipated incidence of GBS has increased from 0.93/100000/year in 2019 to 2.43/100000/year in 2020. [17]

DIAGNOSIS AND DETECTION OF GBS IN COVID 19 PATIENTS:

Gullian-Barre syndrome (GBS) is normally easy to diagnose in people who have typical symptoms, however it might be challenging to distinguish GBS in patients who have atypical symptoms. A lumbar puncture is suggested even in individuals with typical symptoms to exclude diseases other than GBS. [10, 18-21]

Suspected GBS may include some of the clinical presentation such as Rapidly progressive bilateral limb weakness with or without sensory impairments, hyporeflexia or areflexia, facial or bulbar palsy, ophthalmoplegia, and gait problems. The diagnosis entails evaluating the diagnostic criteria and ruling out other possible sources of similar neurological symptoms. To diagnose the syndrome and its types, routine blood testing, cerebrospinal fluid tests, lumbar puncture, muscle and nerve electrophysiology studies and antiganglioside antibodies testing should be performed. Increased amount of mononuclear or polymorphonuclear cells (>50 cells per L) in spinal fluid. [22-24]

The Brighton diagnostic criteria is also used for diagnosing GBS conforming to the clinical symptoms of the patient. The Brighton criteria assign four stages of diagnosing surety.to GBS, ranging from level 1-4 (highest to the lowest). The completeness of the diagnostic criteria is important when using the Brighton criteria to diagnose patients with suspected GBS. [24]

Infectious infections, malignancy, and abnormalities of the neuromuscular junction are among the differential diagnoses for GBS. Differential diagnoses such as Cytomegalovirus (CMV) or HIV (human immunodeficiency virus)-related spinal root inflammation, musculoskeletal problems, Lyme disease, leptomeningeal malignancy, or poliomyelitis should be evaluated in patients with a high CSF cell count. Myasthenia gravis, polymyositis, and dermatomyositis, poliomyelitis, hypermagnesaemia, porphyria, botulism, and lead or organophosphate poisoning are all conditions that should be explored. [19-21]

GBS presents differently in children than it does in adults, and diagnosing childhood GBS, especially in young children under the age of six, can be difficult. The most common presenting symptoms in children are pain, difficulty walking, or refusal to walk, all of which should raise suspicion of GBS. Only one-third of preschool children with GBS are diagnosed correctly at admission. GBS can be misdiagnosed in young children as meningitis, coxitis, or malaise caused by viral illnesses. When the diagnosis is delayed for more than 2 weeks in students less than <6 yrs of age during this period emergency intubation and even death may occur. [25-29]

Assessment scales

Brighton Diagnostic Criteria for GBS	**Level of Diagnostic Certainity**			
Symptoms	**1**	**2**	**3**	**4**
Bilateral and flaccid weakness of limbs	**+**	**+**	**+**	**+/-**
Decreased or absent deep tendon reflexes I weak limbs	**+**	**+**	**+**	**+/-**
Monophasic course and time between onset-nadir=12hrs to 28 days	**+**	**+**	**+**	**+/-**
Absence of alternative diagnosis for weakness	**+**	**+**	**+**	**+/-**
CSF cell count <50/ml	**+**	**+/-[a]**	**-**	**+/-**
CSF protein concentration>60mg/dl	**+**	**+/-[a]**	**-**	**+/-**
Nerve conduction study findings consistent with one of subtyoes of GBS	**+**	**+/-[a]**	**-**	**+/-**

