World Journal of Biology Pharmacy and Health Sciences
eISSN: 2582-5542
Cross Ref DOI: 10.30574/wjbphs
Journal homepage: https://wjbphs.com/

(REVIEW ARTICLE)

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Overview on GBS- Guillain Barre Syndrome

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World Journal of Biology Pharmacy and Health Sciences, 2025, 22(01), 372-382

Publication history: Received on 03 March 2025; revised on 08 April 2025; accepted on 11 April 2025

Article DOI: https://doi.org/10.30574/wjbphs.2025.22.1.0385

Abstract

The acute polyneuropathy known as Guillain-Barré syndrome (GBS) has varying degrees of weakness and peaks in severity in four weeks. Usually, the illness has a monophasic phase and is preceded by an infection. Immunoglobulin (IVIg) and plasma exchange (PE) both works well for GBS. Surprisingly, steroids by themselves don't work. The primary treatment is typically IVIg, mostly for logistical reasons. Miller-Fisher syndrome (MFS), acute motor axonal neuropathy (AMAN), which is more common in Asia and Japan, and acute inflammatory demyelinating polyneuropathy (AIDP), which is the most common form in the western world, are subtypes of GBS. There are overlap syndromes as well (GBS-MFS overlap). A secondary worsening occurs in around 10% of GBS patients within the first 8 weeks following IVIg treatment. It is necessary to administer IVIg repeatedly to address such a treatment-related fluctuation (TRF). Approximately 5% of people who are first diagnosed with GBS end up having acute onset chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) (A-CIDP). It is yet unknown if IVIg is also beneficial for individuals with MFS or GBS patients who are still able to walk (referred to as "mildly affected GBS potients"). GBS is still a serious illness even with modern treatment; roughly 25% of patients need artificial ventilation for a few days to months, 20% are still unable to walk after six months, and 3–10% pass away. Furthermore, a lot of patients experience chronic concerns including pain, exhaustion, or other issues that can last for months or even years. Making a diagnosis can sometimes be quite difficult when pain is present before weakening syndrome (GBS) is a rare appears.

Keywords: GBS; Macrophages; Immunotherapy; EMG

1. Introduction

According to WHO Guillion Barre condition in which a person's Immune system attacks mistakenly the peripheral Nerves. The most prevalent causes of Guillian Barre syndrome are infections with the influenza virus, cytomegalovirus, and campylobacter, a kind of bacteria frequently found in undercooked poultry. A rare but dangerous immune-mediated neuropathy that develops after an infection is Guillain-Barré syndrome (GBS). It is brought on by the autoimmune destruction of peripheral nervous system nerves, which can lead to paralysis. Symptoms include tingling, weakness, and numbness. In the post-polio era, it is the most frequent cause of acute flaccid symmetrical limb paralysis and areflexia. GBS generally encompasses a broad spectrum of clinical symptoms, including muscular weakness, decreased reflexes, and acute inflammatory polyradiculoneuropathy. The pathophysiology of GBS is unclear, however it is believed to be brought on by an abnormal immunological response to infection that damages peripheral neurons. A subset of GBS patients have serum antibodies against gangliosides, which are found in greater quantities in the axolemma and other peripheral nerve components. When the disease is brought on by an outbreak of an infectious disease, the incidence of GBS may rise. The Zika virus outbreaks in French Polynesia in 2013 and Latin America and the Caribbean in 2015–2016 were most recently connected to a rise in GBS diagnoses. Although GBS can affect people of any age, it affects men more often than women and its incidence rises with age. Although there are various different clinical variations and the

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disease's clinical presentation is varied, patients with GBS usually begin with weakness and sensory symptoms in the legs that spread to the arms and cranial muscles. Since GBS was first described in 1859, a great deal of research has been done on its pathophysiology. GBS pathogenesis was first thought to be primarily reliant on the T-cell-mediated immune system. Another important factor in this concept was experimental allergic neuropathy, or EAN, an animal model of GBS. Immunization with PNS myelin proteins (such as P0, P2, and PMP22) or the transfer of sensitized T cells to animals can also cause EAN. It was regarded as an extremely similar model to the AIDP version of GBS. Since EAN won the GBS preclinical research,

