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Current Management Strategies of Guillain - Barré Syndrome – A Comprehensive Review

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ABSTRACT

Since the original report of Guillain-Barré syndrome (GBS) 100 years ago, the understanding of this condition has altered dramatically. GBS is a rare autoimmune disorder. Guillain-Barre syndrome frequently begins with tingling and weakness in the feet and legs and spreads to the upper torso and arms. GBS is often categorized into subtypes based on both pathological involvement and phenotypic differences however numerous therapies may reduce symptoms and shorten the illness duration. Several research and case reports have suggested a link between COVID-19 and Guillain-Barré syndrome (GBS). Here are two therapy options for Guillain-Barré syndrome (GBS) that are currently considered standard of care. These include intravenous immunoglobulin (IVIG) or plasma exchange, as well as biochemical drugs, corticosteroids, and supportive care. This review focuses on the current GBS and management strategy.

1 INTRODUCTION

Guillain Barré syndrome (GBS) is a medical condition marked by the onset of weakness, in the limbs, sensory deficits, involvement of nerves reduced reflexes in tendons, and dissociation of cerebrospinal fluid (CSF). It is reported to affect 100,000 individuals worldwide each year [1]. After being infected with SARS CoV 2, the incidence of GBS ranged from 0.12 to 9.44 cases per 100,000 person-years. Additionally, there were 8.1 cases per 1 million vaccinations associated with the COVID-19 vaccine [3]. The cause of GBS is still not fully understood although past cases have been linked to infections such as Mycoplasma pneumoniae, Campylobacter cytomegalovirus influenza, and Epstein Barr virus. Similarly, COVID-19 can lead to GBS along with symptoms. GBS has variants that include inflammatory demyelinating polyneuropathy, acute motor axonal neuropathy, acute motor sensory axonal neuropathy, and Miller-Fisher syndrome. The evaluation of GBS patients involves testing muscle strength in all four limbs by the use of the Medical Research Council sum score system ranging from 0 (quadriplegic) to 60 (normal). The presence of weakness, in bulbar muscles indicates a prognosis and an increased likelihood of needing mechanical ventilation. Nevertheless, certain therapies, like care, steroids, and immunotherapy can help alleviate the severity of the condition and promote a recovery. The purpose of this review is to offer an up-to-date viewpoint on the approaches and tactics, for managing GBS.

2.Methods

In our study, articles released between 2014 and 2023 were included. Extensive examination was conducted on clinical trials, original publications, retrospective studies, and systemic reviews available in MEDLINE through PubMed, Science Direct, Google Scholar, UpToDate, and the WHO interface. All citations were checked for background information and possibly related articles.

3.Discussion

Experts have discovered that Guillain-Barré syndrome is an autoimmune disease brought on by a prior bacterial or viral infection.

3.1 Clinical features

Weakness and tingling are the first signs of Guillain-Barre syndrome. It frequently begins in the area of the legs before spreading to the face and arms.

1. These symptoms can cause paralysis of the arm, leg, or facial muscles in some people.

2. In about one-third of cases, chest muscle weakness makes breathing difficult.

3. Difficulty with facial movements such as speaking, chewing, and swallowing.

4. Double vision or inability to move the eyes.

5. Difficulty with bladder control or bowel function.

3.2 Pathophysiology

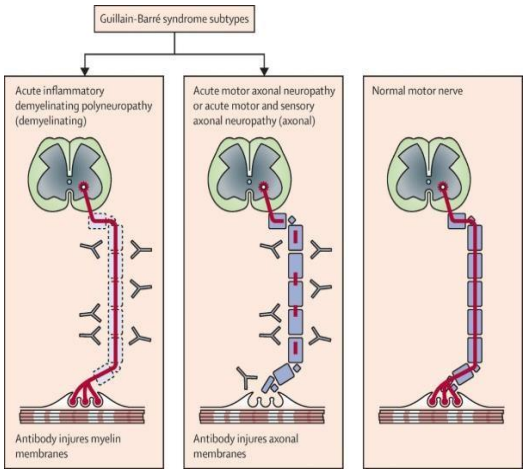


Figure.1 Major subtypes of Guillain-Barré syndrome

The pathophysiology of GBS is not easy to understand. A cross-reaction is caused by the immune response. When the immune system starts attacking the body, there is a reaction in the brain tissue. The breakdown of myelin is the cause of inflammation. Demyelination leads to Schwann cells multiplying and swelling decreasing after 2-3 weeks and the process of remyelinating is initiated[4]. The symptoms can be mild or very severe, leading to the need for mechanical ventilation and even death. As per another comprehensive analysis, 78% of people with GBS[5].

