INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

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Review Article

Guillain-Barré Syndrome: A Comprehensive Review of Clinical Spectrum, Pathophysiology, Diagnostic Approach, and Advances in Management with an Indian Perspective

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ARTICLE INFO

Published: 23 Nov 2026
Keywords:
Guillain-Barré Syndrome, Acute Flaccid Paralysis, Axonal Neuropathy (AMAN), Nodopathy, Molecular Mimicry, Intravenous Immunoglobulin, Small-Volume Plasma Exchange
DOI:
10.5281/zenodo.24459099

ABSTRACT

Guillain-Barré syndrome (GBS) is an acute immune-mediated polyradiculoneuropathy affecting the peripheral nervous system and remains the leading cause of acute flaccid paralysis worldwide in the post-polio era. It is a clinically heterogeneous disorder comprising several variants, including Acute Inflammatory Demyelinating Polyradiculoneuropathy (AIDP), Acute Motor Axonal Neuropathy (AMAN), Acute Motor Sensory Axonal Neuropathy (AMSAN), and Miller Fisher Syndrome (MFS), each with distinct clinical and electrophysiological characteristics. The syndrome is typically preceded by gastrointestinal or respiratory infections, most commonly caused by Campylobacter jejuni, Cytomegalovirus, Epstein–Barr virus, Zika virus, Dengue virus, or SARS-CoV-2. These infections trigger an aberrant immune response through molecular mimicry, leading to antibody-mediated injury of peripheral nerve gangliosides and subsequent neurological dysfunction. Diagnosis is primarily based on the patient's clinical presentation, supported by cerebrospinal fluid findings of albuminocytological dissociation and electrophysiological nerve conduction studies. Early initiation of disease-modifying therapy with intravenous immunoglobulin (IVIg) or plasma exchange (PLEX) has substantially improved patient outcomes; however, access to timely diagnosis and treatment remains a major challenge in many low- and middle-income countries. In India and other Asian regions, axonal variants occur more frequently than in Western populations and are often associated with greater disease severity and prolonged recovery. This review provides a comprehensive overview of the current understanding of GBS, including its epidemiology, pathophysiology, diagnostic approaches, prognostic models, evolving targeted therapies, critical care management,

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

and the unique epidemiological and therapeutic challenges encountered in the Indian healthcare setting.

INTRODUCTION

METHODS:

A comprehensive literature search was conducted using PubMed/MEDLINE, Scopus, Embase, and Google Scholar to identify relevant articles published up to July 2026. Search terms included "Guillain–Barré syndrome," "AIDP," "AMAN," "diagnosis," "IVIg," "plasma exchange," and "emerging therapies." Original articles, randomized controlled trials, systematic reviews, meta-analyses, and clinical practice guidelines published in English were included. Priority was given to recent, high-quality evidence and landmark studies relevant to the pathophysiology, diagnosis, prognosis, and management of Guillain–Barré syndrome

Introduction & Epidemiological Landscape:

Guillain-Barré syndrome (GBS) is an acute immune-mediated disorder of the peripheral nervous system and stands as the primary cause of non-traumatic acute flaccid neuromuscular paralysis globally following the near-eradication of poliomyelitis [1–2]. GBS is considered a true neurological emergency due to its rapid and sometimes unpredictable progression, which can lead to profound quadriplegia, acute respiratory failure, and severe autonomic instability [4–5]. Epidemiological surveys demonstrate a global annual incidence ranging from 0.81 to 1.89 cases per 100,000 person-years, averaging approximately 1 to 2 cases per 100,000 population annually [32,46]. The incidence displays a linear increase with advancing age, showing approximately a 20% increase for every decade of life, thus occurring more frequently in older adults [10,32,46]. Additionally, GBS exhibits a consistent slight male predominance across all age groups, with an overall male-to-female ratio of approximately 1.5:1 [10,32,46].

Although GBS occurs sporadically throughout the year, transient epidemic peaks frequently coincide with local outbreaks of antecedent infectious triggers [19,31,44–45]. The disease is characterized by hyperacute or subacute onset of symmetrical progressive limb weakness, hyporeflexia or areflexia, and variable cranial nerve, autonomic, and respiratory muscle involvement [7,13,18]. Maximum functional disability (disease nadir) is reached within 4 weeks of symptom onset, with over 80% of affected patients reaching nadir within 2 weeks [7,13,18]. Despite major historical advances in neuro-intensive care and immunomodulatory treatments, GBS remains associated with an overall mortality rate of 3% to 7% [9,37]. Furthermore, approximately 20% of affected individuals continue to experience significant residual disability, chronic fatigue, neuropathic pain, or permanent functional impairment at 1-year post-disease onset [27–28].