It has contributed to several research assessing the T cell mechanism in eliciting the inflammatory response seen in GBS for over 20 years, as well as possible treatment targets in its pathophysiology. However, EAN has received a lot of flak for failing to provide GBS and other peripheral neuropathologies with particular antigenic targets for T cell auto-reactivity. Furthermore, AMAN and other GBS spectrum variations other than AIDP cannot be adequately described by EAN. Both the Th-1 and Th-2 immune responses have been implicated in the pathophysiology of GBS. Th-1 (pro-inflammatory) cytokines, such as IFN-γ, IL-1β, TNF, and IL-6, have been observed to increase during the progressive (acute) phase of GBS and EAN, but the recovery phase of the disease is associated with an increase in TH-2 (anti-inflammatory) cytokines, such as TGF-β and IL-4. For example, an increase in the IFN-γ/IL-4 ratio may indicate an imbalance between Th-1 and Th-2 responses, which appears to play a significant role in the pathophysiology of GBS. It is thought that Th-1 responses initiate the disease by attracting and activating macrophages to the peripheral nerve location. This, in turn, causes nerve injury through either the direct action of macrophages or the in situ release of inflammatory and toxic chemicals. Damage to myelin (demyelination), axons, and Schwann cells are the end results of the Th-1 pathway. However, the Th-2 response appears to act as a suppressor and regulator of the Th-1 pathway, which could explain the resolution impact seen during the GBS and EAN recovery phases. Th-17 cells and their distinctive cytokine product, IL-17, have recently been linked to the pathophysiology of GBS. There is overwhelming evidence that cellular infiltrations, not complement fixation or antibody mediation, are frequently linked to AIP (demyelinating GBS). A different known mechanism for GBS is called molecular mimicry, in which antibodies made in response to pathogenic antigens cross-react and attach to self-antigens on peripheral neurons. The complement cascade is triggered by these antibodies' binding of gangliosides in terminal axons and Ranvier nodes. This process will result in the recruitment of macrophages, the deposition of antibodies and immune complexes in the nodal region, and ultimately a full conduct block. AMAN and MFS mutations are thought to share this complement-dependent pathophysiology.

2. History

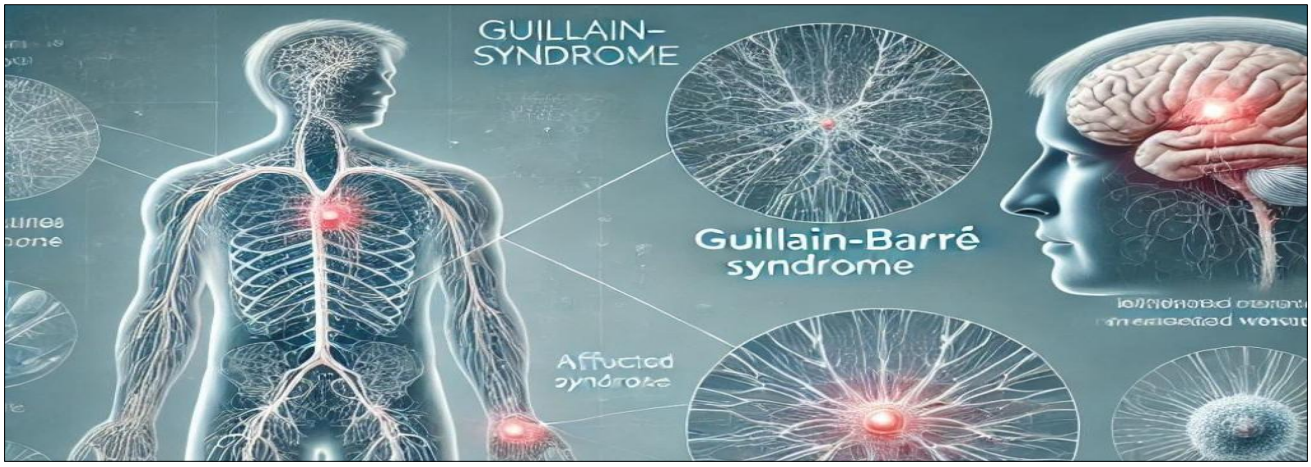

Figure 1 Guillain barre syndrome (GBS)

