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AN IN-DEPTH REVIEW OF GUILLAIN-BARRÉ SYNDROME

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ABSTRACT

Guillain-Barré Syndrome (GBS) is a rare but potentially life-threatening autoimmune condition marked by the sudden onset of muscle weakness and, in some cases, paralysis. This syndrome often develops following an infection, particularly of the respiratory or gastrointestinal tract, and is thought to result from a dysregulated immune response in which the body's immune system mistakenly targets the peripheral nervous system. The clinical course of GBS is highly variable, typically presenting with ascending paralysis, sensory changes, and autonomic dysfunction. At the core of its pathophysiology is the demyelination of peripheral nerves, which disrupts normal nerve conduction. Diagnosis is primarily based on clinical findings, with supportive confirmation through lumbar puncture and electrophysiological studies. Although most individuals with GBS recover, the recovery process can be lengthy, and severe cases may lead to permanent disability or even death. Therapeutic interventions, such as intravenous immunoglobulin (IVIg) therapy and plasmapheresis, focus on reducing symptom severity and accelerating recovery.

Keywords: Guillain-Barre syndrome, Weakness, Paralysis, Infection and Immunoglobulin

INTRODUCTION:

Guillain-Barré Syndrome (GBS) is the leading cause of acute paralytic neuropathy, characterized by inflammation of peripheral nerves. This condition typically presents with sudden onset and rapid progression of symmetric muscle weakness, often accompanied by difficulty with ambulation and reduced or absent reflexes. Initially, the weakness is more pronounced in the distal limbs, with patients frequently experiencing neuropathic pain [1-2]. GBS commonly begins as ascending paralysis, starting in the lower limbs and progressing to the upper limbs and face, often leading to the complete loss of deep tendon reflexes. Although the syndrome can vary, there are several well-established subtypes, each with distinct clinical features [3]. While the precise cause of GBS remains unknown, 50–70% of cases are preceded by a respiratory or gastrointestinal infection or another immune-triggering event that prompts an autoimmune attack on the peripheral nerves and spinal roots. The mechanisms by which microbial infections and host factors influence the immune system's shift towards autoimmunity are still poorly understood. Furthermore, the genetic and environmental factors that determine an individual's susceptibility to GBS are not yet fully identified. Given the rapid progression of paralysis, early diagnosis of GBS is critical for effective intervention [4-6]. Timely monitoring, along with supportive care and the initiation of targeted treatments, can significantly improve patient outcomes. This review aims to outline the clinical manifestations, diagnostic criteria, and management strategies for GBS, offering a comprehensive overview of the current understanding and treatment approaches.

EPIDEMIOLOGY:

Guillain-Barré Syndrome (GBS) has emerged as the most frequent cause of acute and sub-acute flaccid paralysis worldwide, particularly following the successful eradication of poliomyelitis. The annual incidence of GBS is estimated at 0.5 to 2 cases per 100,000 individuals, with the likelihood increasing significantly with age [6]. It is notably rare in children under the age of two years and affects men approximately 1.5 times more frequently than women. This gender disparity, while observed globally, requires further exploration to understand its underlying causes. Epidemiological studies have identified several infectious agents associated with the onset of GBS, although definitive associations have been confirmed for only a limited number of pathogens [7]. Among these, Campylobacter jejuni stands out as the most frequently implicated infection, particularly in adults. It is detected in 25–50% of adult GBS cases and shows a higher prevalence in Asian populations. Additional infectious agents linked to GBS include cytomegalovirus, Epstein–Barr virus, influenza A virus, measles, and Mycoplasma pneumoniae. Emerging pathogens, such as enterovirus D68 and Zika virus, have also been implicated. The first documented association between GBS and Zika virus occurred during an outbreak in French Polynesia between October 2013 and April 2014 [10]. This connection was later substantiated during subsequent Zika virus epidemics, where clusters of GBS cases were reported. For instance, Williams *et al*. described an unusual cluster of 10 adult GBS cases that coincided with four pediatric cases of acute flaccid paralysis in South Wales, United Kingdom, over a three-month period from October 2015 to January 2016. These findings underscore the complex interplay between infectious diseases and autoimmune responses leading to GBS [8]. Globally, the burden of GBS varies geographically, influenced by regional variations in pathogen prevalence, healthcare access, and diagnostic capabilities. In high-income countries, infections such as Campylobacter jejuni and cytomegalovirus predominate as triggers, whereas in low- and middle-income countries, the burden may be shaped by additional endemic pathogens. Understanding the epidemiological patterns of GBS is crucial for early identification and management, particularly during outbreaks of associated infections such as Zika virus [9]. The distribution of Guillain-Barré syndrome (GBS) subtypes, specifically acute inflammatory demyelinating polyneuropathy (AIDP) and acute motor axonal neuropathy (AMAN), differs significantly across regions. In North America and Europe, AIDP is the most common form, accounting for 60–80% of cases. Conversely, the prevalence of AMAN shows substantial geographic variation, with rates of 6–7% reported in the UK and Spain, compared to 30–65% in regions such as Asia, Central America, and South America [17-19].