Indian Perspective: Epidemiological & Phenotypic Profile:

In India and broader South/East Asian regions, the epidemiological and phenotypic profile of GBS differs markedly from North American and European cohorts [17,31]. While demyelinating GBS (AIDP) predominates in Western nations (accounting for 80% to 90% of cases), Indian hospital-based studies report a strikingly higher prevalence of primary axonal variants—specifically Acute Motor Axonal Neuropathy (AMAN) and Acute Motor Sensory Axonal Neuropathy (AMSAN)—comprising 40% to 60% of GBS presentations [16–17,33]. Axonal forms in India are frequently linked to antecedent Campylobacter jejuni gastroenteritis, displaying pronounced seasonal clustering during late summer and monsoon months [17,44–45,49]. Clinically, Indian patients presenting with axonal forms often exhibit higher initial MRC disability scores, increased incidence of early respiratory compromise, and a more prolonged or incomplete recovery trajectory [16–17,33]. Delayed hospital presentation due to regional referral logistics and financial constraints in accessing tertiary neuro-intensive care further impacts overall clinical trajectories and clinical outcomes in the country [6,17,37].

Antecedent Infectious Triggers & Etiology

In approximately 60% to 70% of GBS cases, the neurological illness is preceded by 1 to 4 weeks by an overt gastrointestinal or upper respiratory tract infection [8,32]. Antecedent microbial pathogens stimulate an aberrant host immune response that cross-reacts with

structural glycolipids and gangliosides on peripheral nerve membranes through molecular mimicry [28–29].

Campylobacter jejuni: Identified as the single most common preceding pathogen, present in 25% to 50% of adult GBS cases worldwide [37,49]. C. jejuni enteritis is strongly associated with the AMAN and AMSAN subtypes, high-affinity IgG anti-GM1 and anti-GD1a autoantibodies, pure motor weakness, and acute axonal injury [20,27,37,50].

- **Cytomegalovirus (CMV):** Identified in 10% to 15% of GBS cases globally [32]. CMV infection is strongly linked to the demyelinating (AIDP) phenotype, prominent sensory impairment, severe cranial nerve involvement (especially facial diplegia), and delayed clinical recovery [32].
- **Epstein–Barr Virus (EBV) & Mycoplasma pneumonia:** Common antecedent respiratory infections primarily associated with demyelinating polyneuropathy in children and young adults [32,34].
- **Influenza & Arboviruses (Zika, Dengue):** Arboviral infections have been demonstrated to cause large surge outbreaks of GBS in tropical and subtropical regions [19,31].
- **SARS-CoV-2 & COVID-19 Vaccination:** Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and certain viral-vector COVID-19 vaccines have been identified as rare triggers, necessitating heightened post-viral clinical surveillance [7,35–36].

Pathophysiology and Immunopathogenesis:

The central mechanism involved in the pathogenesis of GBS is molecular mimicry, in which microbial surface antigens resemble structural components of host peripheral nerve glycolipids and gangliosides, resulting in an aberrant immune response against peripheral nerves [12,15]. Gangliosides are sialic acid-containing glycosphingolipids that are highly concentrated within human neural membranes, particularly at the nodes of Ranvier, paranodal axolemma, and Schwann cell membranes, where they play important roles in nerve function and signal transmission [14,50].

During Campylobacter jejuni enteritis, certain bacterial strains express lipooligosaccharides (LOS) containing tetrasaccharide structures that closely resemble the terminal sugar components of human gangliosides, including GM1, GD1a, GD1b, and GQ1b [45,49–50]. In genetically susceptible individuals, this immune activation promotes T-cell-dependent B-cell responses, leading to the production of high-affinity IgG autoantibodies directed against these gangliosides [12,14].

Subtype Pathological mechanisms & The Concept of Nodopathy:

The pathological targets and underlying cellular mechanisms vary considerably among different clinical subtypes of GBS.

AIDP: Acute inflammatory demyelinating polyradiculoneuropathy (AIDP) is primarily mediated by T-cell activation and macrophage infiltration directed against Schwann cell myelin structures [13,15]. Activation of the classical complement pathway (C1q and C3d) on the outer surface of Schwann cells results in focal myelin damage, macrophage infiltration into internodal regions, and segmental demyelination, leading to impaired saltatory nerve conduction [13,15].

AMAN/AMSAN: Acute motor axonal neuropathy (AMAN) and acute motor sensory axonal neuropathy (AMSAN) involve antibody- and complement-mediated injury targeting the nodal and paranodal axonal regions [16,50]. Anti-GM1 and anti-GD1a IgG antibodies bind to gangliosides concentrated at the nodes of Ranvier, activating complement pathways, promoting Membrane Attack Complex (C5b-9) formation, disrupting voltage-gated sodium (Na^+) channels, causing nodal elongation, micro-axonal detachment, and rapid Wallerian-like axonal degeneration [14,50].

Nodopathy / Paranodopathy Concept: Recent advances in neuroimmunology have introduced the concept of "nodopathy," in which immune-mediated injury primarily affects the nodal and paranodal structures without causing classical demyelination or irreversible axonal degeneration [33]. Temporary disruption of nodal sodium channels may result in reversible conduction failure, explaining the rapid clinical improvement observed in some patients after early

immunotherapy despite marked initial electrophysiological abnormalities [33].

Miller Fisher Syndrome: Miller Fisher syndrome is strongly associated with IgG anti-GQ1b antibodies, which demonstrate a sensitivity of more than 90% [18,50]. GQ1b gangliosides are highly expressed in ocular motor nerves (cranial nerves III, IV, and VI) and muscle spindle Ia afferent fibres, explaining the characteristic clinical triad of ophthalmoplegia, ataxia, and areflexia [18,50].