The French neurologists Guillain Barré and Strohl reported two soldiers who experienced acute paralysis with areflexia and then recovered on their own nearly a century ago. They noted that the illness was distinct from poliomyelitis because to albuminocytological dissociation, which is the combination of elevated protein content and a normal cell count in the CSF. Guillain-Barre syndrome (GBS) was the name given to the combination of these clinical and laboratory characteristics, even though Landry had previously documented comparable patients in 1859. Usually caused by *Campylobacter jejuni*, cytomegalovirus, Epstein-Barr virus, or M. pneumoniae, GBS is a post-infectious illness. Within six weeks of the beginning, more than two-thirds of GBS patients report having respiratory or intestinal infections. Fry reported three fatal cases in postpartum mothers in 1938. Campylobacter is the causative agent in 30–40% of GBS cases.

Due to a prior severe streptococcal infection, this was noteworthy. This was noteworthy because group A streptococcus was previously implicated in severe streptococcal infections in that context. Until the early 1960s, when GBS was identified as a major cause of early newborn sepsis in the USA, reports of neonatal illness from GBS were irregular. It had taken over as the predominant pathogen in the early neonatal period by the 1970s. In the UK, GBS meningitis showed a comparable (although somewhat later) time trend. In several affluent nations, GBS was the leading cause of meningitis and newborn sepsis by the early 1980s.