CAUSES:

Infection - Campylobacter Jejuni, a leading global cause of gastroenteritis, is implicated in 30% to 35% of Guillain-Barré Syndrome (GBS) cases, highlighting its significance as a primary infectious trigger. Other pathogens associated with GBS include cytomegalovirus, Mycoplasma pneumoniae, Haemophilus influenzae, Epstein-Barr virus, and HIV. In addition to infectious causes, GBS has been observed in individuals with systemic conditions such as lymphoma, Hodgkin's disease, and systemic lupus erythematosus, with an incidence rate exceeding what could be attributed to chance alone [15].

Vaccinations - vaccinations, while rare, have been historically associated with GBS. The 1976 H1N1 influenza vaccine campaign reported a notable increase in risk, with approximately 1 case per 100,000 individuals vaccinated developing GBS. Subsequent studies showed no such elevated risk in later vaccination efforts. Other vaccines, including those for influenza, rabies, COVID-19, and some bacterial infections, have been linked to sporadic GBS cases [13]. For instance, Hawken *et al*. used simulation models to evaluate the absolute risk associated with seasonal influenza vaccination, incorporating variables such as age, sex, influenza incidence, and vaccine efficacy. Their findings reinforce that while the risk of GBS following vaccination exists, it remains exceedingly low compared to the benefits of immunization in preventing severe disease [14].

Genetic and Environmental factors - The potential role of genetic and environmental factors in GBS is increasingly recognized. Although GBS is not hereditary, specific human leukocyte antigen (HLA) types may predispose individuals to develop the condition, particularly following infections. Environmental exposures, such as contaminated food or water, often leading to Campylobacter jejuni infections, and certain geographical factors, may also influence susceptibility. Genetic factors may also influence the immunobiology of Guillain-Barré Syndrome (GBS). A meta-analysis revealed a moderate link between GBS and a polymorphism in the tumor necrosis factor (TNF) gene. Additionally, research has identified a correlation between the severity of GBS and polymorphisms in the mannose-binding lectin (MBL) gene. This gene plays a role in activating the complement system and facilitating the clearance of apoptotic cells through macrophages and dendritic cells [11-12].

Immunization - A recent study on autoreactive T cell immunity in Guillain-Barré Syndrome (GBS) revealed that individuals with acute inflammatory demyelinating polyneuropathy (AIDP) exhibited CD4+ and CD8+ T cells in their blood, cerebrospinal fluid (CSF), and nerve tissue that reacted to myelin protein 0 (P0), myelin protein 2 (P2), or peripheral myelin protein 22 (PMP22). The autoreactive memory CD4+ T cells displayed a proinflammatory phenotype resembling cytotoxic T helper type 1 (TH1) cells and expressed genes linked to autoimmunity. In contrast, this T cell autoreactivity was not observed in individuals with acute motor axonal neuropathy (AMAN), indicating that demyelinating and axonal subtypes of GBS may involve distinct immunopathological processes. The role of antibody-driven Schwann cell damage and the potential involvement of T cells in B cell activation remain areas requiring further investigation [20].

A minority of GBS cases arise following non-infectious triggers like immunizations, surgeries, trauma, or bone marrow transplantation [16].

CLINICAL FEATURES:

In 1916, French neurologists Guillain, Barré, and Strohl identified two soldiers with acute paralysis and areflexia, who recovered spontaneously. Their observations led to the identification of

