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Clinical Accent and Outcomes of the Guillain - Barre Syndrome (Acute Inflammatory Demyelinating Polyradiculoneuropathy)

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Abstract: ***A polyradiculoneuropathy autoimmune disease called Guillain - Barré syndrome (GBS) is characterized by severe inflammation that damages the peripheral nervous system in a manner that progresses quickly and is primarily seen clinically as muscle weakness. At least 18 of the nation's 24 departments and one constitutional province have recorded at least one incidence of Guillain - Barre Syndrome, according to government records. In response to the unprecedented rise in Guillain - Barre Syndrome, Peruvian authorities announced a 90 - Days nationwide sanitary emergency on July 11, 2023. GBS is now the most frequent cause of acute flaccid paralysis in affluent nations. GBS is still a serious condition despite better detection and care. Anti - GM1 and anti - GQ1B antibodies have been identified as those that attack and harm peripheral neurons or neuromuscular junctions, respectively. Prior research has suggested that the gastrointestinal infection - causing bacteria Campylobacter jejuni predisposes patients to developing GBS. There are multiple subtypes of GBS, but only four of them, acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN), and acute motor, require distinct treatments. Because the subtypes of sensory axonal neuropathy (AMSAN) and Miller - Fisher Syndrome (MFS) differ in their severity and course of treatment. This review seeks to help healthcare professionals better understand GBS and to spread a safety message about the disease.***

Keywords: Guillain - Barre syndrome, Campylobacter jejuni, Polyradiculoneuropathy, Plasmapheresis

1. Introduction

Guillain - Barre Syndrome is a neurological disorder characterized by an unusual immune response that incorrectly assaults the nerve system, according to the National Institute of Neurological Disorder and Stroke (NIK). GBS symptoms may appear gradually over a period of hours, days, or weeks, finally incapacitating some muscles. It was first described in 1916 by two French doctors, Georges Guillain and Jean Alexandre Barré, who gave it their names. Frenchman Jean Baptiste Octave Landry de thé zillat wrote the greatest account of "ascending paralysis" in 1859. [1, 2] GBS is typically brought on by a bacterial or viral illness. Rarely do viral or bacterial components resemble proteins in the body. This causes the immune system to become confused and begin attacking the body. GBS is caused by the immune system attacking the nerves. Numerous antecedent infections have been discovered, including Epstein - Barr virus, Campylobacter jejuni, Cytomegalovirus (CMV), Mycoplasma pneumonia, and Cytomegalovirus (CMV). Parturition and immunization have both been linked to GBS. Campylobacter jejuni infection and the emergence of GBS are linked, according to epidemiological research conducted in numerous nations. The most typical sickness that precedes GBS in individuals is Campylobacter jejuni infection, which is thought to affect between 25 to 40 percent of GBS patients globally 1 to 3 weeks before developing the illness. In GBS patients, polymerase chain reaction seems to be a sensitive method of identifying an earlier C. jejuni infection. [3, 4, 5] Although IVIG and plasma exchange (PE) have been shown to be successful treatments for GBS [6, 7, 8] many patients still have a poor prognosis and long - term effects include persistent discomfort, severe long - term tiredness syndrome, and impaired mobility. [9]