3. Symptoms

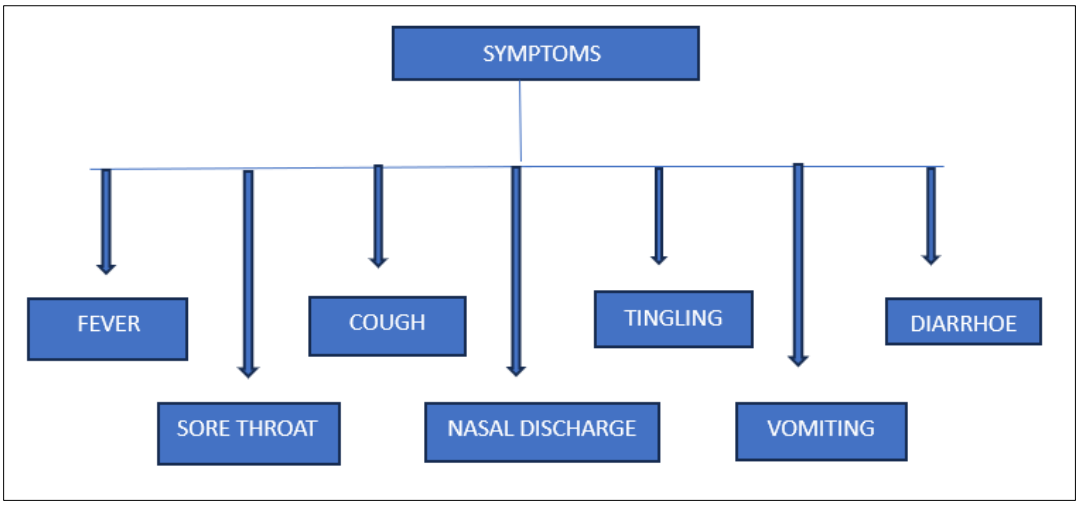

Figure 2 Symptoms of Guillain Barre syndrome

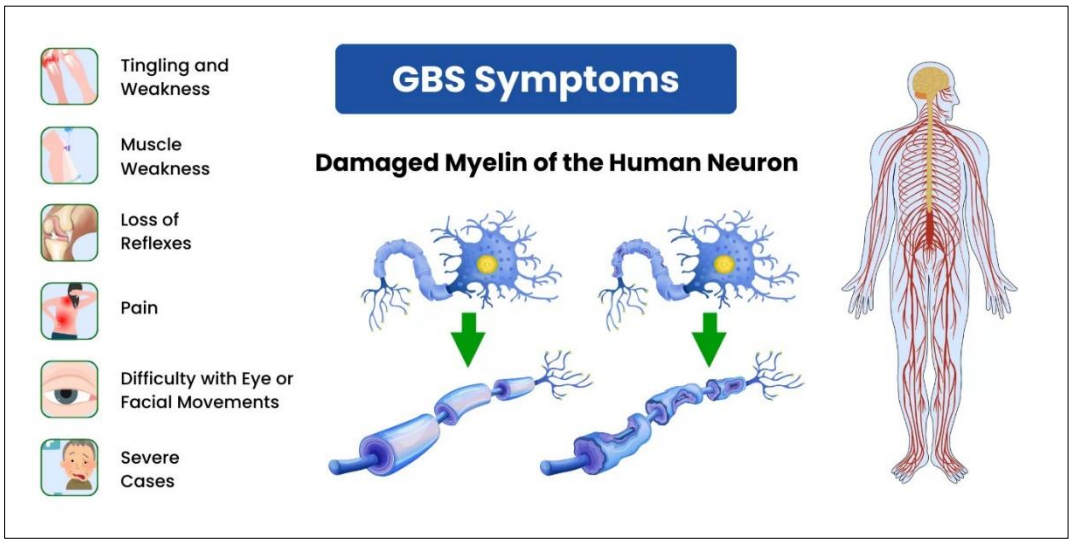

Figure 3 GBS Symptoms

C. jejuni Prior to neuropathic onset, infected patients experienced comparable symptoms: headache, cough, sore throat, and nasal discharge were less frequent, whereas diarrhea and abdominal discomfort were substantial. None of the patients with CMV, EBV, or M. pneumoniae serology had previously reported gastrointestinal symptoms, and there was no discernible correlation between these agents and past symptoms, with the exception of one M. pneumoniae-infected patient who had a history of diarrhea. Out of the 176 patients, 154 (88%) had prior symptoms. Fever was the most commonly reported symptom, followed by cough. The frequency of upper respiratory tract infection prevalence was 62% when combined symptoms of cough, sore throat, and nasal discharge were included. Fifty-one individuals had suffered from gastrointestinal disorders, including vomiting, diarrhea, and digestive pain. Additional symptoms include tinnitus, conjunctival congestion, hoarseness, nausea, lymph nodeswelling, general weariness, joint, neck, or waist pain, and skin itching. Every patient with a history of fever or URTI also had pain, overall exhaustion, or eruption. None of the

patients without antecedent symptoms had ever been admitted, undergone surgery, been seriously injured, or received blood transfusions.

4. Causes

The symptoms of respiratory or digestive illnesses are referred by more than two-thirds of GBS patients within six weeks of the commencement. The causative agent in 30–40% of GBS patients is Campylobacter, and 1/1058 infections are thought to result in GBS. Approximately in 1982, Rhodes and Tattfield. first reported clinical anecdotes linking GBS to *Campylobacter jejuni. Mycoplasma pneumoniae, Haemophilus influenzae, Salmonella species, Mycobacterium bovis, Brucella, Orientia tsutsugamushi, Legionella pneumophila, Bartonella henselae, Helicobacter pylori, Francisella tularensis, Borrelia, Cytomegalovirus, Epstein-Barr virus, varicella-zoster virus, influenza virus, human immunodeficiency virus, parainfluenza virus* type 1, adenovirus, herpes simplex virus, and hepatitis (A, B, and E) are additional infections that may arise prior to GBS. West Nile virus, Zikavirus, Hantavirus, measles, Parvovirus B19, Norovirus, parechovirus, Coxsackieviruses, echovirus, mumps, rubella, polio (wild type 3), dengue, chikungunya, enterovirus (D68, 71), Japanese encephalitis virus.