Guillain-Barré syndrome (GBS), a condition characterized by elevated cerebrospinal fluid (CSF) protein levels without increased cell count. Over time, GBS has been recognized as a spectrum of acute, idiopathic, and typically monophasic peripheral neuropathies. Classic GBS commonly presents with symptoms such as pain, paresthesia, numbness, and rapidly progressing bilateral limb weakness, often beginning in the lower limbs and ascending to affect the arms and facial muscles, potentially leading to bulbar weakness and respiratory issues. In some cases, the weakness starts in the arms or affects both arms and legs simultaneously. Subtypes like Miller Fisher syndrome, which involves cranial nerve weakness, have been described. Symptoms usually peak within 2–4 weeks, though rare cases experience persistent paraparesis. Patients may also have sensory disturbances, ataxia, and autonomic dysfunction, with muscle or radicular pain observed in about 30% of cases. Reflexes may be normal or hyperreflexic in some instances. GBS can progress for up to six weeks, with 20–30% of patients experiencing complications such as respiratory failure, sepsis, cardiac arrhythmias, and autonomic disturbances like sweating abnormalities, gastrointestinal dysmotility, and urinary retention. These symptoms are more common in severe cases, particularly those with respiratory failure. GBS typically starts with subtle prodromal symptoms such as fever, respiratory or gastrointestinal infections, which precede the rapid onset of motor, sensory, and autonomic dysfunction. The characteristic feature of GBS is symmetrical, ascending weakness that often results in flaccid paralysis. Sensory impairments like paresthesia often accompany the motor symptoms. GBS includes several subtypes, such as Acute Inflammatory Demyelinating Polyneuropathy (AIDP), which involves segmental demyelination of peripheral nerves, and Acute Motor Axonal Neuropathy (AMAN) and Acute Motor-Sensory Axonal Neuropathy (AMSAN), which are characterized by axonal damage. Autonomic dysfunction, manifesting as blood pressure fluctuations, arrhythmias, respiratory issues, and gastrointestinal dysmotility, is common and requires close monitoring. The disease typically peaks within four weeks and follows with a plateau and recovery phase. Recovery times vary, ranging from full recovery to persistent disabilities. In pediatric cases, GBS can be more severe, leading to quadriplegia, cranial nerve involvement, respiratory failure, and pronounced autonomic dysfunction. Advanced imaging, including MRI and CSF analysis, aids in assessing disease severity and prognosis. MRI findings, along with elevated CSF protein levels, correlate with the degree of disability, offering important prognostic information. Bickerstaff's Brainstem Encephalitis (BBE), which can overlap with GBS, poses diagnostic challenges, particularly in children, as its clinical features share similarities with GBS, necessitating careful differentiation [21-29].

TYPES OF VARIANTS OF GBS:

Acute Inflammatory Demyelinating Polyneuropathy:

Acute Inflammatory Demyelinating Polyneuropathy (AIDP) is the most prevalent subtype of Guillain-Barré Syndrome (GBS), accounting for approximately 85–90% of cases. This rare autoimmune disorder is characterized by acute inflammation and demyelination of peripheral nerves, leading to rapid and progressive neurological impairment. AIDP primarily targets the myelin sheath of motor and sensory nerves, resulting in symmetrical muscle weakness, diminished reflexes, and sensory disturbances. Initial symptoms often include tingling or paraesthesia in the extremities, typically progressing to ascending muscle weakness that may involve the upper limbs and respiratory muscles in severe cases. The underlying pathology involves immune-mediated destruction of the myelin sheath. This process is often triggered by preceding infections, such as Campylobacter jejuni, Epstein-Barr virus, or cytomegalovirus, which initiate an aberrant immune response through molecular mimicry. Activated macrophages strip myelin, while T-cell infiltration exacerbates inflammation, causing conduction block and impaired signal transmission. In severe cases, axonal damage may occur secondary to prolonged demyelination. The complement system, particularly the membrane attack complex (MAC), plays a role in terminal axonal injury, disrupting the cytoskeleton and mitochondrial function. Diagnosis relies on clinical presentation, supported by electrophysiological studies demonstrating slowed conduction velocities or conduction blocks, and cerebrospinal fluid (CSF) analysis showing elevated protein levels without an increase in white blood cells (albuminocytologic dissociation). Prompt recognition and treatment are crucial, as severe cases can lead to respiratory failure, necessitating mechanical ventilation, and autonomic dysfunction [31-34].