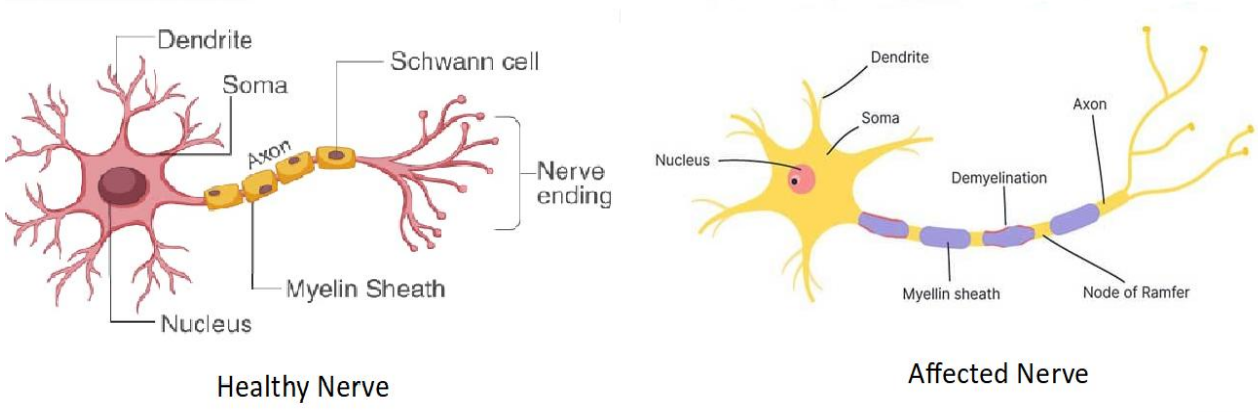
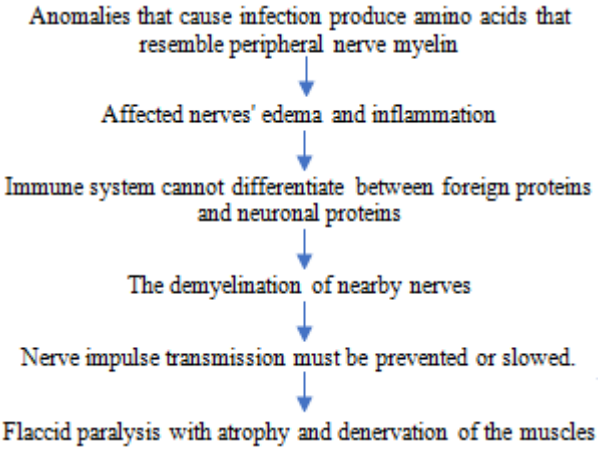


Figure 1: Healthy and affected nerve with Guillain - Barre Syndrome

Pathogenesis:

Although the precise pathophysiology of GBS is not yet fully understood, immunologic processes cause GBS to manifest. As a predisposing bacterial or viral illness, most frequently an upper respiratory tract infection or gastroenteritis, GBS is thought to be an autoimmune disease. [10, 11] According to estimates, infections have a role in the onset of GBS because examinations conducted in the past revealed that 70% of GBS patients had a history of infections. [12] At least one - third of these infections are caused by C. jejuni. [13, 14, 15] Cytomegalovirus, Epstein - Barr virus, Mycoplasma pneumonia, Haemophilus influenzae, and influenza virus are other microorganisms that cause GBS - related antecedent infections. [13, 14, 16] earlier demonstrated this by demonstrating how the lipooligosaccharide that is widely present in the structure of campylobacter jejuni and the gangliosides located within peripheral nerves share comparable molecular structures. [17] GBS is believed to be brought on through molecular mimicry. The production of antibodies that cross react with particular gangliosides, which are not formed during uncomplicated C. jejuni gastroenteritis, is a crucial stage in GBS pathogenesis after C. jejuni infection. [18, 19] Cross reactive antibody production, on the other hand, is only induced in vulnerable individuals. [18] Antibodies that cross - react with several gangliosides have been identified in GBS patients. [13, 20, 21, 22] Some antibody specificities are linked to specific GBS subtypes and neurological impairments, reflecting the distribution of various gangliosides in human peripheral nerves. Different regions of the peripheral nervous system are attacked by antibodies that concurrently develop against the host gangliosides. GM1 and GQ1B antibodies have been identified as two of the reported antibodies that attack and harm either neuromuscular junctions or peripheral neurons. [23, 24] Additionally, it has been discovered that anti - GD1a antibodies in patients bind to the neuromuscular junction, the nodes of Ranvier of the peripheral nerves, and the paranodal myelin of the afflicted neurons. [25, 26] As was already mentioned, it has been discovered that specific antibodies may predispose individuals to particular GBS variations and clinical symptoms. For instance, it has been shown that anti - GM1 antibodies predispose to the development of the form of axonal motor neuropathy whereas anti - GQ1B antibodies have been linked to Miller - Fisher syndrome in the past. [27, 28] These antibodies should only be taken into consideration for confirmation of the evaluation and diagnosis because their validity, including both specificity and sensitivity in detection and identification of the various variations, remains poor. The tendency to create cross reactive, carbohydrate - targeted antibodies may also be a patient - related feature that influences the development of GBS following a C. jejuni infection. The fact that GBS has a relapse rate of 5%, which is obviously higher than would be predicted by chance, lends weight to this concept. [29] GBS development is significantly influenced by the initial pathogen - host interaction. Siglec - 7 (sialic acid - binding immunoglobulin - like lectin 7) is bound by C. jejunilipo - oligosaccharides, which then stimulate dendritic cells via CD14 and Toll - like receptor 4. TNF and type 1 interferon, which are both produced by these dendritic cells and encourage B cell growth. [19, 30, 31] Genetic variants might have an impact on this immunological activation, but up to now, genetic influences have only been examined in limited patient populations. Unexpectedly, a meta - analysis discovered a weak correlation between GBS and a specific TNF variation. [32] Additionally, it has been established that there is a link between polymorphisms in the MBL2 gene, which codes for the mannose - binding protein C, and the severity and outcome of GBS. [33] To determine the significance of host factors in the etiology of GBS, future genome - wide association studies in sizable, adequately controlled cohorts will be necessary.