Table 1: Clinical, Pathophysiological, and Prognostic Features of Guillain- Barré Syndrome Variants [5, 13, 16, 18, 33, 39, 50]:

GBS Variant	Clinical Features	Pathophysiology& Target	Associated Antibodies	Prognosis & Outcome
AIDP	Ascending weakness, sensory loss, areflexia, cranial nerve involvement, autonomic Dysregulation [11,15,16].	Macrophage-mediated demyelination& Schwann cell damage [16, 42].	Variable (Anti-LM1,anti-galactocerebroside) [16].	Generally favorable recovery; gradual improvement over months [9,16].
AMAN	Pure motor weakness, rapid progression, preserved sensation, Hyperreflexia in rare subsets[20,27].	Antibody & complement mediated nodal axolemma injury [20, 29].	Anti-GM1,Anti-GD1a,Anti-GalNac-GD1a [27,37].	Variable; rapid recovery if reversible nodal failure, or prolonged if axonal loss occurs[33].
AMSAN	Severe acute motor and sensory loss, early respiratory involvement ,marked muscle wasting [13, 33].	Direct axonal degeneration of motor and sensory nerve fibers [13, 20].	Anti-GM1,Anti-GD1a [27, 37].	Poorer prognosis, high risk of permanent disability and incomplete recovery [9,33].
MFS	Triad of ophthalmoplegia, ataxia, and areflexia; minimal limb weakness [38- 39].	Immune-mediated injury to CN III, IV, VI & muscle spindles [38].	Anti-GQ1b,Anti-GT1a (>90% sensitivity) [38-39].	Excellent prognosis; spontaneous recovery usually within 1–3 months [38].
PCB	Prominent facial, pharyngeal, cervical, and upper limb weakness ; preserved 1leg strength [13].	Localized immune-mediated cranial and brachial plexus neuropathy [13].	Anti-GT1a,Anti-GQ1b [13, 39].	Variable; requires close airway monitoring due to severe bulbar palsy [13].
BBE	Ophthalmoplegia , ataxia ,altered consciousness/ hypersomnia, Hyperreflexia [39].	Central CNS and peripheral brainstem inflammatory Involvement [39].	Anti-GQ1b [39].	Variable; Favorable with early Aggressive immunotherapy and ICU care [5, 39].

Abbreviations:

AIDP, acute inflammatory demyelinating polyradiculoneuropathy; AMAN, acute motor axonal neuropathy; AMSAN, acute motor and sensory axonal neuropathy; MFS, Miller Fisher syndrome; PCB, pharyngeal-cervical-brachial variant; BBE, Bickerstaff brainstem encephalitis; CNS, central nervous system; CN, cranial nerve

This figure illustrates the Immunopathogenesis of Guillain–Barré syndrome, including antecedent Campylobacter jejuni infection, molecular mimicry, activation of T and B lymphocytes, production of anti-ganglioside antibodies, complement activation, and immune-mediated injury leading to acute inflammatory demyelinating polyradiculoneuropathy (AIDP) and acute motor axonal neuropathy (AMAN)

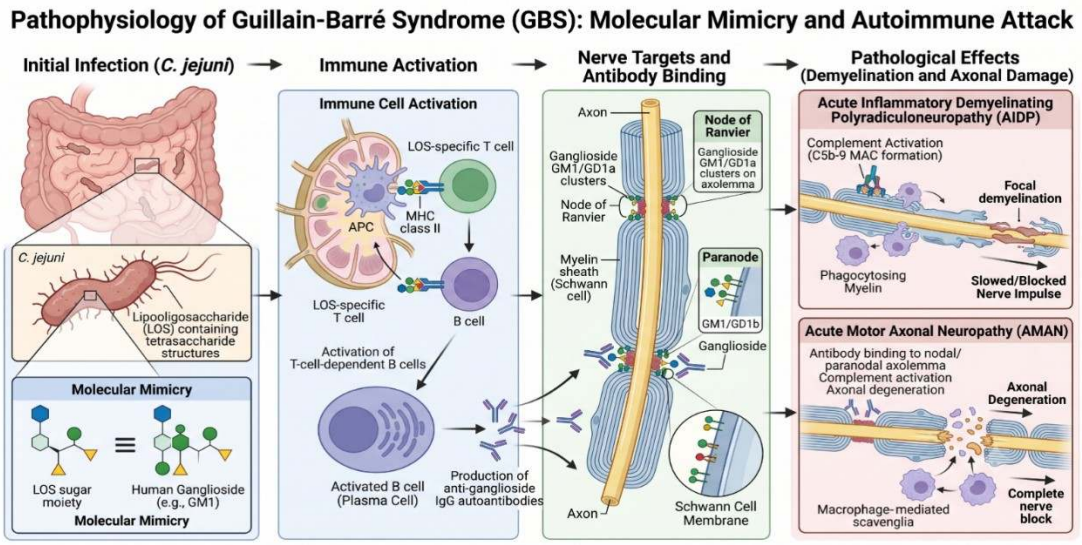

Figure 1: Pathophysiology and Immunopathogenesis of Guillain–Barré Syndrome (GBS): Molecular Mimicry, Immune Activation, and Peripheral Nerve Injury