Acute Motor Axonal Neuropathy:

Acute Motor Axonal Neuropathy (AMAN) is a distinct subtype of Guillain-Barré Syndrome (GBS), is characterized by acute flaccid paralysis caused by motor axonal damage with minimal or no sensory involvement. It is predominantly observed in children and young adults, particularly in East Asia, including China and Japan, with a notable seasonal peak in the summer months. AMAN is often triggered by infections, most commonly by

Campylobacter jejuni, though other pathogens like Mycoplasma pneumoniae and various viruses have also been implicated. The pathogenesis of AMAN involves an immune-mediated attack on motor nerve axons, especially at the nodes of Ranvier. This process is driven by molecular mimicry, where microbial antigens resemble gangliosides (e.g., GM1, GD1a, GD1b) present on motor nerve membranes. This mimicry leads to the production of specific IgG antibodies, which activate the complement system, resulting in inflammation, macrophage invasion, axonal damage, and disruption of neuromuscular transmission. Clinically, AMAN presents with a rapid onset of symmetrical weakness, typically starting in the lower limbs and progressing to the upper limbs. In severe cases, cranial nerve involvement and respiratory muscle paralysis may occur. Unlike other GBS variants, sensory symptoms are minimal or absent, and tendon reflexes, though often reduced or absent, may sometimes be preserved. Autonomic dysfunction is less common in AMAN compared to other subtypes. The diagnosis of AMAN is guided by clinical evaluation and supported by ancillary tests. Electrophysiological studies reveal specific patterns of axonal involvement, such as reduced motor nerve conduction velocities and diminished or absent compound muscle action potentials (CMAPs). Cerebrospinal fluid (CSF) analysis may show albuminocytologic dissociation that elevated protein levels without an increase in cell counts, though this finding is not unique to AMAN. The detection of anti-ganglioside antibodies, particularly anti-GM1 and anti-GD1a, provides valuable diagnostic clues [35-37].

Miller Fisher Syndrome (MFS):

Miller Fisher Syndrome (MFS) is a Guillain-Barré Syndrome (GBS) variant marked by the classic triad of ataxia, areflexia, and ophthalmoplegia. Approximately 25% of patients may develop limb weakness. Electrophysiological studies often show sensory conduction failure, and anti-GQ1b antibodies, strongly linked to ophthalmoplegia, are present in about 90% of cases. Pathological evidence, though limited, includes nerve root demyelination. Distinguishing MFS from other GBS variants like acute inflammatory demyelinating polyneuropathy (AIDP) or acute motor axonal neuropathy (AMAN) involves the presence of anti-GQ1b and anti-GT1a antibodies targeting oculomotor and bulbar nerves, which are rich in these gangliosides. Representing 5% of GBS cases, MFS is the second most common variant after AIDP. Diplopia, due to asymmetric ocular motor weakness, is a hallmark of classical MFS, often progressing to complete ophthalmoplegia, with the sixth cranial nerve typically affected first. Ptosis and various forms of nystagmus are common, while pupillary involvement is rare. Ataxia, usually truncal or gait-related, typically follows diplopia but can precede it in one-third of cases. Hypotheses for ataxia pathogenesis include cerebellar dysfunction or selective muscle spindle afferent involvement by anti-GQ1b antibodies. Distal paresthesias, though frequent, do not involve sensory loss. Up to 43% of MFS patients develop descending limb weakness within a week, indicating possible MFS-GBS overlap. Therefore, close monitoring during the first week is critical. CSF analysis often reveals albuminocytological dissociation within three weeks, while anti-GQ1b IgG antibodies peak early, detected in 80–100% of cases. Nerve conduction studies may be normal in one-third of patients or show sensory axonal or demyelinating changes. Brain MRI is usually normal but may occasionally show cranial nerve enhancement. MFS has a favorable prognosis, with most patients recovering within 2–3 months, correlating with declining antibody levels. Ataxia typically resolves first, followed by ophthalmoplegia, while reflex recovery is slower [44-45].

Acute motor and sensory axonal neuropathy:

Acute motor and sensory axonal neuropathy (AMSAN) are a severe subtype of Guillain-Barré syndrome (GBS), characterized by acute onset of motor and sensory deficits due to axonal degeneration affecting peripheral nerves and their roots. Unlike the demyelinating forms of GBS, AMSAN primarily involves direct damage to the axons of motor and sensory nerves without significant demyelination. This form is more commonly reported in Asia and Latin America and is associated with preceding infections, part icularly with Campylobacter jejuni, which triggers an immune-mediated response. The pathological hallmark of AMSAN includes the presence of antibodies, such as anti-ganglioside antibodies (e.g., GM1, GD1a), which target components of the axonal membrane, leading to complement activation and subsequent axonal injury. Clinically, AMSAN presents with rapid progression of symmetrical weakness, severe distal muscle atrophy, and profound sensory loss, often accompanied by diminished or absent reflexes. Sensory deficits may include pain, paresthesias, and loss of proprioception and vibration sense, severely impacting mobility and function. The condition typically progresses rapidly, peaking in severity within days to weeks, and may result in respiratory compromise necessitating mechanical ventilation in severe cases. Nerve conduction studies in AMSAN reveal markedly reduced or absent motor and sensory action potentials, reflecting extensive axonal degeneration, with relatively preserved conduction velocities and latencies, distinguishing it from demyelinating forms. Cerebrospinal fluid analysis often shows albuminocytological dissociation, characterized by elevated protein levels without significant pleocytosis. The prognosis of AMSAN tends to be poorer compared to other GBS subtypes due to the extensive axonal damage, which requires prolonged recovery and may result in residual deficits [38-40].