3.3 Guillain Barre Syndrome associated with SARS-CoV-2

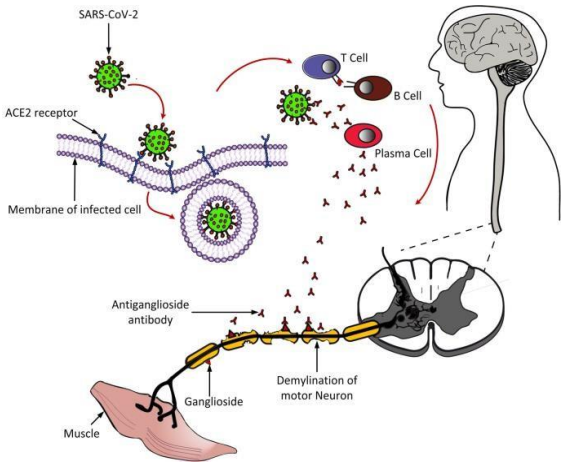


Figure.2 a visual representation of pathophysiology of GBS related with COVID-19

The coronavirus disease 2019 pandemic, which was caused by a severe acute respiratory syndrome infection, has been linked to a range of neurological symptoms, including complications with the brain, spinal cord, and neuromuscular system [6]. COVID-19 was hyper-responsive to intravenous immunoglobulin (Ig) [7]. T-cell and B-cell interactions generated by SARS-CoV-2 infection led to the development of SARS-CoV-2-specific antibodies, but molecular mimicry of the similarity between the virus and ganglioside peptide- sequences May lead to self-infection. May cause loss-tolerance. as shown in Figure 2 [8]. COVID-19-GBS is not only more difficult to treat but also has a poorer prediction, including, gastroparesis, heart failure, respiratory failure, multiple organ failure and other symptoms, and extreme nervousness. It is a disease characterized by severe autonomic nerve dysfunction manifested by muscle symptoms. The autonomic and peripheral neurologic consequences of COVID-19 infection are often accompanied by Bradycardia or weakness or paralysis[9]. GBS is a rare condition.

3.4 Guillain Barre Syndrome associated with COVID-19 vaccination

The effectiveness and safety of vaccination have been demonstrated in all populations. However, like all vaccinations, it can cause many side effects. COVID-19 vaccination may cause neurological side effects Among the side effects is the development of Guillain-Barre syndrome. The exact occurrence is still uncertain, and further research is necessary to determine the cause. The structural similarities between SARS-CoV-2 spike protein and myelin protein

suggest a pathophysiological explanation for GBS after COVID-19 vaccination. This process is known as molecular mimicry [11]. Vaccination against the SARS-CoV-2 Spike protein can cause antibody cross-reactivity. It has long been believed that vaccination can lower the risk of infectious disease because it increases the immune system's activity, which in turn increases autoimmune diseases such as GBS [10].

3.5 Diagnosis

Early diagnosis of Guillain-Barre syndrome can be difficult. The manifestations differ among individuals but are reminiscent of other neurological ailments. CSF findings and clinical characteristics are the main factors used in GBS diagnosis. Electromyography and blood testing are examples of laboratory tests.

Spinal tap (lumbar puncture).

In the lumbar area, just a small quantity of fluid is removed from the spinal canal.

People with Guillain-Barre syndrome often have specific changes that are detected in their body fluids.

Electromyography.

The physician places a fine needle electrode in the muscle that they intend to examine. Electrodes track muscle nerve activity.

Study of nerve conduction.

A nerve was covered with electrodes through the skin. By administering a small shock, the nerve's transmission rate can be determined.