Clinical Presentation and Variants:

GBS typically begins with subtle distal sensory symptoms, such as tingling sensations or numbness involving the toes and fingers [11,15,22]. Over the following days, these symptoms gradually progress to ascending, symmetrical flaccid weakness that starts in the lower limbs and extends proximally, resulting in increasing difficulty with activities such as walking, climbing stairs, and maintaining posture [11,15–16]. Deep tendon reflexes are usually reduced or completely absent in the affected limbs, which remains a key clinical feature of the disorder [11,17]. Symptoms generally continue to worsen over a period of 2 to 4 weeks before reaching a temporary plateau phase [11,16].

The major clinical subtypes of GBS include acute inflammatory demyelinating polyradiculoneuropathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor sensory axonal neuropathy (AMSAN), and Miller Fisher syndrome (MFS). In addition, several regional variants have been described, including the Pharyngeal-Cervical-Brachial (PCB) variant, characterized by facial, bulbar, and upper limb weakness; the Paraparetic variant, presenting with isolated lower limb weakness; and Bickerstaff Brainstem Encephalitis (BBE), which involves central nervous system brainstem manifestations with ophthalmoplegia and ataxia [13,38–39,43–44].

This figure illustrates the typical clinical presentation and progression of Guillain–Barré syndrome (GBS), beginning with distal paraesthesia, followed by ascending symmetrical flaccid weakness and generalized areflexia. It summarizes the temporal course of disease progression and highlights the major clinical variants, including acute inflammatory demyelinating polyradiculoneuropathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor and sensory axonal neuropathy (AMSAN), Miller Fisher syndrome (MFS), pharyngeal-cervical-brachial (PCB) variant, paraparetic variant, and Bickerstaff brainstem encephalitis (BBE), along with their characteristic clinical manifestations and anatomical involvement

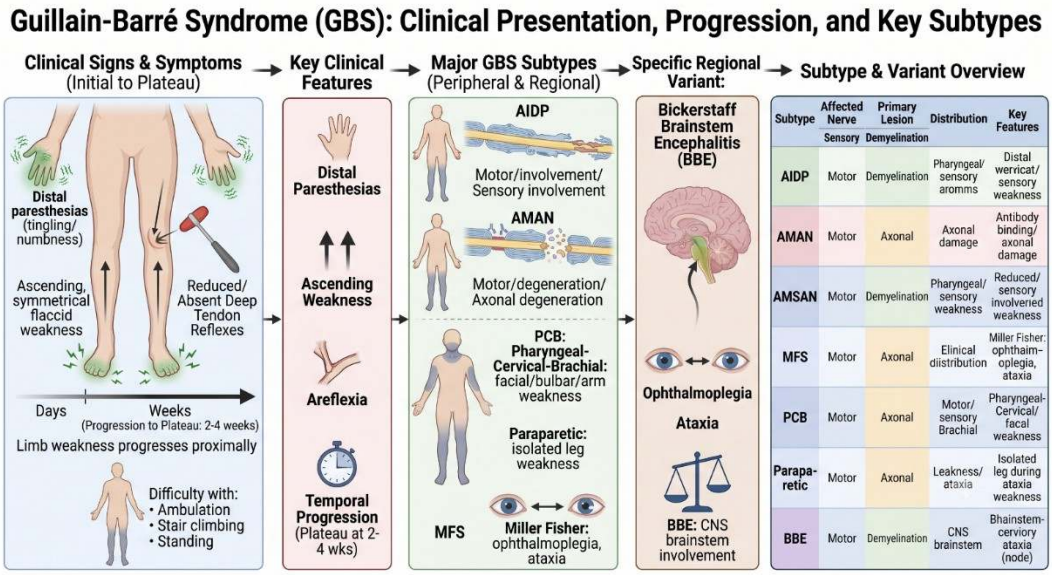

Figure 2: Clinical Presentation, Disease Progression, and Major Clinical Variants of Guillain–Barré Syndrome (GBS).

Diagnostic Approach & Diagnostic Frameworks:

The diagnosis of GBS is primarily based on a comprehensive clinical assessment, supported by cerebrospinal fluid (CSF) analysis, nerve conduction studies (NCS), and careful exclusion of conditions that may mimic the clinical presentation [4,17,47].

Clinical Diagnostic Criteria & Brighton Criteria:

The classic Asbury and Cornblath (1990) criteria established the essential diagnostic features of GBS, including progressive bilateral flaccid weakness involving the legs and arms along with areflexia or hyporeflexia. Supportive features include a monophasic disease course of ≤4 weeks, symmetrical weakness, cranial nerve involvement, autonomic dysfunction, and cerebrospinal fluid (CSF) albuminocytological dissociation [2]. The standardized Brighton Collaboration Criteria further categorizes GBS cases into Levels 1 through 4 based on diagnostic certainty, with detailed criteria presented in Section 10 (Table 2) [3].