Phathophysiology of GBS



Subtypes of GBS:

Axonal forms, variants based on particular fibre types involved (sensory or autonomic), and MFS are examples of variations that are frequently identified. Additionally, there are variations with a regional or notably lopsided distribution. [34] There are several known subtypes of GBS, each with unique clinical and pathophysiology characteristics:

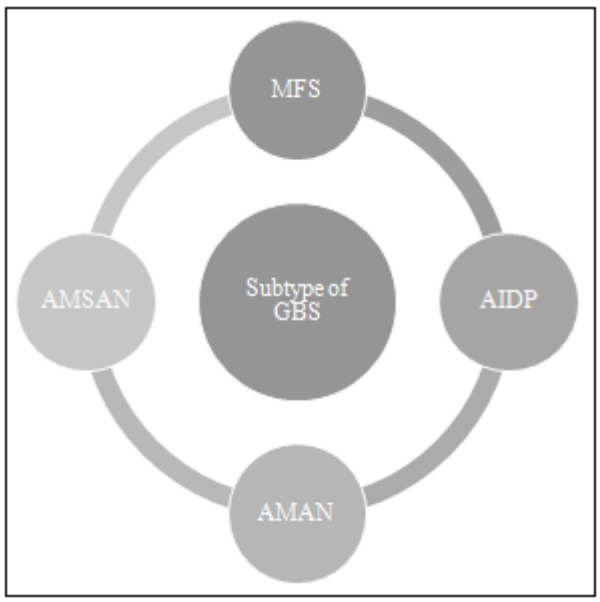


Figure 2: Subtypes of Guillain - Barre Syndrome (GBS)

1) Acute Inflammatory Demyelinating Polyneuropathy (AIDP)

The most prevalent type, known as Acute Inflammatory Demyelinating Polyneuropathy (AIDP), affects 85–90% of patients and is pathologically characterized by demyelination, lymphocytic infiltration, and macrophage - mediated removal of myelin. Clinical signs include areflexia and symmetrical ascending motor weakening. In severe cases, axonal damage could develop later. Antibody binding and complement fixation occur after AIDP - induced injury to nerve terminal axons. The breakdown of the terminal axonal cytoskeleton and mitochondrial damage are the main effects of complement pathway activation, which also results in the development of membrane attack complexes (MAC). [35]

2) Acute motor Axonal Neuropathy (AMAN)

Acute motor axonal neuropathy (AMAN) is more prevalent in young people and during the summer in China and Japan. It has a connection to prior Campylobacter jejuni infection. [36, 37, 38]. The pathogenic process in AMAN includes macrophage invasion, inflammation, binding of antibodies to ganglioside antigens on the axon cell membrane, and axonal destruction. [35]

3) Miller Fisher Syndrome (MFS)

Ataxia, areflexia, and ophthalmoplegia are symptoms of Miller Fisher syndrome (MFS). Leg weakness may occur in 25% of individuals. There haven't been many pathological investigations of MFS, however nerve root demyelination has been proven. The activation of anti - GQ1b and anti - GT1a antibodies that target the oculomotor and bulbar nerves, which are believed to have relatively high GQ1b and GT1a ganglioside densities, distinguishes MFS from AIDP or acute motor axonal neuropathy. [35, 39]

Table 1: GBS subtypes, including symptoms and disease progression [40, 11, 1]