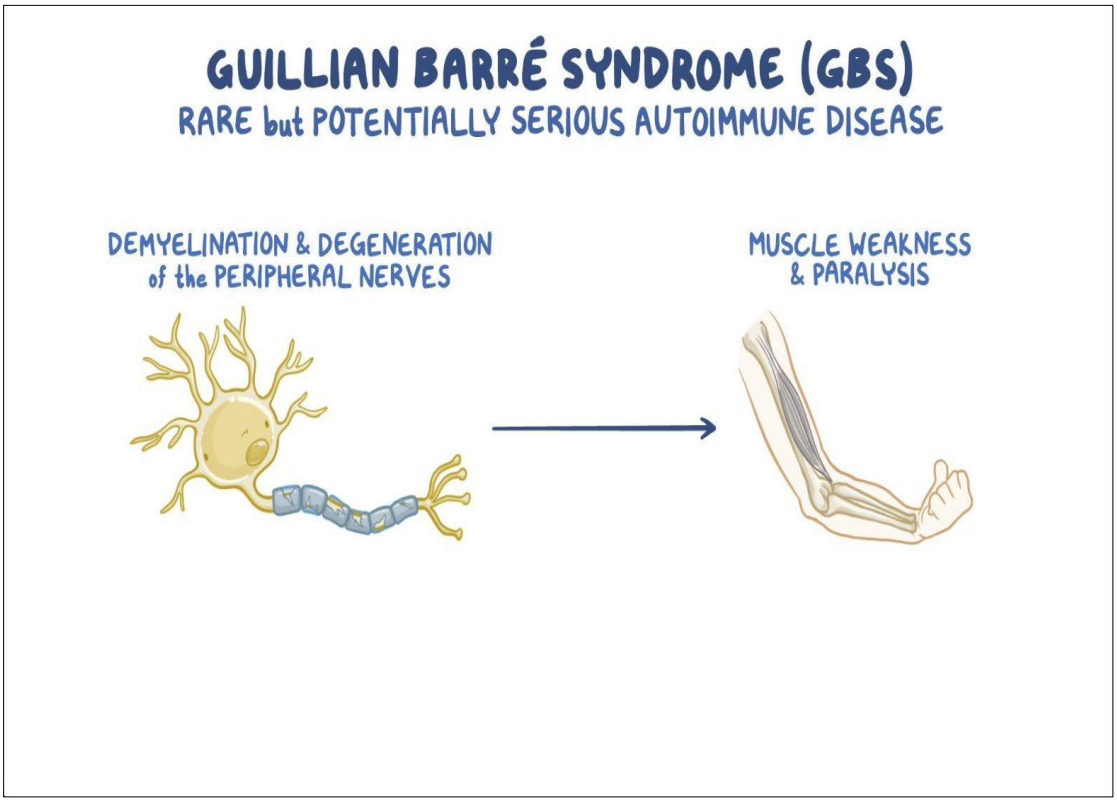

Figure 4 Causes of Guillain Barre Syndrome

Table 1 The proposed link between guilliain barre syndrome and infection from c. jejuni to zika virus

Agent	Epidemiology	Physiopathology mechanism	Pathogen characteristics
Bacterial Campylobacter Jejuni	About 25% of patients had C. jejuni, which has been repeatedly found to be the most common antecedent infection on GBS	Molecular mimicry: cross-reactivity between peripheral nerve gangliosides and C jejuni epitopes The expression of gangliosides is tissue-specific, and the profile of anti-gangliosides determines	Based on the existence of unique LOS loci, C. jejuni epitopes subtypify into seven classes (A-G) and surface LOS. Class B (MFS) and Class A (GBS) loci

		the neurological environment's patterns	
Mycoplasma pneumonia	M. pneumoniae seropositivity in GBS patients ranges significantly (1-25%)	Molecular Mimic	Presence of GMI Pneumon Epitope in M.pnemonia
Influenza Virus	Four to seven cases per 100,000cases Of influenza	Influenza virus does not share structural Homiologies with known gangliosides The mechanism linking Influenza virus and GBS Are poorly understood And probably relate to Increased risk of secondary infection	Influenza A (H1N1), Influenza B virus
HIV	18% had antecedent influenza-like illness and 3.5% had serological evidence of recent infection HIV GBS is a well-known but rare complication of primary HIV infection	Immune mechanisms poorly understood Increased susceptibility to infection, direct action of HIV on nerves, and generation of myelin specific antibodies	Immune mechanisms poorly understood Increased susceptibility to infection, direct action of HIV on nerves, and generation of myelin specific antibodies
Zika Virus	GBS incidence was increased four- to ninefold during 2014–2015 (French Polynesia), suggesting a link to CHIKV infection 2.4/10,000 ZIKV infections AMAN Incidence was 20-fold higher than expected during the time coinciding with the ZIKV epidemic in French Polynesia	A causal relationship between ZIKV and neurological complications are very likely due to molecular mimicry mechanism	Neutralizing antibodies against ZIKV