Cerebrospinal Fluid (CSF) Analysis:

The characteristic CSF finding in GBS is albuminocytological dissociation, defined by an increased CSF protein concentration with a normal total white blood cell count (<10–50 cells/μL) [19,36]. However, clinicians should consider the timing of CSF evaluation, as protein levels may remain normal in up to 30% to 50% of patients during the first week of illness [19]. CSF protein concentration generally increases during the second and third weeks after symptom onset [19]. A CSF cell count exceeding 50 cells/μL should raise suspicion for alternative diagnoses, including HIV polyradiculitis, Lyme disease, CMV radiculitis, or leptomeningeal malignancy [4,19].

Electrophysiology, Neuroimaging & Differential Diagnosis:

Nerve conduction studies are essential for confirming peripheral neuropathy, differentiating demyelinating from axonal subtypes, and providing valuable prognostic information [3,20,48]. Repeat electrophysiological testing after 3 to 6 weeks can help resolve transient conduction abnormalities and establish definitive subtype classification [3,40]. Contrast-enhanced spinal MRI with T1-gadolinium may demonstrate smooth enhancement of the cauda equina and anterior spinal nerve roots, supporting the diagnosis in appropriate clinical settings [4,38]. Important differential diagnoses include severe hypokalemia, myasthenia gravis, botulism, transverse myelitis, diphtheritic neuropathy, organophosphate poisoning, and vasculitic neuropathy [39]

Table 2: Brighton Collaboration Diagnostic Criteria for Guillain- Barré Syndrome [3,47]

Level of Certainty	Clinical Features	CSF Findings	Electrophysiology (NCS)	Exclusion of Alternates
Level 1 (Definite)	Bilateral flaccid weakness +decreased/ absent reflexes; monophasic course (nadir ≤4 weeks) [17, 47].	Elevated protein with cell count <50/μL (Albuminocytological dissociation) [36, 47].	Consistent with GBS subtype (AIDP or AMAN/AMSAN) [18,48].	Required (Alternative causes ruled out) [47].
Level 2 (Probable)	Bilateral flaccid weakness + decreased/ absent reflexes; monophasic course [17, 47].	Supportive CSF OR Supportive NCS (One of the two is positive) [36, 47].	Supportive NCS OR Supportive CSF [18,47].	Required [47].
Level 3 (Possible)	Bilateral flaccid weakness + decreased/ absent reflexes ;monophasic course [17, 47].	Not available or Inconclusive [47].	Not available or Inconclusive [47].	Required [47].
Level 4 (Reported)	Clinical features present but data Incomplete or non-classifiable [47].	Not available [47].	Not available [47].	Not clearly excluded [47].

Abbreviations:

GBS, Guillain–Barré syndrome; CSF, cerebrospinal fluid; NCS, nerve conduction studies; AIDP, acute inflammatory demyelinating polyradiculoneuropathy; AMAN, acute motor axonal neuropathy; AMSAN, acute motor and sensory axonal neuropathy

Schematic illustration of the diagnostic evaluation of Guillain–Barré syndrome, including clinical assessment and Brighton Collaboration diagnostic criteria, cerebrospinal fluid analysis, electrophysiological studies, neuroimaging, and important differential diagnoses.

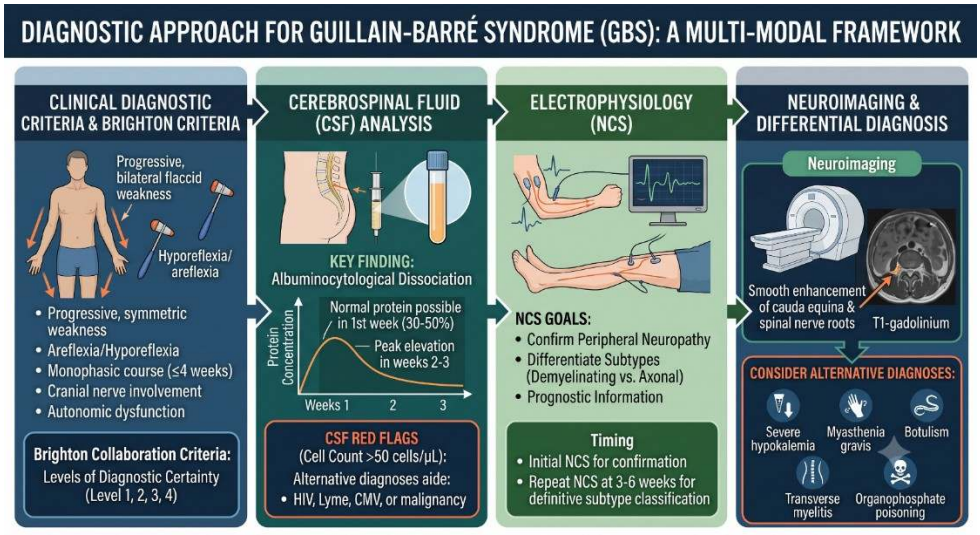

Figure 3: Diagnostic Approach to Guillain–Barré Syndrome.

Management Strategies and Therapeutic Advances:

Management of GBS requires early hospitalization, continuous supportive critical care, and timely initiation of disease-modifying immunotherapy in patients with progressive neurological deterioration [4,16,24].