3.6 MANAGEMENT

Studies comparing immunoglobulins and PE subsequently proven the therapeutic efficacy of these two approaches [12]. Besides monoclonal antibody treatment, no evidence is there to support the use of other drugs for GBS, such as steroids and interferon beta. Most GBS clinical trials use his GBS Disability Scale as an outcome measure. Levels 0 to 6 make up the GBS disorder scale. [13]

3.6.1 IVIg

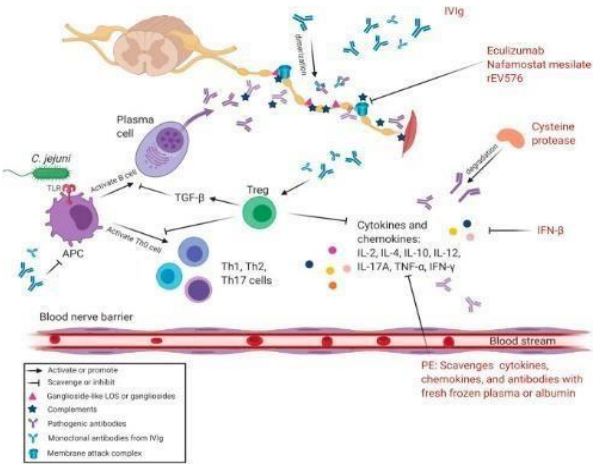


Figure 3. Pharmacological therapeutic targets of GBS.12

In 1992, the first RCT using IVIg was published, showing that IVIG was just as effective as PE. A blood product that contains polyclonal IgG antibodies is known as an IVIg. By using IVIG to treat Fc-mediated treatment, immune cell activation, anti-ganglioside antibody binding to brain targets, and local complement activation can all be avoided. Currently, 2 g/kg body weight is the generally accepted empirical dosage of IVIg for GBS. Various treatment regimens have been proposed, including 0.4 g/kg over 5 days or, more frequently, an overall dosage of 2 g/cover 2 days in successive days [14,15]. One course of IVIg did not improve the overall progress of the disease in patients with moderate GBS (Cornblath DR, et al., 2021)[16]. Being able to remove immunoglobulins and immune complexes from plasma selectively makes immunoadsorption a popular treatment for many autoimmune disorders. Using immunoadsorption in routine clinical practice has been done safely and with good patient tolerance[17]. IVIg therapy has been utilized for several COVID-19-related neurological conditions. A positive outcome appears to be dependent on the administration's time. They propose that the earliest IVIG administration in the context of COVID-19 produces the biggest benefits.

3.6.2 Plasma Exchange

The early administration of COVID-19 is considered to be the most advantageous aspect of IVIG, according to their recommendation. Plasma exchange was improved, leading to an improvement in GBS. Plasma the liquid part of blood is separated from blood cells [19,20]. Cells are reinfused into the GBS patient at the same time as plasma collection [21]. TPE is recommended for the treatment of GBS because it is cheaper than IVIg and widely available in developing countries. Five sessions of 40–50 mL/kg plasma exchange were conducted over seven to fourteen days, with 200–250 mL of plasma exchanged per kilogram of body weight. [22].

Due to citrate toxicity and complications, plasmapheresis cycles reach 3 cycles, but not all patients are recommended to perform 5 cycles of TPE was found to be one of the most effective treatment strategies for his GBS considering the reduction in hospital stay and intensive care period. Plasmapheresis most likely increases the chance of complete recovery of muscle strength after 1 year. TPE was administered in combination with standard treatment for severe COVID-19, which includes oxygen therapy, anticoagulation, and corticosteroids. The combined therapy proved to be therapeutically effective in our patients[23].

3.6.3 Supportive Care

Supportive care remains the mainstay of treatment, although the evidence for supportive care treatments is insufficient, and consensus treatment guidelines have not been established. The main care components of supportive are supportive pharmacotherapies like biological drugs, steroids, and supplements, with multidisciplinary care. Typically, respiratory, cardiovascular, or autonomic problems are the causes of mortality [31, 28, 29]. Joint stiffness and muscle strength are improved with physical therapy. A rehabilitation clinic is frequently where patients undergo physical and occupational treatment once their conditions are stabilized. Throughout the disease, psychological support is essential [30].