5. Pathogenesis

Various mechanisms are suggested for AMAN and AIDP. In the first instance, segmental demyelination limited to nerve areas invaded by T cells and macrophages was initially documented by Asbury et al. in 1969 in four patients who passed away from GBS. This led to the realization that active macrophages are primarily responsible for myelin destruction, as they pierce the basement membrane surrounding nerve fibers and ultimately produce demyelination. Additionally, compared to controls, patients with acute GBS have decreased peripheral CD4+ CD25+ T-cell counts, which further supports the idea that T cells play a part in the pathophysiology of GBS. Through activated T cells and MMP9, macrophages target antigens on the surface of Schwann cells or the myelin sheath. Toxic nitric oxide radicals generated by activated macrophages cause Schwann cell damage, which is followed by peripheral nerve invasion. Moreover, in severe cases of AIDP, inflammatory mediators and cells may cause axonal damage through a process known as secondary degeneration. The imbalance of Th1/Th2/Th17/Treg and cytokines that C. jejuni causes is essential for the onset of GBS. Immune-mediated illness progression may be linked to early disease course increase of Th1 cytokines because of neuronal inflammation, but overexpression of Th2Recovery from the illness is aided by the immunological response in the latter stages. Furthermore, Th17 is also harmful, and increased levels of Th22 cells in the blood are linked to illness severity but not to GBS subphenotypes . GBS patients' Th17 and Th22 cells may express a suitable cytokine profile during the acute phase, such as interleukin (IL)-17, IL-22, and others (such as IL-6 and tumor necrosis factor-α), which can exacerbate the inflammatory and autoimmune response and lead to the development of GBS.

Early alterations in the pathophysiology of AMAN include the extension of the Ranvier node with myelin deformation, while macrophages that are on top of it infiltrate the gap between the axon and the Schwann cell, preserving the internodal myelin sheath and Schwann cytoplasm. Some patients may recover quickly because these alterations may be initially reversible. A barrier of axonal conduction or axon terminal degeneration may be linked to AMAN, as evidenced by the faster recovery seen in certain patients.The preserved neuromuscular transmission at axonal-stimulating single-fiber electromyography (EMG) in AMAN has provided experimental evidence that challenges this assumption, suggesting that transmission may be compromised in the motor terminal axons close to the neuromuscular junction.

6. Diagnosis

6.1. Examination of cerebrospinal fluid (CSF)

A CSF analysis is also useful in ruling out other potential reasons of weakness, such as HIV-related radiculitis or Lyme disease, both of which are linked to elevated mononuclear cell counts. When there are certain non-typical characteristics, an elevated total protein in the cerebrospinal fluid (without cellular reactivity) may aid in the diagnosis. However, it is crucial to understand that in the first week following the onset of symptoms, roughly 50% of GBS patients still have a normal CSF protein, and thus the diagnosis is not ruled out in the absence of an elevated CSF protein.

6.2. EMG examination

EMG is especially helpful when it shows signs of a polyneuropathy in clinically not yet involved areas, for example when it shows signs of a polyneuropathy in the arms in patients with weakness only in the legs. It also enables to differentiate GBS in AMAN (axonal features) and AIDP (demyelinating features) Clinical characteristics. When weakness is accompanied by an infection within 1-3 weeks of beginning, the diagnosis of GBS is frequently simple. However, diagnosing certain people might be more challenging, particularly if pain is evident prior to the start of weakness or if the weakness initially only affects the legs. Additionally, in children, pain may at first be mistaken for other conditions such discitis, which could cause a significant delay in diagnosis and possibly be quite problematic since developing respiratory weakening could go unnoticed. As a result, a few characteristics in particular ought to cast doubt on the diagnosis. Before a diagnosis of GBS can be made, a number of illnesses or conditions that could resemble it must be ruled out or made unlikely.