PATHOPHYSIOLOGY OF COVID 19 AND GBS

COVID-19 has a variety of neurological mechanisms. The virus spreads to ACE2 protein on cells in the CNS via olfactory neurons and hematogenous dissemination. When the virus's receptor connects to ACE2, it causes a cytokine storm and a disruption of the blood-brain barrier. Dizziness, headache, changed mental status, stroke, ataxia, seizure, anosmia, visual abnormalities, nerve pain, skeletal muscle injury linked with sepsis, and multiple organ injury are some of the neurological consequences of Covid. [13] Anthor mechanism that may include SARS-CoV-2 can trigger an immunological response involving an increase in interleukin-6 (IL-6), which increases the inflammatory cascade and destroys tissues. As a result, inflammatory variables may play a significant role in the organ dysfunction of patients infected with Covid 19. The majority of neurological symptoms are most likely caused by these immune mechanisms. [30-32] In patients with co morbidity condition such as Diabetes mellitus (DM) can worsen the clinical and electrophysiological features of coexisting peripheral neuropathies, including GBS The specific mechanism underlying the DM-induced aggravation is unknown; however, it could be linked to the chronic inflammatory diseases associated with DM, as well as peripheral nerve neurovascular impairment. [33]

TYPES OF GBS:

There are mainly 4 variants of GBS that include AIDP (Acute Inflammatory Demyelinating Polyneuropathy) is the first. Inflammatory demyelinating is thought to begin at the nerve roots, resulting in electrophysiological conduction slowness and conductivity blockages, as well as acute muscle weakness. Peripheral nerves can undergo remyelination. It is primarily the most prevalent subtype of this illness that manifests. The second form Acute Motor Sensory Axonal Neuropathy (AMSAN), one of most extreme form of AMAN, Axon degeneration is most likely to impact sensory motor neuron fibres, resulting in delayed and poor recovery that can be reversible or irreversible. Acute Motor Axonal Neuropathy is functionally similar, albeit with additional sensory complaints. The third for is Miller Fisher Syndrome (MFS) which is characterised by ataxia, difficulty with eye movement, and areflexia. Antibodies that is against GQ1b (a ganglioside element of the nerve) are found in the majority of patients with this variation. Anti-GQ1b ganglioside is a common antigenic target which is not proportionally visible in the motor neurons that do not directly innervate peripheral muscles. AMAN (Acute Motor Axonal Neuropathy) differs from Acute Inflammatory Demyelinating Polyneuropathy in that it affects just motor nerves and has a distinct electrophysiological pattern of axonal involvement. [34,35] In terms of the distribution of GBS electrophysiological variations, the findings revealed that COVID-19-related GBS is most commonly linked with AIDP and, to a smaller extent, AMSAN and AMAN, similar to classic GBS in Western countries. [23,36] AIDP affects 60–80 percent of patients with GBS in Europe and the United States, while AMAN affects only 6–7%. This number is about 30–65 percent across Asia, Central and South America. This has to do with the population's genetic traits and its exposure to various pathogens. [37]

OUTCOME AND TREATMENT OF GBS IN COVID 19 PATIENTS:

Among the various GBS variant and subtypes found most of the patient infected with GBS were male. Latency between the onset of disease among the patient with covid 19 and GBS is 10-90 days'. GBS patients can receive IVIG or plasma exchange treatment. [38] Treatment is typically reserved for patients who are unable to walk independently, have increasing symptoms, bulbar weakness, or have respiratory compromise. Intravenous immunoglobulin (IVIG) at a dose of 2g/kg/ per day for 5 days was administered within 24 hours of the patient's arrival at the hospital. Previous case studies have demonstrated that Intravenous Immune Globulin treatment has had variable results, with certain patients reporting complete recovery and others indicating modest or delayed responses. [39,40] treating with Intra Venous Immune Globulin is associated with thromboembolic events as COVID-19 may be associated with a pro-thrombotic state, there may be concern about administering Intravenous Immune globulin but none of the reports described thrombotic complications. [41,42]

Plasmapheresis and steroids were administered among the patient and they are best when offered within 4 weeks of onset of the symptoms but the largest effect is seen when treatment is started within the first 2 weeks. [43-46] According to some research, patients with AMAN may have better outcomes with plasma exchange treatment than with Intravenous Immune Globulin therapy, and plasma exchange seems to be the most cost-effective approach. Plasma exchange followed by Intravenous Immune Globulin isn't considerably superior than either plasma exchange or Intravenous Immune Globulin on its own. In people with GBS, oral steroids and intravenous methylprednisolone are ineffective. Eighty-five percent of patients are able to return to their previous level of function. Long-term issues afflict 20% of patients, including severe impairment, pain, and exhaustion, with a 5% mortality rate. During the admission process to the hospital, 20-30% of patients require mechanical ventilation and intubation. [43,47-49] Plasma exchange (PLEX) was used to treat GBS without reported complications in two patients that we reviewed, but Plasma exchange is associated with hypotension in a small percentage of patients and can also affect the balance of clotting factors potentially leading to thromboembolic events. [50,51]