First-Line Disease-Modifying Immunotherapy:

Intravenous immunoglobulin (IVIg; total dose of 2.0 g/kg administered over 5 days) and plasma exchange (PLEX; 4–6 exchanges performed over 1–2 weeks) are established first-line therapies with comparable clinical efficacy [22–25]. Combining IVIg and PLEX does not provide additional therapeutic benefit, and systemic corticosteroids have not demonstrated efficacy in improving outcomes [22,23].

Table 3: Comparison of First-Line Treatment Modalities in Guillain- Barré Syndrome [22-25,39]:

Aspect	Intravenous Immunoglobulin(IVIg)	Plasma Exchange(PLEX)
Mechanism of Action	Neutralizes pathogenic autoantibody , blocks Fc receptors ,inhibits complement, modulates cytokines [11, 27].	Directly clears circulating autoantibodies, immune complexes, complement, and cytokines [23,39].
Standard Regimen	0.4g/kg/day IV for 5 consecutive days (Totaldose:2.0 g/kg) [23, 25].	4–6exchanges (40–50mL/kgpersession,total200–250mL/kg) over 1–2weeks[23,39].
Onset of Action	Gradual immunomodulatory effect [25].	Rapid reduction in circulating autoantibody titer [23,39].
Clinical Indication	First-line therapy ;preferred in early disease or when PLEX access is limited [4, 25].	First-line alternative;highly effective in severe or rapidly progressive disease [23,39].
Advantages	Non-invasive, easy administration, widely available in tertiary facilities [4, 25].	Direct, rapid physical clearance of pathogenic immune mediators [23,39].
Limitations &Risks	High acquisition cost; risk of fluid overload, aseptic meningitis, or thrombosis [23, 25].	Requires specialized aphaeresis equipment, central venous access, ICU setup [23,39].
Adverse Effects	Headache, fever, allergic reactions, rarely acute renal failure [23, 25].	Hypotension, bleeding/ coagulopathy ,infection, line sepsis, electrolyte shifts [23,39].
Resource Suitability	Preferred in general hospital settings ; limited by financial cost in LMICs [21,25].	Restricted to tertiary care hospitals with aphaeresis infrastructure [21,23].

Abbreviations:

IVIG, intravenous immunoglobulin, PLEX, plasma exchange , LMIC , low and middle income countries

Indian Perspective: Resource Optimization & Small-Volume Plasma Exchange (SVPE):

In India and other resource-limited healthcare settings, the high acquisition cost of IVIg can impose substantial financial burden on patients and families, particularly among those without insurance coverage [21,25]. To address this challenge, South Asian clinical researchers have explored Small-Volume Plasma Exchange (SVPE), which utilizes lower plasma volumes (10–15 mL/kg per session) administered over 8–10 sessions using basic blood bank centrifuge technology [43]. Available studies suggest that SVPE may provide therapeutic effectiveness comparable to conventional PLEX and IVIg while substantially reducing treatment costs, thereby improving access to care in resource-constrained public hospitals [21,43]

Treatment-Related Fluctuations & Emerging Biotherapies:

Treatment-related fluctuations (TRFs) occur in approximately 6% to 10% of patients and may require a second course of immunotherapy in selected cases [26,48]. Emerging targeted approaches, including complement inhibitors (Eculizumab, ANX005), FcRn antagonists (Efgartigimod), B-cell depletion strategies (Rituximab), and selective immunoadsorption, are currently under clinical investigation [6,12].

Table 4: Emerging and Investigational Therapeutic Strategies in Guillain- Barré Syndrome [11-12,15]:

Therapy Class	Mechanism of Action	Representative Examples	Clinical Rationale &Target	Developmental Status
Complement Inhibitors	Blocks terminal complement Cascade (C5orC1q), preventing MAC assembly [11,15].	Eculizumab,ANX005 [11, 12]	Prevents acute neuroaxonal degeneration at nodes of Ranveer ,especially in axonal GBS [15].	Phase II / Phase III clinical trials [11,12].
FcRn Inhibitors	Blocks neonatal Fc receptor, accelerating degradation of endogenous pathogenic IgG [11, 12].	Efgartigimod, Rozanolixizumab [11,12]	Rapidly lowers serum IgG levels without donor blood supply constraints or fluid overload [11, 12].	Under clinical evaluation for autoimmune Neuropathies [11,12].
Cytokine-Targeted Therapy	Inhibits pro-inflammatory Cytokine networks(IL-6receptor antagonism) [11].	Tocilizumab[11]	Suppresses systemic inflammatory cascades contributingtonerveroot swelling [11].	Experimental / Early translational stage [11].
B-Cell Targeted Therapy	DepletesCD20+Blymphocytes, eliminating autoantibody-secreting precursor cells [11].	Rituximab [11]	Targets the source of persistent ganglioside autoantibody production [11].	Limited case series/Refractory cases [11].
Immunoadsorption	Selectively adsorbs and removes immunoglobulin from plasma via columns [11, 12].	Selective Ig columns [11]	Alternative to PLEX without requiring donor plasma Replacement or albumin substitution [11, 12].	Investigational/ Limited regional use [11].