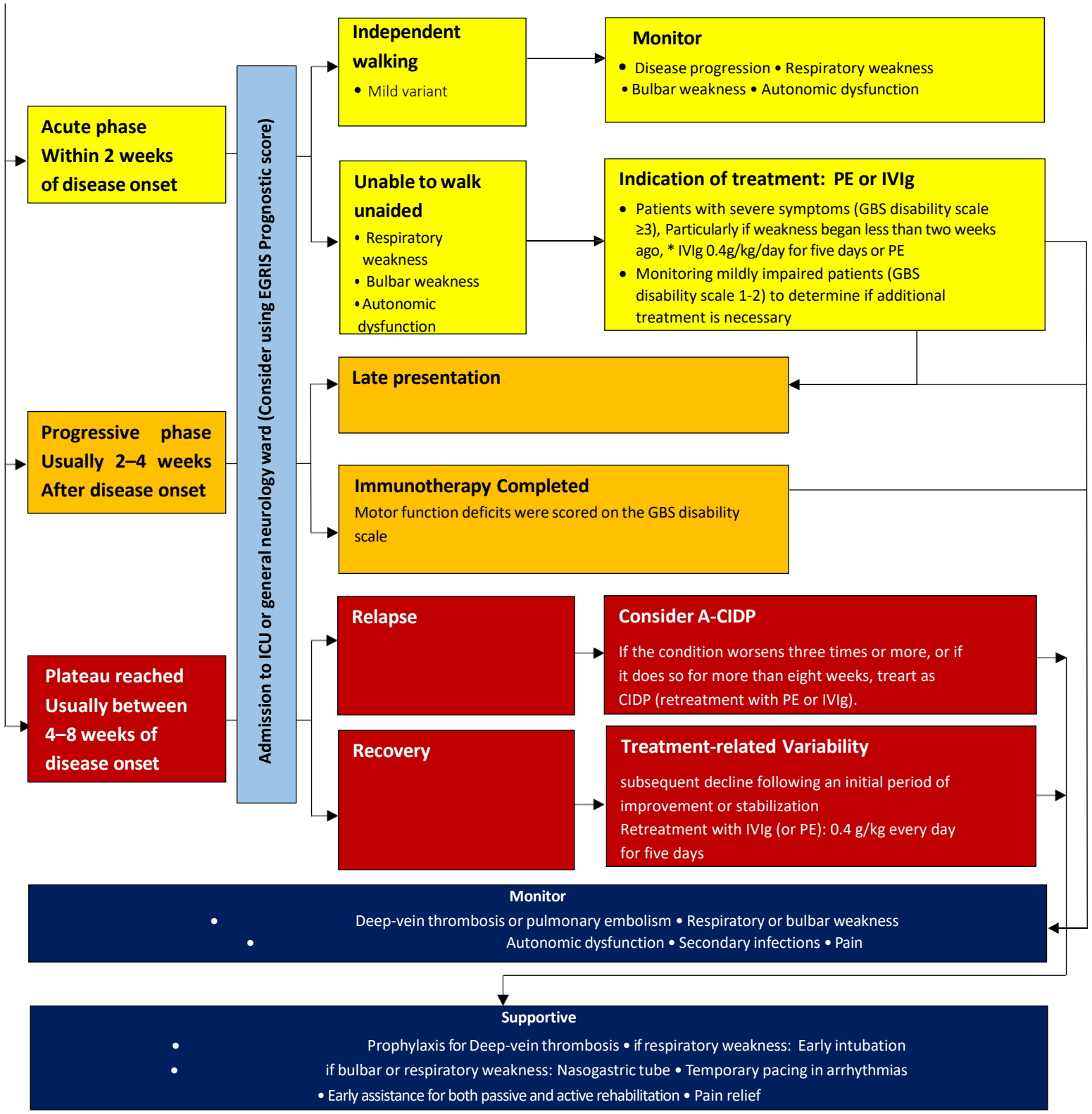
3.6.4 Biological Drugs

The significance of biological agents in treating several immune-mediated inflammatory or malignant illnesses has been studied. Authors here focused on literature data on novel biological therapeutic agents, such as cytokine targets and monoclonal antibodies against C5 (Eculizumab), C1q (Eculizumab), T cell, CD2, L-selectin, CD52, and other emerging agents. None of these medications have yet received FDA approval for the treatment of GBS [24]. Novel biological drugs such as eculizumab showed significant efficacy and were well tolerated in acute GBS patients and may be used safely in combination with IVIg[25, 26].