7. Precaution

7.1. General care is crucial for people with Guillain-Barré syndrome (GBS).

To avoid and treat the potentially deadly consequences, patients with GBS in particular require first-rate multidisciplinary treatment. This suggests that infections should be avoided and that cardiac and respiratory function should be closely monitored. Ventilation is necessary for around 25% of patients with significant involvement, thus its necessity must be carefully and frequently assessed. This entails timely transfer to an intensive care unit, when necessary, as well as routine monitoring of respiratory frequency and vital capacity. The likelihood that a certain patient would require mechanical breathing can be predicted using a new, straightforward scale that can be used as soon as the patient is admitted to the hospital. Prophylaxis for deep vein thrombosis, cardiac and hemodynamic monitoring (among other signs of autonomic dysfunction), pain management, management of potential bladder and bowel dysfunction, psychosocial support, and rehabilitation are a few more concerns that require attention early in the course of the disease. Joining a patient organization like the GBS/CIDP Foundation International is beneficial for many patients and their families.

8. Treatment

8.1. Immunotherapy

8.1.1. The advantages of immunotherapy

Plasma exchange (PE) has been demonstrated to be helpful when administered within the first four weeks after beginning; however, the greatest impact was observed when initiated early (within the first two weeks). Five Pes over the course of two weeks, with a total exchange of roughly five plasma volumes, is the standard protocol. Two PE sessions are more beneficial than no PE for patients with mild GBS, according to a French PE trial. Ig is just as effective as PE, according to the 1992 publication of the first RCT on the use of IVIg (0.4 g IVIg/kg bodyweight/day for five days in a

row). Due primaRILy to Its IncrEASed availability and simpliciTY, IVig has supplanted PE aS the recommended treatment in numerous centers since these findings were released. The Cochrane study on IVIg's application to GBSshowed that there was no difference between IVIg and PE withrespect to the improvement in disability grade after 4 weeks, the duration of mechanical ventilation, mortality, or residual disability.

Table 2 allopathy drug therapy

DRUGS	BIOLOGICAL APPROACH	EFFICIENCY	YEAR
Cobra venom factor (CVF)	Complement modulation	Efficient	1987
Eculizumab	Complement modulation	Efficient	2008
Anti-GD3 anti-idiotype mAb (BEC2)	Autoantibody modulation	Efficient	2010
Linomide	Cytokine modulation	Effecient	1997
IFNβ	Cytokine modulation	Effecient	1999