Abbreviations:

GBS, Guillain–Barré syndrome; C5, complement component 5; C1q, complement component 1q; MAC, membrane attack complex; FcRn, neonatal Fc receptor; IgG, immunoglobulin G; IL-6, interleukin-6; CD20, cluster of differentiation 20; PLEX, plasma exchange

Critical Care, Autonomic & Rehabilitation Management:

Approximately 20% to 30% of patients with GBS may require intensive care support with endotracheal intubation and mechanical ventilation [5,37]. Bedside respiratory monitoring incorporates the "20-30-40 Rule" (forced vital capacity [FVC] <20 mL/kg, negative inspiratory force [NIF] <−30 cmH_2O, and maximum expiratory pressure [MEP] <40 cmH_2O), along with the Erasmus GBS Respiratory Insufficiency Score (EGRIS), to identify patients at risk of respiratory failure [5,48]. Autonomic dysfunction, Thromboembolic complications, infections, and neuropathic pain require structured monitoring and multidisciplinary management approaches [5, 16, 22].

Table 5: Major Systemic Complications in Guillain-Barré Syndrome [5, 16, 22, 37,46]

Category	Specific Complication	Underlying Cause/Mechanism	Clinical Management &Significance
Respiratory	Acute respiratory failure, atelectasis, aspiration pneumonia [5, 37].	Diaphragmatic and intercostals muscle paralysis, bulbar muscle weakness[5, 37].	ICU admission, elective intubation, mechanical ventilation, chest physiotherapy [5, 37].

Category	Specific Complication	Underlying Cause/Mechanism	Clinical Management &Significance
Autonomic	Severe bradycardia , sinus arrest, hypertension/ hypotension , paralytic ileus [5, 16].	Immune-mediated damage to Sympathetic and parasympathetic fibers [5, 16].	Continuous cardiac telemetry, short-acting vasoactive drugs, temporary cardiac pacing [5].
Thromboembolic	Deep vein thrombosis (DVT), Pulmonary embolism (PE) [5, 46].	Prolonged limb immobility, venous stasis, hypercoaguable state [5, 46].	Mandatory low-molecular-weight heparin (LMWH) and sequential compression devices [5].
Infectious	Ventilator-associated pneumonia , catheter-sepsis , urinary tract infection [5].	Invasive lines , prolonged mechanical ventilation, neurogenic bladder [5].	Strict aseptic protocols, line care, targeted antimicrobial therapy[5].
Neurological / Musculoskeletal	Persistent neuropathic pain, muscle atrophy, joint contractures [22].	Axonal loss, central/peripheral pain sensitization, immobilization [22].	Gabapentinoids (gabapentin /pregabalin), early passive/active physical therapy [22, 25].
Psychological	Severe anxiety , depression, post-traumatic stress disorder (PTSD) [22].	Sudden onset paralysis , ICU stay , loss of functional independence [22].	Psychological support, communication boards, targeted pharmacotherapy [22].

Abbreviations:

GBS, Guillain–Barré syndrome; ICU, intensive care unit; DVT, deep vein thrombosis; PE, pulmonary embolism; LMWH, low-molecular-weight heparin; PTSD, post-traumatic stress disorder

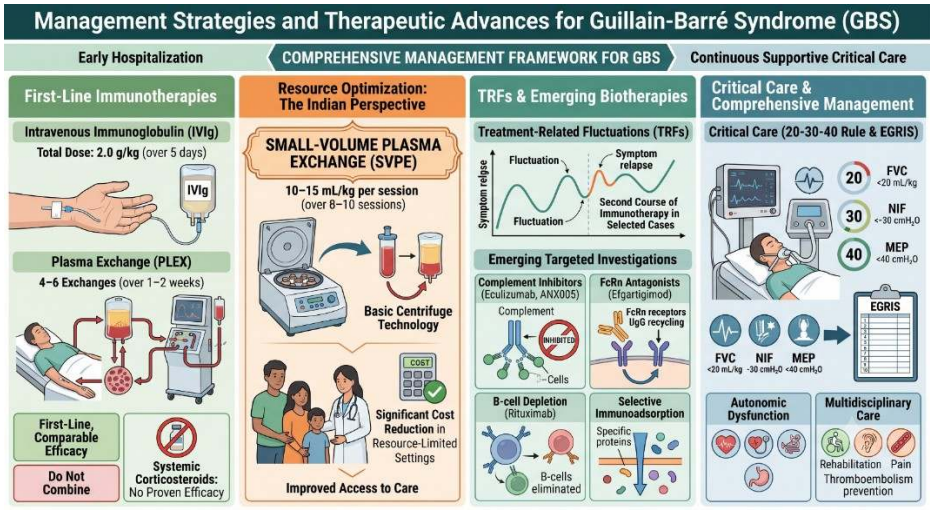

Figure 4: Management Strategies and Therapeutic Advances for Guillain–Barré Syndrome (GBS). Overview of the Evidence-Based Management of GBS, Including First-Line Immunotherapies (Intravenous Immunoglobulin and Plasma Exchange), Resource-Optimized Approaches Such as Small-Volume Plasma Exchange, Treatment-Related Fluctuations, Emerging Targeted Biotherapies, Critical Care, Respiratory Monitoring, Autonomic Management, Rehabilitation, and Multidisciplinary Supportive Care.