In contradiction to those with a positive prognosis, patients with no improvement or a poor outcome had a somewhat greater (but not statistically significant) incidence of clinical history and/or a radiological image of COVID-19 pneumonia (73.7 percent). Furthermore, the first group of patients was much older than the latter (mean age 51.8 16.6 years), but had similar sex and electrophysiological subtype distributions, as well as similar delay between COVID-19 and GBS ($p = 0.588$) and nadir ($p = 0.825$). [52]

Rehabilitation, physiotherapy, Logopaedic help, Psychological support are the treatment plan for people who are disabled as a result of Guillain-Barré syndrome. The rehabilitation is important to be started as early as possible. [53]

Treatment options are influenced by both patient-related and socioeconomic factors. Plasma exchange, for example, necessitates specialised equipment that is not always available in all hospitals. Furthermore, plasma exchange can be difficult to execute in young children, and due to the substantial volume shifts required in the plasma exchange operation, caution should be exercised in patients with autonomic cardiovascular instability [54,55]

DISCUSSION:

GBS is a rare but catastrophic post-infectious neuropathy that has a 3-13 percent fatality rate. [56] with a rapidly progressive immune theory mediated polyradiculo-neuropathy. It is usually associated with post infections

syndrome as defined by an onset that is delayed from the acute symptoms of infection and by a mechanism that is distinct from the infection The discovery of auto-antibodies that result from an immune response directed against an epitope of the infectious agent that then cross reacts with a structurally similar component of peripheral nerve, result in slow immune-mediated damage to peripheral nervous system, supports the post infectious mechanism of GBS. [57] Most of the patients have symptoms of infection in preceding 3–6 weeks. [(13)] Some studies have shown that bacterial and viral pathogens have been discovered in GBS patients, but the factors that cause immune-mediated nerve tissue destruction have not been identified. [58] The Epstein–Barr virus, CMV, Campylobacter jejuni, human immunodeficiency virus (HIV), and ZiKa virus are among the pathogenic agents linked to GBS. [59,60] Campylobacter jejuni is the likely the most common infection causing Guillain-Barré syndrome. [13] In most patients, the delay between the development of infectious and neurological symptoms and a negative PCR supports a post-infectious rather than a direct infectious cause. The role of the peripheral nervous system in the development of GBS in SARS-CoV-2-infected patients is uncertain. The majority of patients developed GBS on average 10 days after the initial non-neurological signs of SARS-CoV-2 infection, implying a causal link. Moreover, no particular SARS-CoV2 RNA has been observed in the Cerebrospinal Fluid of any of the patients. GBS is triggered by an immune-mediated process instead of a direct viral attack on nerves, such as antibody precipitation on myelin sheaths or axons, as previously thought. [61]

GBS can develop in persons who are generally asymptomatic or have mild COVID-19 signs. Moreover, the severity of GBS is unrelated to the severity of COVID-19. Due to the sheer limited timeframe between the SARS-CoV-2 infection and the start of GBS (8–23 days), GBS-related neurological symptoms frequently overlap with COVID19-related symptoms. As a result, it is clear that the overlap adds to a worse prognosis. In the majority of cases, there was an increase in protein level as well as albuminocytological separation. This pattern distinguishes GBS from other illnesses in which both the protein and the cell count are high, such as lymphoma and poliomyelitis. Furthermore, protein levels in CSF have been linked to illness activity, progression, and therapy response. [62] A viral infection can produce neuromuscular injury through a variety of pathways, including direct damage such as neuritis or myositis during an active infection, systemic inflammatory response syndrome, or cross-immunity. The inflammation generated by some coronaviruses can cause immunological dysfunction, resulting in the release of various pro-inflammatory immune factors that might harm other organs and/or nerves in addition to the lungs. A systemic hyper inflammation in COVID-19 patients with macrophage activation syndrome has recently been recognized. In addition, certain cases of GBS caused by the Zika virus have led to speculation about a possible non-infectious aetiology. [60]