8.2. Homeopathic drug therapy

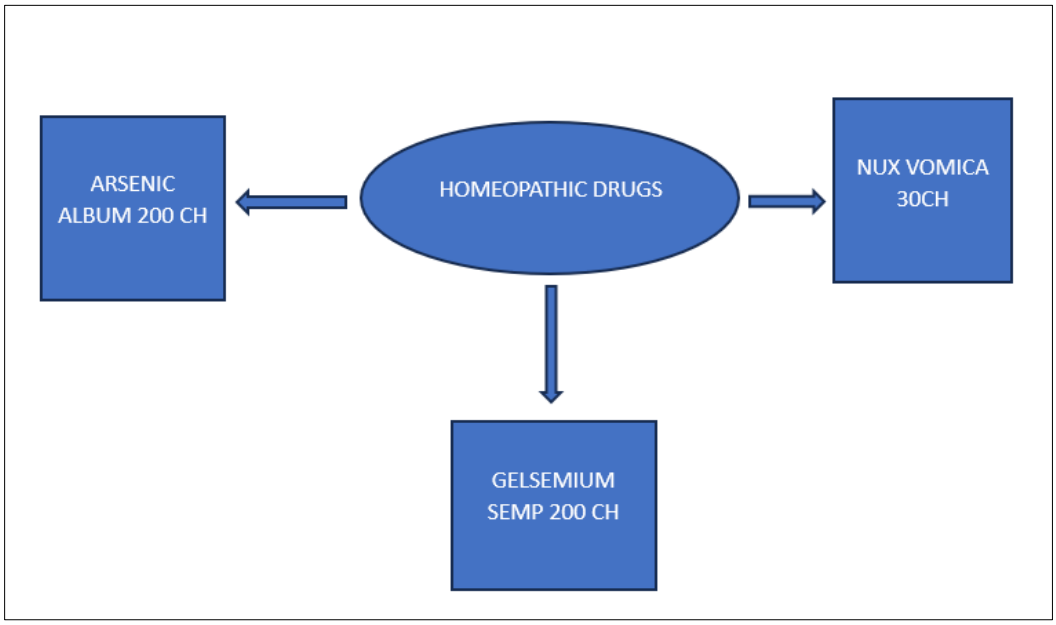

Figure 5 Homeopathic drug used in GBS

9. Epidemiology

The incidence of typical GBS is more common in men than in women (sex ratio 1.5:1), with a range of 0.81 to 1.89 (median 1.11) instances per 100,000 person-years. Age-specific GBS rates are 0.62 cases per 100,000 person-years among individuals aged 0–9 to 2.66 cases per 100,000 person-years among persons aged 80–89. The prevalence and incidence of GBS rise with age. elderly people. With seasonal variation and a peak in May, Bangladesh had the highest crude incidence rate of GBS (2.5 per 100,000 person-years), whereas Brazil had the lowest (0.40 per 100,000 person-years). There is little information available on the epidemiology of the AMAN subphenotype of GBS, and the frequency according to electrodiagnostic criteria is highest (65%) in Chinese patients as opposed to 6–7% in North American and European series. It has been proposed that a higher incidence of diarrhea and inadequate hygienic facilities are associated with a higher prevalence of AMAN. Particularly in cases of AMAN group and Bickerstaff's brain stem encephalitis requiring mechanical ventilation, which account for 4% of GBS cases in Japan, 6% in India, and 11% in Bangladesh, the severity of GBS cases also shows varying prevalence rates in different regions, with China having the highest prevalence rates compared to Europe and the USA.

Table 3 Patient reviews in all over world of Guillain Barre Syndrome

Author	Yearly incidence (/100000)	Country
Deceuninck	0.81	Canada
Winner and Evans	1.1	England
Govoni	1.89	Italy
Bogliun and Beghi	1.55	Italy
Chiò	1.44	Italy
Sedano	1.03	Spain
Aladro-Benito	1.04	Spain
Cuadrado	0.85	Spain
Cuadrado	1.25	Spain
Cheng	1.63	Sweden
Beghi	1.68	USA

10. Future prospect

Since the prognosis for a sizable population of GBS patients is dire, new therapeutic alternatives are required. far from good, still. A second IVIg treatment for patients with a bad prognosis could be an option during the acute period. Both the international second-dose IVIg study (I-SID-GBS) and the SIDS-GBS RCT are underway in the Netherlands.

In the very early stages of GBS, drugs that disrupt complement activation may be appealing candidates for testing, according to recent experiments. With improved accuracy in predicting patient outcomes, new medications such as eculizumab or other regimens may be explored, particularly in a limited GBS population with a bad prognosis. A more individualized approach to treatment may result from concentrating on the pathophysiological effects of treatment, such as researching the mechanism of action of IVIg, after it is demonstrated that certain patients need different IVIg dosages or treatment plans. In uncommon diseases in particular, it typically takes a long time to enroll enough patients in treatment trials.

11. Conclusion

Clinical and immunological patterns that are not always dependent on infection by a common trigger pathogen may be indicated by antecedent symptoms in GBS and kindred illnesses. In a complex group of GBS patients, determining antecedent symptoms may be useful in identifying order, even though it does not always identify individual infections. On the basis of earlier research on the genesis, pathophysiology, and therapy of GBS have been examined. The most common factor that predisposes people to developing GBS is viral infections. For those patients who are at risk, appropriate interventions should be provided.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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