Special Populations & Prognostic Scoring Frameworks:

Pediatric GBS may present with hyperacute pain, refusal to walk, or gait disturbances, with IVIg considered the preferred treatment option [18,38]. During pregnancy, GBS most commonly occurs during the third trimester or postpartum period, and IVIg has been reported to be safe and effective in this population [4,24]. Prognostically, the Modified Erasmus GBS Outcome Score (mEGOS), assessed at admission and incorporating age, preceding diarrhea, and Medical Research Council (MRC) sum score, provides accurate prediction of independent ambulation at 6 months [26,48].

Table 6: Modified Erasmus GBS Outcome Score (mEGOS) at Admission [48]:

Predictor Variable	Categories /Subscores	Points
Age at Onset (years)	≤40years	0
	41–60years	1
	>60years	2
Preceding Diarrhea	Absent	0
	Present	1
MRC Sum Score at Admission	51–60	0
	41–50	1
	31–40	2
	≤ 30	3

**Note: Total mEGOS score ranges from 0 to 6 [51]. Higher scores correlate with a significantly lower probability of regaining independent ambulation at 6months[48]*

Abbreviations: mEGOS, modified Erasmus Guillain–Barré Syndrome Outcome Score; MRC, Medical Research Council.

DISCUSSION:

Guillain–Barré syndrome (GBS) is a heterogeneous immune-mediated polyradiculoneuropathy with diverse clinical presentations and outcomes. Although molecular mimicry remains the accepted pathogenic mechanism, recent studies have emphasized the roles of antiganglioside antibodies, complement activation, and nodal/paranodal dysfunction. Yuki and Hartung highlighted molecular mimicry as the key trigger of autoimmune nerve injury, whereas Uncini and Kuwabara proposed nodopathies as a distinct pathological spectrum, suggesting that future classifications may incorporate immunological biomarkers alongside electrophysiological findings.[7,10–12]

Diagnostic strategies have evolved considerably over the past decade. While the Brighton Collaboration criteria remain the standard diagnostic framework, their accuracy is enhanced when combined with cerebrospinal fluid analysis and electrophysiological studies. In addition, Walgaard et al. demonstrated that prognostic tools such as the modified Erasmus Guillain –Barré Syndrome Outcome Score (mEGOS) and the Erasmus Guillain–Barré Syndrome Respiratory Insufficiency Score (EGRIS) improve early prediction of functional outcomes and respiratory failure, supporting individualized patient management.[18,24–26]

Current evidence supports intravenous immunoglobulin (IVIg) and plasma exchange (PLEX) as equally effective first-line therapies when initiated early. Hughes et al. and van Doorn et al. reported no significant difference in long-term neurological recovery between the two modalities. However, IVIg is often preferred because of its ease of administration and favorable safety profile, while PLEX remains an effective option where expertise is available. Despite these advances, treatment-related fluctuations and incomplete recovery continue to occur in some patients, highlighting the need for more targeted therapies.[29–31]

Emerging immunotherapies, including complement inhibitors, FcRn antagonists, and immunoadsorption, have shown promising early results. However, the current evidence is limited by small sample sizes and short follow-up periods, and larger multicenter

randomized controlled trials are needed before these therapies can be incorporated into routine clinical practice.[35–38]

In India, delayed diagnosis, limited access to neurophysiological investigations, and the high cost of immunotherapy remain important barriers to optimal care. Resource-adapted strategies such as small-volume plasma exchange may provide practical alternatives in selected settings, although further validation is required. Future research should focus on biomarker-guided therapy, validation of prognostic models, and evaluation of emerging targeted therapies to improve long-term outcomes.[40,43–45]

CONCLUSION:

Guillain–Barré syndrome remains a major cause of acute immune-mediated paralysis and requires prompt recognition, accurate diagnosis, and early initiation of treatment to achieve the best possible outcomes. Advances in the understanding of its Immunopathogenesis have improved disease classification, diagnostic approaches, and prognostic assessment, while intravenous immunoglobulin and plasma exchange continue to be the standard of care. Emerging targeted therapies offer promising new avenues for treatment, although further high-quality clinical evidence is needed before their routine use can be recommended. In resource-limited settings, strengthening early diagnosis, improving access to specialized neurological care, and ensuring timely treatment remain key priorities. Continued research into biomarkers, prognostic models, and novel immunotherapies is expected to support more personalized management and improve long-term functional outcomes for patients with Guillain–Barré syndrome.

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HOW TO CITE: Dr. Mandeep Singh Juneja, Dr. Sunny Jaiswal, Dr. Bondada Hemanth Kumar, Guillain-Barré Syndrome: A Comprehensive Review of Clinical Spectrum, Pathophysiology, Diagnostic Approach, and Advances in Management with an Indian Perspective, Int. J. of Pharm. Sci., 2026, Vol 4, Issue 11, 4342-4356. https://doi.org/10.5281/zenodo.24459099