Around one-fifth of COVID-19-associated GBS participants required mechanical breathing during hospitalisation, similar to classic GBS. Cases with no improvement or a bad prognosis appeared slightly older age (but not statistically significant) than those with a positive prognosis in this aspect, confirming similar findings in both classic GBS and COVID-19, as well as a marginally greater frequency (without reaching statistical significance) of past or concurrent COVID-19 pneumonia. [63-66]

As the prevalence of GBS has been risen since the pandemic due to various reason First, SC2-GBS may go unnoticed because it's mistaken for greater weakness or sensory abnormalities caused by a pre-existing neuropathy. Second, SC2-GBS could be confused with critical ill neuropathy. Third, due to modest symptoms or onset during an ICU stay, a neuropathy work-up may be incomplete. Alternative conditions must be ruled out before SC2-GBS may be diagnosed. These include neuropathy that has already existed, critical ill myopathy, critical ill neuropathy, toxic neuropathy, and neuropathy or myopathy caused by pharmacological adverse effects. Neuropathy has been linked to lopinavir and tocilizumab. [67,68] There were also reports that chloroquine can cause neuropathy.

The majority of the studies did not specify whether SC2-GBS patients' respiratory failure was caused by brainstem encephalitis, BFE, respiratory muscle involvement in GBS, acute pneumonia, respiratory distress syndrome (ARDS), pulmonary embolism, heart failure, or a combination of these conditions. However, determining the aetiology of respiratory failure is critical because therapy and outcomes might vary greatly between various disorders. [13]

CONCLUSION:

GBS can be caused by the SARS-CoV-2 infection. The underlying theory that causes this disease to develop is still unknown. since the virus has not been found in CSF of any SC2-GBS patient reported. Even though SC2- GBS occurs at any age most of the cases are seen above 50yrs. SC2-GBS patients do not differ from non-SC2-GBS patients in terms of clinical manifestations or therapy, but their outcomes are poorer. The prevalence/incidence of GBS most likely increased since the outbreak of the pandemic Pedi should be aware of GBS as a rare complication associated with COVID-19. Diagnosis can be difficult and time-consuming, particularly in asymptomatic patients or those who have had a mild respiratory illness week before. Early detection and treatment can help to enhance the clinical result.

REFERENCES:

1. Li X, Zai J, Zhao Q, et al., Evolutionary history, potential intermediate animal host, and cross-species analyses of SARS-CoV-2. J Med Virol. 2020; 92(6):602-611. https://doi.org/10.1002/jmv.25731

2. WHO Director-General's opening remarks at the media briefing on COVID-19 (2020). Available online at: https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-themedia-briefing-on-covid-19 (accessed August 24, 2021).

3. Huang C, Wang Y, Li X, et al., Clinical features of patients infected with 2019 novel Coronavirus in Wuhan, China. Lancet. 2020; 395(10223):497-506. https://doi.org/10.1016/S0140-6736(20)30183-5

4. Zhou P, Yang X-L, Wang X-G, et al., A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020; 579(7798):270-273. https://doi.org/10.1038/s41586-020-2012-7

5. Mao L, Jin H, Wang M, et al., Neurologic manifestations of hospitalized patients with Coronavirus Disease 2019 IN WUHAN, CHINA. JAMA Neurol. 2020; 77(6):683. https://doi.org/10.1001/jamaneurol.2020.1127

6. Orlikowski D, Porcher R, Sivadon TV, et al., Guillain-Barre syndrome following Primary Cytomegalovirus Infection: A prospective cohort study. Clin. Infect. Dis. 2011; 52(7):837-844. https://doi.org/10.1093/cid/cir074