Pharyngeal–cervical-brachial variant:

The pharyngeal–cervical-brachial (PCB) variant of Guillain-Barré syndrome (GBS) is a rare and distinct subtype characterized by acute weakness primarily affecting the pharyngeal, cervical, and brachial muscles without significant involvement of the lower limbs. It is often mistaken for other neuromuscular disorders due to its unique clinical presentation, which typically includes difficulty swallowing (dysphagia), weakness in neck flexor and extensor muscles, and proximal upper limb weakness, sometimes progressing to respiratory compromise. Unlike classical GBS, PCB variant usually spares the legs, although mild involvement can occur. The pathophysiology of PCB variant is believed to be immune-mediated, similar to other forms of GBS, and involves molecular mimicry triggered by antecedent infections, often respiratory or gastrointestinal, leading to autoantibody production. Notably, anti-GT1a IgG antibodies are frequently detected in patients, reflecting their role in targeting gangliosides expressed in the affected nerves. Diagnosis relies on clinical assessment, electrophysiological studies showing demyelination or axonal changes, and cerebrospinal fluid (CSF) analysis, which may reveal albuminocytological dissociation. Misdiagnosis as myasthenia gravis or brainstem stroke can occur due to overlapping symptoms like bulbar palsy [41-43].

PATHOGENESIS:

Guillain-Barré Syndrome (GBS) is a post-infectious neurological disorder, with approximately two-thirds of patients reporting prior respiratory or gastrointestinal infections. Specific infections can be identified in nearly half of GBS cases, with Campylobacter jejuni responsible for at least one-third. Other notable pathogens include cytomegalovirus, Epstein-Barr virus, Mycoplasma pneumoniae, Haemophilus influenzae, and influenza A virus [12, 46-49]. A notable association has also been observed with hepatitis E virus (HEV); for instance, a study in the Netherlands found HEV in 5% of GBS cases compared to 0.5% in healthy controls. Similarly, 10% of GBS cases in Bangladesh had antecedent HEV infections, confirming its global relevance as a GBS trigger.

Despite these associations, GBS remains rare. Only 1 in 1,000 to 5,000 individuals with C. jejuni enteritis develops GBS within two months, underlining its sporadic nature. However, outbreaks following C. jejuni infections have been reported occasionally. A critical pathogenic mechanism in GBS after C. jejuni infection is the production of antibodies that cross-react with gangliosides in peripheral nerves. These antibodies are generated only in genetically or immunologically susceptible individuals. Furthermore, only specific C. jejuni strains possess lipo-oligosaccharides mimicking human gangliosides, a feature dependent on polymorphic genes and enzymes [50-53]. For example, the Thr51 variant of the cstII gene in C. jejuni is linked to GBS, while the Asn51 variant correlates with Miller Fisher Syndrome (MFS). Patients with GBS often have antibodies against gangliosides like GD1b, GD3, GT1a, and GQ1b, which are associated with clinical features such as ataxia and ophthalmoplegia. In cases related to cytomegalovirus, anti-GM2 antibodies are frequently detected, though these can also appear in uncomplicated infections. Complexes of ganglioside epitopes, located within lipid rafts, may also elicit antibody responses. These antibodies, particularly when targeting ganglioside complexes, may cross-react with C. jejuni lipo-oligosaccharides, further implicating molecular mimicry in GBS pathogenesis [54-56]. Complement activation plays a significant role in nerve damage in GBS. Studies in animal models of acute motor axonal neuropathy (AMAN) have shown complement-induced disruption of the nodal and paranodal structures essential for nerve function. Inhibiting complement activation has been demonstrated to prevent clinical manifestations of antiganglioside-mediated neuropathy. The presence of such antiganglioside antibodies, along with genetic susceptibility, likely explains the 5% relapse rate observed in GBS. Polymorphisms in genes such as TNF and MBL2 have been implicated in disease susceptibility and severity, warranting further research in larger, well-controlled cohorts [57-58]. Vaccination-related GBS is rare but draws public attention. During the 1976 H1N1 influenza vaccination campaign in the USA, the attributable risk was about 1 in 100,000 [59]. In subsequent campaigns, such as in 2009, the risk was lower, with 1.6 excess cases per million vaccinated individuals—comparable to seasonal vaccines. Notably, influenza infection itself carries a 4–7 times higher risk of GBS than vaccination. Current guidelines suggest that influenza vaccination is generally safe for individuals with a history of GBS, provided the onset was not shortly after vaccination and more than three months have elapsed since recovery [60-61].