3.6.5 Corticosteroid

From the early 1950s onwards, corticosteroid (methylprednisolone) therapy has been used in individual case reports for GBS. Many authors reported on potentially beneficial outcomes from uncontrolled comparative studies or limited series [27]. In inflammatory neuropathy, corticosteroids.

Diagnosis and treatment of Guillain Barre Syndrome



• GBS-Guillain Barre Syndrome • IVIg- Intravenous Immunoglobulin • PE- Plasma Exchange
• A-CIDP- Acute Chronic Inflammatory Demylating Polyneuropathy • ICU- Intensive Care Unit
• EGRIS- Erasmus GBS Respiratory Insufficiency Score.

should theoretically reduce inflammation thereby lessening nerve damage. Therefore, a thorough analysis of the risk-benefit ratio of corticosteroid therapy in GBS is necessary. Whereas GBS is an immune-mediated sickness, corticosteroids are ineffective when the condition is severe.

CONCLUSION

Immunoglobulin therapy and plasma exchange are both equally successful treatments. Combining them or administering them sequentially will not be as successful as using either approach alone. A person with Guillain-Barre syndrome requires physical support and rehabilitation before and during recovery. Adults recovering from Guillain-Barre syndrome include: Six months after diagnosis, around 80% are ambulating independently with appropriate treatment. About 60% regain full exercise strength one year after diagnosis. In about 5-10%, recovery is very slow and incomplete. Children, who rarely develop GBS, generally recover more fully than adults. Research continues to identify new treatments for GBS. Clinicians should be aware of neurological symptoms of GBS, which are likely related to SARS-CoV-2 infection. Patients with moderate and variable forms of GBS, as well as those who experience treatment- related fluctuations or treatment failure, are routinely treated in current practice, but there is a lack of research evidence to support this decision. For GBS patients, we found that IVIG or PE was much more efficient. Research on the combinations of IVIG + PE, IVIG + immunoadsorption, and IVIG + biological medications need to be done further. GBS is not significantly affected by corticosteroids.

REFERENCES:

[1] Leonhard, S.E., Mandarakas, M.R., Gondim, F.A.A., Bateman, K., Ferreira, M.L.B., Cornblath, D.R., van Doorn, P.A., Dourado, M.E., Hughes, R.A.C., Islam, B., Kusunoki, S., Pardo, C.A., Reisin, R., Sejvar, J.J., Shahrizaila, N., Soares, C., Umapathi, T., Wang, Y., Yiu, E.M. and Willison, H.J. (2019). Diagnosis and Management of Guillain–Barré Syndrome in Ten Steps. *Nature Reviews Neurology*, Nov;15(11):671-683. doi: 10.1038/s41582-019-0250-9. Epub 2019 Sep 20.

[2] Dimachkie, M.M. and Barohn, R.J. (2013). Guillain-Barré Syndrome and Variants. *Neurologic Clinics*, may31(2), pp.491–510. doi10.1016/j.ncl.2013.01.005

[3] Kim, J.-E., Min, Y.G., Shin, J.-Y., Kwon, Y.N., Bae, J.S., Sung, J.-J. and Hong, Y.-H. (2021). Guillain-Barré Syndrome and Variants following COVID-19 Vaccination: Report of 13 Cases. Frontiers in Neurology, 2022 Jan 27:12:820723. doi: 10.3389/fneur.2021.820723.

[4] Gonçalves, N.P., Mohseni, S., El Soury, M., Ulrichsen, M., Richner, M., Xiao, J., Wood, R.J., Andersen, O.M., Coulson, E.J., Raimondo, S., Murray, S.S. and Vægter, C.B. (2019). Peripheral Nerve Regeneration Is Independent from Schwann Cell p75NTR Expression. Frontiers in Cellular Neuroscience, 2019 May 29:13: 235.doi: 10.3389/fncel.2019.00235.