7. Wakerley BR, Yuki N. Infectious and non-infectious triggers in Guillain-Barre syndrome. Expert Rev. Clin. Immunol.2013;9:627-639. https://doi.org/10.1586/1744666X.2013.811119

8. Cao-Lormeau VM, Blake A, Mons S, et al., Guillain-Barre syndrome outbreak associated with Zika virus infection in French

Polynesia: a case-control study. Lancet.2016; 387(10027):1531-1539. https://doi.org/10.1016/S0140-6736(16)00562-6

9. Uncini A, González BDC, Acosta AYY, et al., Clinical and nerve conduction features in Guillain-Barre syndrome associated with Zika virus infection in Cúcuta, Colombia. Eur. J. Neurol.2018; 25:644-650. https://doi.org/10.1111/ene.13552

10. Hughes RAC, Cornblath DR. Guillain-Barré syndrome. Lancet. 2005; 366(9497):1653-1666. https://doi.org/10.1016/S0140-6736(05)67665-9

11. Sejvar JJ, Baughman AL, Wise M, Morgan OW. Population incidence of Guillain Barré syndrome: a systematic review and meta-analysis. Neuroepidemiology.2011; 36:123-133. https://doi.org/10.1159/000324710

12. Jacobs BC, Rothbarth PH, van der Meché FG, et al., The spectrum of antecedent infections in Guillain-Barré syndrome: a case-control study. Neurology.1998; 51(4):1110-5. https://doi.org/10.1212/WNL.51.4.1110

13. Patanik UJ. Review article On COVID-19 and GUILLAIN-BARRÉ SYNDROME. Front. Biosci. 2021; 13(1):97. doi:10.52586/s555 https://doi.org/10.52586/S555

14. Nguyen TP, Taylor RS. Guillain Barre syndrome. 2021 July 10. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021. Jan-. [last accessed 17 August 2021] Available at https://www.ncbi.nlm.nih.gov/books/NBK532254/

15. Finsterer J, Scorza FA. Guillain-Barre syndrome in 220 patients With covid-19. The Egypt. J. Neurol. Psychiatry Neurosurg. 2021; 57(1). https://doi.org/10.1186/s41983-021-00310-7

16. Webb AJ, Brain SA, Wood R, Rinaldi S, Turner MR. Seasonal variation in Guillain-Barré syndrome: a systematic review, meta-analysis and Oxfordshire cohort study. J. Neurol Neurosurg Psychiatry.2015; 86:1196-1201. https://doi.org/10.1136/jnnp-2014-309056

17. Filosto M, Cotti Piccinelli S, Gazzina S, et al., Guillain-Barré syndrome and COVID-19: An observational Multicentre study from two italian hotspot regions. J. Neurol. Neurosurg Psychiatry. 2020; 92(7):751-756. https://doi.org/10.1136/jnnp-2020-324837

18. van Doorn PA, Ruts L, Jacobs BC. Clinical features, pathogenesis, and treatment of Guillain-Barré Syndrome. Lancet Neurol. 2008; 7(10):939-950. https://doi.org/10.1016/S1474-4422(08)70215-1

19. Parry GJ. Guillain-Barré Syndrome 42-55 (Thieme Medical Publishers, 1993).

20. Hughes RA. Guillain-Barré Syndrome 124-130 (Springer-Verlag, 1990). https://doi.org/10.1007/978-1-4471-3175-5

21. Ropper AH, Wijdicks EF, Truaxm BT. Guillain- Barré Syndrome 175-224 (F. A. Davis, 1991).

22. Camdessanche JP, Morel J, Pozzetto B, Paul S, Tholance Y, Botelho NE. COVID-19 may induce Guillain-Barré syndrome. Rev Neurol.2020; 176(6): 516-518. https://doi.org/10.1016/j.neurol.2020.04.003

23. Parasher A. COVID-19: Current understanding of its Pathophysiology, Clinical presentation and Treatment. Postgrad Med. J. 2020; 97(1147):312-320. https://doi.org/10.1136/postgradmedj-2020-138577