DIAGNOSIS:

Several diagnostic criteria have been developed to assist clinicians in identifying Guillain-Barré syndrome (GBS). Following the 1976–77 swine flu vaccination campaign, the US National Institute of Neurological Disorders and Stroke (NINDS) established criteria to evaluate whether the incidence of GBS increased post-vaccination. These guidelines were later reviewed and reaffirmed with clarifications. In 2011, the Brighton Collaboration Guillain-Barré Syndrome Working Group introduced case definitions for GBS and Miller Fisher syndrome (MFS) to standardize global data collection for post-vaccination GBS surveillance. Recognizing limited resources in some regions, the Brighton criteria emphasized diagnostic certainty based on available evidence. Both the NINDS and Brighton criteria remain widely utilized. A minimum requirement for diagnosing GBS is symmetrical flaccid weakness with reduced reflexes, in the absence of other explanations [62-63]. The Brighton criteria further provide a separate definition for MFS, requiring the triad of bilateral ophthalmoplegia, ataxia, and reduced reflexes, without limb weakness or central nervous system involvement, to meet Level 3 diagnostic certainty. Higher diagnostic certainty levels for GBS and MFS necessitate a monophasic illness peaking within 28 days, cerebrospinal fluid showing albumin-cytological dissociation, and electrodiagnostic confirmation of neuropathy. Clinically, GBS presents variably. Though not part of formal diagnostic criteria, up to 76% of patients report a preceding illness within four weeks. Weakness patterns in GBS are not limited to limbs and may involve cranial nerves, respiratory muscles, or autonomic functions. Rarely, atypical presentations may serve as the initial indication of GBS [64].

Cerebrospinal fluid analysis:

Cerebrospinal fluid (CSF) analysis is primarily utilized to exclude other potential causes of weakness apart from Guillain-Barré Syndrome (GBS) and should be part of the initial assessment. The characteristic finding in GBS is albumino-cytological dissociation, where CSF protein levels are elevated, but the cell count remains normal [65-66]. However, in the first week after symptom onset, 30–50% of patients may have normal protein levels, and this occurs in 10–30% during the second week. Consequently, a normal protein level does not exclude GBS. Significant pleocytosis (>50 cells/µL) often indicates alternative conditions, such as leptomeningeal malignancies or infectious/inflammatory disorders affecting the spinal cord or nerve roots. While mild pleocytosis (10–50 cells/µL) can occur in GBS, it necessitates consideration of other potential causes, such as infectious polyradiculitis [67].

Electrodiagnostic studies:

Electrodiagnostic studies are not essential for diagnosing Guillain-Barré syndrome (GBS) but are highly recommended when feasible, particularly for atypical cases. These tests often reveal sensorimotor polyradiculoneuropathy or polyneuropathy, characterized by slowed conduction velocities, reduced sensory and motor amplitudes, abnormal temporal dispersion, and/or partial motor conduction blocks. A hallmark feature in GBS is the "sural sparing pattern," where the sural sensory nerve remains unaffected while the median and ulnar sensory nerves show abnormalities or are absent [68-69]. However, electrodiagnostic results may appear normal early in the disease (within the first week) or in cases with proximal weakness, mild symptoms, slow progression, or certain clinical variants. For these patients, repeating the tests after 2–3 weeks can provide more diagnostic clarity. In Miller Fisher syndrome (MFS), findings are typically normal or show reduced sensory nerve action potential amplitudes [70]. Electrodiagnostic studies are also useful in distinguishing between the main GBS subtypes: acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN), and acute motor-sensory axonal neuropathy (AMSAN). Although several diagnostic criteria exist for classifying these subtypes based on motor nerve characteristics, no international consensus has been established. Approximately one-third of patients may not meet the criteria for any subtype and are categorized as "equivocal" or "inexcitable." Repeated testing 3–8 weeks after symptom onset may help classify these cases or reclassify previously defined subtypes, though this practice remains debated [71].