Sr. No.	Subtypes	Symptoms	Disease Progression	Antibodies
1	AIDP	Axonal injury and motor inflammatory demyelination.	Intact myelin sheaths are invaded by macrophages, which disrobe the axons.	Various
2	AMAN	Participation of the motor, respiratory, and main axonal systems.	Invading macrophages leave the myelin sheath intact by inserting between the axon and the surrounding Schwann - cell axolemma at the nodes of Ranvier.	GM1a, GM1b GD1a GalNAc - GD1a
3	AMSAN	Respiratory dysfunction, sensory and motor problems, and primary axonal degeneration with prognosis.	ventral and dorsal roots are also involved, similar to AMAN.	GM1, GD1a
4	MFS	Areflexia, sensory ataxia, and ophthalmoplegia.	abnormality in sensory conduction, involvement of cranial nerve proteins. increase of a certain type of antiganglioside antibody.	GQ1b, GT1a

2. Diagnosis

Areflexia and progressive weakness in both the upper and lower extremities over the course of four weeks are necessary for a diagnosis. CSF analysis and electrodiagnostic testing are examples of supportive auxiliary GBS testing. The National Institute of Neurological Disorders and Stroke (NINDS) created the two sets of diagnostic criteria for GBS that are most frequently used in 1978 (and 1990, respectively). [41, 42] The following section goes into greater detail about the function auxiliary investigations have in confirming a GBS diagnosis.

1) Laboratory investigations:

Laboratory testing is based on the differential diagnosis for each patient, but in general, all patients with suspected GBS will undergo complete blood counts as well as tests for glucose, electrolytes, renal function, and liver enzymes. Further specific tests may be performed with the goal of excluding other diseases that can mimic GBS. Testing for prior infections does not typically contribute to the diagnosis of GBS but can provide crucial epidemiological information during infectious disease outbreaks, as was seen in previous outbreaks of Zika virus and C. jejuni infection. [43, 44] Antiganglioside antibody serum levels have limited diagnostic relevance and rely on the assay. Even when the diagnosis is unclear, a positive test result can be helpful, while a negative test result does not necessarily rule out GBS. [45] Since anti - GQ1b antibodies are present in up to 90% of MFS patients [46], they are more useful for diagnosing MFS than they are for diagnosing classic GBS or other variations. We advise against waiting for the results of an antibody test before beginning treatment when GBS is suspected.

2) Cerebrospinal fluid examination:

A patient is first being evaluated, a CSF test should be done primarily to rule out reasons of weakness other than GBS. Combining an increased CSF protein level with a normal CSF cell count, or albumino - cytological dissociation, is the hallmark GBS result. [47] However, in the first week following the commencement of the condition, 30–50% of patients and 10–30% of patients, respectively, have normal protein levels. [48, 49, 50, 51] As a result, normal CSF protein levels do not exclude a GBS diagnosis. Significant pleocytosis (>50 cells/l) raises the possibility of further illnesses such leptomeningeal cancer or inflammatory or viral diseases of the spinal cord or nerve roots. Even while mild pleocytosis (10–50 cells/l) is compatible with GBS, physicians should still evaluate other diagnosis, like infectious causes of polyradiculitis. [48, 49]

3) Electrodiagnostic studies:

GBS can be diagnosed without electrodiagnostic tests. However, given their value in bolstering the diagnosis, we advise having these studies done whenever possible. Electrophysiological testing on GBS patients typically reveals a sensorimotor polyradiculoneuropathy or

polyneuropathy, which is manifested by aberrant temporal dispersion, lower conduction velocities, reduced sensory and motor evoked amplitudes, and/or partial motor conduction blocks. [52, 53] A 'sural sparing pattern', which is typical for GBS, is characterized by normal sural sensory nerve action potentials but aberrant or non - existent median and ulnar sensory nerve action potentials. [52, 53] When taken early in the illness course within a week of the onset of symptoms or in patients with initially proximal weakness, moderate disease, sluggish progression, or clinical variations, electrophysiological data may, nevertheless, be normal. [54, 55, 56] A second electrodiagnostic examination two to three weeks later may be beneficial for these patients. Results of electrodiagnostic investigations in patients with MFS are often normal or simply show a lower amplitude of sensory nerve action potentials. [57, 58] AMAN, AMSAN, and AIDP are the three electrophysiological subtypes of classical GBS that can be distinguished using electrodiagnostic testing. There are numerous lists of electrodiagnostic standards that are intended to categorize patients into these various electrophysiological subtypes based on the presence of particular electrodiagnostic traits in at least two motor nerves. On which set of standards the electrophysiological subtypes are best defined, there is still no universal agreement. [54, 44, 59]