24. Fokke C, van den Berg B, Drenthen J, Walgaard C, van Doorn PA, Jacobs BC. Diagnosis of Guillain-Barré syndrome and validation of Brighton criteria. Brain. 2014; 137(1):33-43. https://doi.org/10.1093/brain/awt285

25. Devos D, Magot A, Perrier BJ, et al., Guillain-Barré syndrome during childhood: Particular clinical and electrophysiological features. Muscle Nerve. 2013; 48(2):247-251. https://doi.org/10.1002/mus.23749

26. Korinthenberg R, Schessl J, Kirschner J. Clinical Presentation and Course of Childhood Guillain-Barré Syndrome: A Prospective Multicentre Study. Neuropediatrics. 2007; 38(1):10-17. https://doi.org/10.1055/s-2007-981686

27. Roodbol J, Wit M, Walgaard C, Hoog M, Catsman BC, Jacobs B. Recognizing Guillain-Barre syndrome in preschool children. Neurology. 2011; 76(9):807-810. https://doi.org/10.1212/WNL.0b013e31820e7b62

28. Ryan MM. Guillain-Barré syndrome in childhood. J. Paediatr Child Health.2005; 41(5-6):237-241. https://doi.org/10.1111/j.1440-1754.2005.00602.x

29. Wit MC, Roodbol J, Hoog M, Catsman-B, Jacobs, BC. Imminent respiratory insufficiency in children resulting from Guillain-Barré syndrome [Dutch]. Nederlands Tijdschrift voor Geneeskunde.2011; 155:A3808.

30. Carod-Artal FJ. Neurological complications of coronavirus and COVID-19. Revista de Neurologia.2020; 70(9):311-322. https://doi.org/10.33588/rn.7009.2020179

31. Helms J, Kremer S, Merdji H, Clere-Jehl R, Schenck et.al., Neurologic features in severe SARSCoV-2 infection. N. Engl. J. Med. 2020; 382(23):2268-2270 https://doi.org/10.1056/NEJMc2008597

32. Sedaghat Z, Karimi N. Guillain Barre syndrome associated with COVID-19 infection: a case report. J. clin. Neurosci.2020;76:233-239. https://doi.org/10.1016/j.jocn.2020.04.062

33. Bae JS, Kim YJ, Kim JK. Diabetes mellitus exacerbates the clinical and electrophysiological features of Guillain-Barré syndrome. Eur. J. Neurol. 2016; 23(3):439-46. https://doi.org/10.1111/ene.12885

34. Rahimi K. Guillain-Barre syndrome during COVID-19 pandemic: an overview of the reports. Neurol. Sci.2020; 41:3149-3156. https://doi.org/10.1007/s10072-020-04693-y

35. Martín-Aguilar L, Camps-Renom P, Lleixà C, Díaz-Manera J, Rojas-García R, et al. Serum neurofilament light chain predicts long-term prognosis in Guillain-Barré syndrome patients. J. Neurol. Neurosurg. Psychiatry. 2021; 92:70-77. https://doi.org/10.1136/jnnp-2020-323899

36. Arcila-Londono X, Lewis RA. Guillain-Barré syndrome. Seminars in Neurology. 2020; 32(3):179-186. https://doi.org/10.1055/s-0032-1329196

37. Van den Berg, B.; Walgaard, C.; Drenthen, J.; Fokke, C.; Jacobs, B.C.; van Doorn, P.A. Guillain-Barré syndrome: Pathogenesis, diagnosis, treatment, and prognosis. Nat. Rev. Neurol. 2014; 10(8):469-482. https://doi.org/10.1038/nrneurol.2014.121

38. Finsterer J, Scorza FA. Guillain-Barre syndrome in 220 patients with covid-19. Egypt. J. Neurol. Psychiatr. Neurosurg. 2021; 57(1) 1-7. https://doi.org/10.1186/s41983-021-00310-7