[5] Gizem Çifter, Gholamreza Hoseinzadeh, Elif Simin Issı, Demet İlhan Algın, Oğuz Osman Erdinç. Twelfth Cranial Nerve Involvement in Guillain-Barre Syndrome: A Case Report. Turk J Neurol. 2020; 26(4): 353-356. doi.10.4274/tnd.2020.60948

[6] Toscano, G., Palmerini, F., Ravaglia, S., Ruiz, L., Invernizzi, P., Cuzzoni, M.G., Franciotta, D., Baldanti, F., Daturi, R., Postorino, P., Cavallini, A. and Micieli, G. (2020). Guillain–Barré Syndrome Associated with SARS-CoV-2. New England Journal of Medicine. 2020; 382:2574-2576 DOI: 10.1056/NEJMc2009191

[7] Kanou, S., Wardeh, L., Govindarajan, S. and Macnay, K. Guillain-Barre Syndrome (GBS) Associated with COVID-19 Infection That Resolved without Treatment in a Child. BMJ Case Reports CP, 15(3). 2022;15: e245455. doi:10.1136/bcr-2021-245455

[8] Röltgen, K. and Boyd, S.D. Antibody and B Cell Responses to SARS-CoV-2 Infection and Vaccination. Cell Host & Microbe,2021 Jul 14;29(7):1063-1075. doi: 10.1016/j.chom.2021.06.009.

[9] Shastri, A., Ahmad Al Aiyan, Kishore, U. and Maria Elena Farrugia. Immune-Mediated Neuropathies: Pathophysiology and Management. International Journal of Molecular Sciences, 24(8). 2023, 24(8), 7288; doi.org/10.3390/ijms24087288

[10] Mahdi Malekpour, Shaghayegh Khanmohammadi, Javad, M., Dorsa Shekouh, Mohammad Reza Rahmanian, Kardeh, S. and Negar Azarpira . COVID-19 as a trigger of Guillain-Barré syndrome: A review of the molecular mechanism. Pubmed,2023 May;11(5): e875. doi: 10.1002/iid3.875.

[11] Felipe Cuspoca, A., Isaac Estrada, P. and Velez-van-Meerbeke, A. Molecular Mimicry of Sars-Cov-2 Spike Protein in The Nervous System: A Bioinformatics Approach. Computational and Structural Biotechnology Journal. 2022:20:6041-6054. doi: 10.1016/j.csbj.2022.10.022.

[12] Rajabally, Y.A. Immunoglobulin and Monoclonal Antibody Therapies in Guillain-Barré Syndrome. Neurotherapeutics,2022 Apr;19(3): 885-896.doi: 10.1007/s13311-022-01253-4.

[13] van den Berg, B., Walgaard, C., Drenthen, J., Fokke, C., Jacobs, B.C. and van Doorn, P.A. (2014). Guillain–Barré syndrome: pathogenesis, diagnosis, Treatment and Prognosis. Nature Reviews Neurology, 10(8), pp.469–482. doi:10.1038/nrneurol.2014.121

[14] van Doorn, P.A., Kuitwaard, K., Walgaard, C., van Koningsveld, R., Ruts, L. and Jacobs, B.C. (2010). IVIG Treatment and Prognosis in Guillain-Barré Syndrome. Journal of Clinical Immunology, 30 Suppl 1(Suppl 1), pp. S74-8. doi: 10.1007/s10875-010-9407-4.

[15] Hughes, R.A., Swan, A.V. and van Doorn, P.A. Intravenous immunoglobulin for Guillain-Barré syndrome. Cochrane Database of Systematic Reviews. 2014 Sep 19;2014(9):CD002063. doi: 10.1002/14651858.CD002063.pub6.

[16] Verboon C, Harbo T, Cornblath DR, et al. Intravenous immunoglobulin treatment for mild Guillain-Barré syndrome: an international observational study. Journal of Neurology, Neurosurgery & Psychiatry 2021 Oct;92(10): 1080-1088.doi: 10.1136/jnnp-2020-325815.

[17] Fuchs, K., Rummler, S., Ries, W., Matthias Helmschrott, Selbach, J., Ernst, F., Morath, C., Adelheid Gauly, Saynab Atiye, Stauss-Grabo, M. and Giefer, M. Performance, Clinical effectiveness, and Safety of Immunoadsorption in a Wide range of indications. Therapeutic Apheresis and Dialysis, 26(1). 2022 Feb;26(1):229-241. doi: 10.1111/1744-9987.13663.