Nerve conduction studies:

Nerve conduction studies (NCS) are valuable for confirming the diagnosis of Guillain-Barré syndrome (GBS) and distinguishing between its axonal and demyelinating subtypes. Early diagnosis of GBS can be challenging, particularly during the initial stages when reflexes are intact or weakness presents atypically, such as in paraparesis [81]. NCS can detect abnormalities in asymptomatic regions, such as the upper limbs, and reveal evidence of peripheral neuropathy or polyradiculopathy, which aids in diagnostic confirmation. Typically, NCS abnormalities peak over two weeks after symptom onset. However, delaying testing for this duration is impractical in acute cases. Although early NCS may produce normal findings, prolonged or absent F-waves are often the first detectable abnormalities. To optimize diagnostic accuracy, NCS should evaluate at least four motor nerves, three sensory nerves, and F-waves. The specific NCS findings depend on the GBS subtype. In acute inflammatory demyelinating polyneuropathy (AIDP), NCS reveals demyelination indicators such as prolonged distal motor latency, reduced conduction velocity, prolonged F-wave latency, temporal dispersion, and conduction block, with the sural sensory potential often preserved [82-83]. Axonal subtypes, including acute motor axonal neuropathy (AMAN) and acute motor-sensory axonal neuropathy (AMSAN), typically show reduced motor and sensory amplitudes without demyelinating features. Sensory nerve studies help distinguish between AMAN and AMSAN. In AMAN, neurophysiological patterns may include transient conduction block or slowing, known as reversible conduction failure, which resolves during recovery and is thought to result from nodal conduction impairment linked to antiganglioside antibodies. These transient abnormalities can mimic demyelination, leading to misdiagnosis as AIDP. Additional demyelinating features may also appear transiently in early axonal GBS. Serial NCS are often necessary to differentiate accurately between AIDP and AMAN. For instance, an Italian study found that 24% of patients initially diagnosed with AIDP were later reclassified as AMAN following serial testing [84-86].

Antiganglioside antibodies:

Antiganglioside antibodies play a role in the pathogenesis of Guillain-Barré syndrome (GBS); however, their utility as a diagnostic tool remains unproven. The low prevalence of specific antibodies limits the negative predictive value of detection tests, meaning a negative result cannot definitively exclude GBS [77-78]. Additionally, these tests have restricted positive predictive value, as antiganglioside antibodies—particularly IgM—isotypes—can also be associated with other conditions. Notable exceptions include anti-GQ1b antibodies, which are detected in over 90% of patients with Miller Fisher syndrome (MFS), and anti-GM1 and anti-GD1a IgG antibodies, commonly found in acute motor axonal neuropathy (AMAN). When validated assays are employed, these specific antibodies may aid in diagnosis [79-80].

Lumbar puncture:

A lumbar puncture is commonly performed in patients with suspected Guillain-Barré Syndrome (GBS), primarily to rule out alternative diagnoses rather than confirm GBS. The characteristic finding in GBS is an elevated protein level with normal cell counts in the cerebrospinal fluid (CSF), a phenomenon known as albuminocytological dissociation. However, this is not universally present, as only 64% of GBS patients exhibit this feature [90]. Initially, elevated CSF protein levels are seen in about 50% of patients within the first three days of symptom onset, rising to approximately 80% after the first week. If CSF cell counts exceed 50 cells/μL, other conditions such as leptomeningeal malignancies, lymphoma, cytomegalovirus radiculitis, HIV-associated polyneuropathy, or poliomyelitis should be considered. A normal CSF protein level generally does not warrant repeated lumbar punctures, as albuminocytological dissociation is not a prerequisite for diagnosis. It is also noteworthy that treatment with high-dose intravenous immunoglobulin (IVIg) can elevate CSF protein levels and cell counts, potentially complicating interpretation during repeat lumbar punctures due to transudation or aseptic meningitis [91].

Magnetic resonance imaging:

Magnetic resonance (MRI) is not routinely used in diagnosing Guillain-Barré syndrome (GBS) but can be valuable in ruling out other conditions, such as brainstem infections, stroke, spinal cord or anterior horn cell inflammation, nerve root compression, or leptomeningeal malignancies. Gadolinium-enhanced MRI may reveal nerve root enhancement, a sensitive but nonspecific indicator of GBS, which can be particularly helpful in diagnosing young children, where clinical and electrophysiological evaluations may be difficult [72-74]. This is especially relevant in distinguishing GBS from acute flaccid myelitis (AFM), a condition with a similar clinical presentation that has been observed in recent outbreaks. However, it is important to note that nerve root enhancement can also occur in a subset of AFM cases. Additionally, ultrasound imaging of peripheral nerves has emerged as a potential diagnostic tool, identifying early cervical nerve root enlargement, suggesting inflammation of spinal roots as an initial pathological feature of GBS. While promising for early diagnosis, this technique requires further validation [75-76].