39. Andrea A, Luana B, Silvia DM, Erika S, Massimo DS. New clinical manifestation of COVID 19 related Guillain Barrè syndrome highly responsive to intravenous immunoglobulins: Two Italian cases. J. Neurol. Sci. 2020; 41:1657-1668. https://doi.org/10.1007/s10072-020-04484-5

40. Frontera J, Mainali S, Fink E et al. Global Consortium Study of Neurological Dysfunction in COVID-19 (GCS-NeuroCOVID): Study Design and Rationale. J. Neurocrit Care. 2020; 33(1):25-34. https://doi.org/10.1007/s12028-020-00995-3

41. Research C for BE and. Safety & Availability (Biologics) - FDA Safety Communication: New boxed warning for thrombosis related to human immune globulin products. Accessed April 22, 2020. http://wayback.archiveit.org/7993/20170112095644/http://www.fda.gov/biologicsbloodvaccines/safetyavailability/ucm375096.html

42. Hess DC, Eldahshan W, Rutkowski E. COVID-19-Related Stroke. Transl. Stroke Res. 2020; 11(3):322- 325. https://doi.org/10.1007/s12975-020-00818-9

43. Hughes RAC, Swan AV, Raphaël J-C, et al. Immunotherapy for Guillain-Barré syndrome: a systematic review. Brain.2007; 130(9):2245-2257. https://doi.org/10.1093/brain/awm004

44. Raphael, J. C., Chevret, S., Hughes, R. A. & Annane, D. Plasma exchange for Guillain-Barré syndrome.Cochrane Database of

Systematic Reviews. 2012; 7:CD001798. https://doi.org/10.1002/14651858.CD001798.pub2

45. [No authors listed] Plasmapheresis and acute Guillain-Barré syndrome. The Guillain-Barré syndrome Study Group. Neurology.1985; 35(8);1096-1104. https://doi.org/10.1212/WNL.35.8.1096

46. [No authors listed] Efficiency of plasma exchange in Guillain-Barré syndrome: role of replacement fluids. French Cooperative Group on Plasma Exchange in Guillain-Barré syndrome. Ann. Neurol.1987; 22(6):753-761. https://doi.org/10.1002/ana.410220612

47. Hughes, R. A. & van Doorn, P. A. Corticosteroids for Guillain-Barré syndrome. Cochrane Database of Systematic Reviews, Issue 8. Art. No.: CD001446.

48. Van Koningsveld R, Schmitz P, van der Meché F, Visser L, Meulstee J, van Doorn P. Effect of methylprednisolone when added to standard treatment with intravenous immunoglobulin for Guillain-Barré syndrome: randomised trial. Lancet. 2004; 363(9404):192-196. https://doi.org/10.1016/S0140-6736(03)15324-X

49. Willison HJ, Jacobs BC, van Doorn PA. Guillain-Barré syndrome. Lancet 2016; 388(10045):717-27. https://doi.org/10.1016/S0140-6736(16)00339-1

50. Rodnitzky RL, Goeken JA. Complications of Plasma Exchange in Neurological Patients. Arch. Neurol. 1982; 39(6):350-354. https://doi.org/10.1001/archneur.1982.00510180028007

51. Jin PH, Shin SC, Dhamoon MS. Risk of thrombotic events after inpatient intravenous immunoglobulin or plasma exchange for neurologic disease: A case-crossover study. Muscle Nerve.2020:62(3); 327-332. https://doi.org/10.1002/mus.26884

52. 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. 2020; 268(4):1133-1170. https://doi.org/10.1007/s00415-020-10124-x

53. Winer JB. Treatment of Guillain-Barré syndrome. Monthly J. Assoc. Physicians. 2002; 95(11):717-721. https://doi.org/10.1093/qjmed/95.11.717

54. Gajjar, M D. et al. Efficacy and cost effectiveness of therapeutic plasma exchange in patient of Guillain-Barré syndrome-a prospective study. SEJCRR.2013; 2(4):218-228.