[18] Tzilas, V., Manali, E., Papiris, S. and Bouros, D. Intravenous Immunoglobulin for the Treatment of COVID-19: A Promising Tool. Respiration, 2020;99(12): 10871089.doi:10.1159/000512727

[19] Mayo Clinic (2018). Guillain-Barre syndrome - Diagnosis and treatment - Mayo Clinic. Available from: https://www.mayoclinic.org/diseases-conditions/cancer/diagnosis-treatment/drc-20370594

[20] Mathew J, Sankar P, Varacallo M. Physiology, Blood Plasma. 2023 Apr 24. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan–. PMID: 30285399.

[21] Chevret, S., Hughes, R.A. and Annane, D. Plasma exchange for Guillain-Barré syndrome. Cochrane Database of Systematic Reviews. 27 February 2017 doi.org/10.1002/14651858.CD001798.pub3

[22] Islam, S.S., Ferdous, J., Hoque, A. and Rahman, A. Therapeutic Plasma Exchange in Guillain Barre Syndrome: an Experience of Bangabanhu Sheikh Mujib Medical University, Bangladesh. European Journal of Medical and Health Sciences, Jan 5, 2022 4(1). doi.org/10.24018/ejmed.2022.4.1.937

[23] Duong-Quy S, Huynh-Truong-Anh D, Tran-Xuan Q, Nguyen-Quang T, Nguyen-Thi-Kim T, Nguyen-Chi T, Tran-Ngoc-Anh T, Nguyen-Van-Hoai N, Do-Thi-Thu M, Tang-Thi-Thao T, Bui-Diem K. Bradycardia unresponded to atropin testing was successfully treated with therapeutic plasma exchange in a patient with

severe COVID-19 complicated by Guillain-Barré syndrome: A case report. Frontiers in cardiovascular medicine. 2023 Jan 19; 9:1035896. doi: 10.3389/fcvm.2022.1035896

[24] Nehal, shah and Manisha, shrivastava Role of Physiotherapy in Guillain Barre Syndrome a Narrative Review. ResearchGate5(9):529 Available from https://www.researchgate.net/publication/352438961

[25] Davidson, A.I., Halstead, S.K., Goodfellow, J.A., Chavada, G., Mallik, A., Overell, J., Lunn, M.P., McConnachie, A., van Doorn, P. and Willison, H.J. Inhibition of complement in Guillain-Barré syndrome: the ICA-GBS study. Journal of the Peripheral Nervous System. 2017 Mar;22(1):4-12. doi: 10.1111/jns.12194.

[26] Querol, L. and Lleixà, C. Novel Immunological and Therapeutic Insights in Guillain-Barré Syndrome and CIDP. Neurotherapeutics. 2021 Oct;18(4):2222-2235. doi: 10.1007/s13311-021-01117-3.

[27] Hughes, R.A., Brassington, R., Gunn, A.A. and van Doorn, P.A. Corticosteroids for Guillain-Barré syndrome. Cochrane Database of Systematic Reviews. 24 October 2016 doi: 10.1002/14651858.CD001446.pub5.

[28] Physiotherapy, P. (2020). Guillain-Barré Syndrome Treatment. Propel Physiotherapy. Available from https://propelphysiotherapy.com/neurological/guillain-barre-syndrome-treatment

[29] Connors, C., McNeill, S. and Hrdlicka, H.Occupational and Physical Therapy Strategies for the Rehabilitation of COVID-19 Related Guillain-Barré Syndrome in the Long-Term Acute Care Hospital Setting: A Case Report (Preprint). JMIR Rehabilitation and Assistive Technologies, 2022 Feb 10;9(1): e30794. doi: 10.2196/30794.

[30] Torok, Daniel P., "Physical Therapy Rehabilitation in A Patient with Guillain-Barre Syndrome with Acute Respiratory Failure: A Case Report" (2020). Physical Therapy Scholarly Projects. 694. Available from https://commons.und.edu/pt-grad/694

[31] van den Berg, B., Bunschoten, C., van Doorn, P.A. and Jacobs, B.C. (2013). Mortality in Guillain-Barre syndrome. Neurology, April 30, 2013 issue 80 (18) 1650-1654 doi.org/10.1212/WNL.0b013e3182904fcc.