Management Strategies and Treatment For GBS Patient:
GBS patients who are symptomatic but stable and able to walk unassisted for more than 5 m can be treated conservatively at outlying locations. However, if they are still in the first week after the disease's onset, they should be monitored for disease development. Variations in blood pressure and heart rate, as well as any clinical symptoms of respiratory failure, should be methodically and carefully tracked. Keep an eye out for ileus clinical symptoms. When any of these symptoms are noticed, the patient should be sent right away to specialized facilities for further therapy. Although there is no known cure for Guillain - Barre Syndrome, two therapies, intravenous immunoglobulin therapy and plasma exchange, can lessen the severity of the condition.

1) Intravenous Immunoglobulin Therapy:
Immunoglobulin, a protein that the immune system normally produces to fight infection - causing organisms, is administered intravenously as part of this treatment. When given within two weeks of the start of symptoms, it is most helpful. IVIg is superior to plasma exchange in a number of ways. It has fewer adverse effects, is more readily accessible, and requires less labour. By inhibiting Fc receptors, IVIg, which is made up of pooled donor IgG antibodies, may lessen the severity of autoimmune inflammation in GBS. IgA deficiency (linked to allergic reactions to blood products) and prior anaphylactic reactions to IVIg are among the contraindications to IVIg. IVIg side effects include nausea, headaches, fluid overload, abnormal liver function tests, venous thromboembolism, acute renal failure, and anaphylaxis. These effects can be moderate or severe. There is no proof that additional rounds of therapy are helpful. [35, 40, 60, 61]

2) Plasma Exchange Therapy (Plasmapheresis):
Using a catheter, a bit of blood is extracted for this therapy, the plasma is removed, and the blood is then returned. It is most effective when started within a week of the commencement of symptoms, but it can still be helpful up to thirty days afterwards. [40] Depending on the severity of the condition, plasma exchange has been successfully employed in mild, moderate, and severe GBS patients. Blood must flow through an extracorporeal cell separator in order to exchange plasma. The human albumin solution or FFP is used to replenish the blood's plasma fraction. The process involves the administration of anticoagulants. Plasma exchange attempts to get rid of antibodies linked to the underlying autoimmune response. Plasma exchange is contraindicated in cases of coagulopathy, severe sepsis, haemodynamic instability, and shock. Included in the side effects, which range in severity from mild to severe, are nausea, vomiting, diarrhoea, fevers, coagulopathy, immuno suppression, hypocalcaemia due to citrate usage, and difficulties with lines. [35, 62, 63] Complications were seen in the PE group slightly more in the IVIg group. Hypotension, septicemia, pneumonia, irregular clotting, and hypocalcemia are among the serious side effects of PE. PE is not recommended in cases of severe hemostatic problems, unstable cardiovascular status, active infection, or pregnancy. In addition to these therapies, a particular treatment is required to manage the many problems that can arise during paralysis. Some patients may endure persistent weakness or long - term problems even after fully recovering with GBS.

3. Conclusion

Due to its rapid and unanticipated onset, Guillain - Barré Syndrome can be a severe condition. For patients, adjusting to unexpected paralysis and needing assistance with daily tasks from others can be extremely challenging. Therefore, raising awareness of this disease among patients and medical professionals will undoubtedly assist to improve the existing state of care. We have examined the results of earlier investigations on the pathogenesis, subtypes, and treatment of GBS. There are numerous variations with various symptoms and pathophysiology. In terms of illness management, plasma exchange and IVIG continue to be the most important and effective strategies. Equally crucial to lowering GBS morbidity and mortality is attentive anticipatory supportive care. We want to use this consensus report as a foundation for the creation of online information resources, training materials, and instructional courses in an effort to further improve the global management of GBS. These materials will be geared for medical professionals, such as clinical neurologists, as well as GBS patients and their families.

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