55. Winters JL., Brown D., Hazard E., Chainani A. Andrzejewski, C. Jr. Cost-minimization analysis of the direct costs of TPE and IVIg in the treatment of Guillain-Barré syndrome. BMC Health Ser.Res. 2011; 11(1). https://doi.org/10.1186/1472-6963-11-101

56. van den Berg B, Bunschoten C, van Doorn PA, Jacobs BC. Mortality in Guillain-Barre syndrome. Neurology. 2013; 80(18):1650-1654. https://doi.org/10.1212/WNL.0b013e3182904fcc

57. Willison HJ, Jacobs BC, van Doorn PA. Guillain-Barré syndrome. Lancet. 2016; 388(10045):717- 727. https://doi.org/10.1016/S0140-6736(16)00339-1

58. Hardy TA, Blum S, McCombe PA, Reddel SW. Guillain-Barré syndrome: modern theories of etiology. Curr. Allergy. Asthma. Rep. 2011; 11(3):197-204. https://doi.org/10.1007/s11882-011-0190-y

59. Ottaviani D, Boso F, Tranquillini E, Gapeni I, Pedrotti G, Cozzio S, Guarrera GM, Giometto B. Early Guillain-Barré syndrome in coronavirus disease 2019 (COVID-19): a case report from an Italian COVID-hospital. Neurol. Sci. 2020; 41(6):1351-1354. https://doi.org/10.1007/s10072-020-04449-8

60. Parra B, Lizarazo J, Jiménez-Arango JA, Zea-Vera AF, GonzálezManrique G, Vargas J, Angarita JA, Zuñiga G, Lopez-Gonzalez R, Beltran CL, Rizcala KH, Morales MT, Pacheco O, Ospina ML, Kumar A, Cornblath DR, Muñoz LS, Osorio L, Barreras P, Pardo CA. Guillain-Barré syndrome associated with Zika virus infection in Colombia. N. Engl. J. Med. 2016; 375(16):1513-1523 https://doi.org/10.1056/NEJMoa1605564

61. Finsterer J, Scorza FA, Ghosh R, COVID-19 polyradiculitis in 24 patients without SARS-CoV-2 in the cerebro-spinal fluid. J. Med. Virol. 2020; 93(1): 66-68. https://doi.org/10.1002/jmv.26121

62. Domingues R, Fernandes G, Leite F et al. The cerebrospinal fluid in multiple sclerosis: far beyond the bands. Einstein (São Paulo). 2017; 15(1):100-104. https://doi.org/10.1590/s1679-45082017rw3706

63. Willison HJ, Jacobs BC, van Doorn PA. Guillain-Barré syndrome. Lancet. 2016; 388(10045):717-727. https://doi.org/10.1016/S0140-6736(16)00339-1

64. Walgaard C, Lingsma HF, Ruts L et al. Prediction of respiratory insufficiency in Guillain-Barré syndrome. Ann. Neurol.2010; 67(6):781-787. https://doi.org/10.1002/ana.21976

65. van K R, Steyerberg E, Hughes R, Swan A, van D P, Jacobs B. A clinical prognostic scoring system for Guillain-Barré syndrome. Lancet Neurol. 2007; 6(7):589-594. https://doi.org/10.1016/S1474-4422(07)70130-8

66. Liu Y, Mao B, Liang S et al. Association between age and clinical characteristics and outcomes of COVID-19. Eur. Respir. J. 2020; 55(5):2001112. https://doi.org/10.1183/13993003.01112-2020

67. Khanlou H, Valdes-Sueiras M, Farthing C. Peripheral Neuropathy Induced by Lopinavir-Saquinavir-Ritonavir Combination Therapy in an HIV-Infected Patient. J. Intern Ass. Physicians AIDS Care. 2007; 6(3):155-155. https://doi.org/10.1177/1545109707302756

68. Sugiura F, Kojima T, Oguchi T, Urata S, Yuzawa Y, Sakakibara A, et al. A case of peripheral neuropathy and skin ulcer in a patient with rheumatoid arthritis after a single infusion of tocilizumab. Mod Rheumatol. 2009; 19(2): 199-203. https://doi.org/10.3109/s10165-008-0132-2