Children diagnosis of GBS:

The clinical presentation and outcomes of Guillain-Barré Syndrome (GBS) differ between children and adults, making diagnosis in younger children, particularly those under six years of age, more challenging. Pain, difficulty walking, or refusal to walk are the most common initial symptoms in pediatric cases and should prompt suspicion of GBS. However, only about one-third of preschool-aged children receive an accurate diagnosis upon admission. In this age group, GBS is frequently misdiagnosed as meningitis, coxitis, or viral-related malaise, often leading to delays in diagnosis, which can exceed two weeks in some cases. Diagnosing GBS in children is further complicated by substantial pain, which may obscure limb weakness and delay recognition of the condition [87-88]. Although the clinical features and disease progression are generally comparable to those seen in adults, nerve conduction studies, often used for diagnosis, may not be well-tolerated by children. In such instances, diagnostic support can be provided by imaging modalities such as MRI or ultrasound. Despite the challenges, children with GBS generally have favorable outcomes. However, delayed diagnosis and insufficient monitoring may result in severe complications, including emergency intubation or death due to autonomic dysfunction. Early intervention and treatment strategies, similar to those used in adult GBS management, are essential to prevent adverse outcomes [89].

TREATMENT:

The most effective treatments for GBS are immunotherapy with IVIg or plasma exchange, which are generally started when patients are unable to walk independently (GBS Disability Scale score ≥3). Both therapies have immunomodulatory effects, but the precise mechanisms behind their efficacy remain unclear. IVIg may work by inhibiting immune cell activation and ganglioside antibody binding, while plasma exchange is believed to remove harmful antibodies and inflammation mediators [92-95]. Treatment within the first two weeks of weakness onset offers the most significant benefits. Though small-volume plasma exchange is a potential cost-effective alternative, its efficacy needs further validation. In regions with limited resources, small-volume plasma exchange or exchange transfusion could be considered, though this approach lacks large-scale evidence [95-97]. Despite the higher costs, IVIg remains the treatment of choice in many hospitals, especially since it does not require specialized equipment. Immunoabsorption is occasionally used as an alternative to plasma exchange, but no large trials support its superiority. Studies on additional treatments like corticosteroids, interferons, and neurotrophic factors have failed to show beneficial effects. Patients with the Miller Fisher Syndrome (MFS) variant of GBS tend to recover spontaneously, making immunotherapy less necessary. However, treatment with IVIg or plasma exchange remains an option for MFS–GBS overlap cases. Children with GBS are typically treated using the same protocols as adults, given the lack of specific pediatric studies. Neither IVIg nor plasma exchange is contraindicated during pregnancy. However, as plasma exchange requires additional considerations and monitoring, IVIg might be preferred [98-102].

Intravenous immunoglobulin (IVIg) and plasma exchange are both effective treatments for Guillain-Barré Syndrome (GBS), with IVIg being the preferred option due to its easier administration and broader availability. IVIg is typically given at a dose of 0.4 g/kg daily for five days, while plasma exchange involves 200-250 ml plasma/kg body weight over five sessions. Despite both treatments showing similar efficacy, plasma exchange has a higher risk of being discontinued due to complications. Early studies on corticosteroids in GBS have shown no significant benefits, and corticosteroid treatment may even worsen outcomes. Additionally, combining plasma exchange with IVIg does not offer additional advantages compared to either treatment alone [103-107].

CONCLUSION:

Guillain-Barré Syndrome (GBS) is a rare yet severe neurological condition marked by the rapid development of muscle weakness and paralysis, often following an infection. It is important to understand the various forms and subtypes of GBS, such as acute inflammatory demyelinating polyneuropathy (AIDP), Miller Fisher syndrome (MFS), and acute motor axonal neuropathy (AMAN), for accurate diagnosis and treatment planning. Although the exact cause is not fully understood, GBS is commonly triggered by an infection, with immune system abnormalities playing a central role in its development. Prompt diagnosis and treatment, which may include supportive care and immunotherapy, are crucial for improving outcomes. While many patients recover, the disease's variable severity and potential for long-term complications emphasize the need for continued research into its causes and treatment options.

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