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A Review

Immune system involvement and neuropathology in Guillain-barré syndrome: Approaches to therapy

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Guillain-Barré Syndrome (GBS) is increasing in incidence and is associated with significant morbidity, emphasizing the urgent need for improved therapeutic options beyond current treatments. While intravenous immunoglobulin (IVIG) and plasmapheresis are the primary therapies, their limited ability to prevent long-term neuromuscular impairments highlights the necessity for innovative approaches. GBS is an acute autoimmune disorder that often follows infections, leading to demyelination or damage to nerve axons and resulting in paralysis. This review discusses emerging immunomodulatory treatments, such as monoclonal antibodies aimed at B-cell depletion and complement system inhibition, which provide targeted mechanisms to modulate abnormal immune responses. Additionally, regenerative strategies, including mesenchymal stem cell therapy and neuroprotective agents, are explored for their potential to promote nerve repair and improve recovery. Advances in gene-editing technologies also offer promising possibilities for correcting immune dysregulation at the molecular level. Beyond pharmacological interventions, the review highlights the importance of addressing the complex physical, psychological, and socioeconomic burdens of GBS. Comprehensive rehabilitation comprising physiotherapy, occupational therapy, and psychological supportis vital for restoring independence and enhancing quality of life. Future research should focus on personalized treatment approaches, biomarker-guided monitoring, and large clinical trials to improve outcomes and lessen the global impact of GBS.

Keywords: Autoimmune neuropathy, Autoimmune response, Biomarkers, Guillain-Barré Syndrome (GBS), Immunological triggers, Neuropathic consequences

Introduction

Guillain-Barré Syndrome (GBS) is an acute, immune-mediated disorder of the peripheral nervous system that manifests with rapidly progressing muscle weakness, sensory loss, and, in severe cases, respiratory failure requiring intensive care support. It remains one of the most common causes of acute flaccid paralysis across the globe, underscoring the importance of understanding its complex pathogenesis, evolving treatment options, and the profound impact it has on patients' functional recovery and quality of life. Despite notable progress in the field of neuromuscular medicine, GBS continues to pose major clinical challenges owing to its unpredictable course, heterogeneous immunopathological subtypes, and inconsistent response to both standard and advanced therapeutic modalities.

The condition is primarily driven by an abnormal immune reaction triggered by preceding infections, most frequently caused by *Campylobacter jejuni*, cytomegalovirus, Epstein–Barr virus, or influenza. These infectious agents initiate molecular mimicry, in which immune cells mistakenly target ganglioside components of peripheral nerves due to structural similarities between microbial antigens and neural tissue. This misguided immune attack results in either demyelination or axonal injury, depending on the specific clinical variantsuch as Acute Inflammatory Demyelinating Polyneuropathy (AIDP), Acute Motor Axonal Neuropathy (AMAN), or Acute Motor and Sensory Axonal Neuropathy (AMSAN). Each subtype is characterized by distinct immunological and pathological mechanisms, which account for differences in disease severity, progression, and therapeutic responsiveness, making individualized management essential for optimal patient outcomes[1].

GBS commonly begins with symmetrical ascending weakness, loss of reflexes, and sensory disturbances that progress rapidly over days or weeks. Severe cases may involve autonomic dysfunctions, including cardiac arrhythmias, blood pressure fluctuations, and respiratory failure, necessitating

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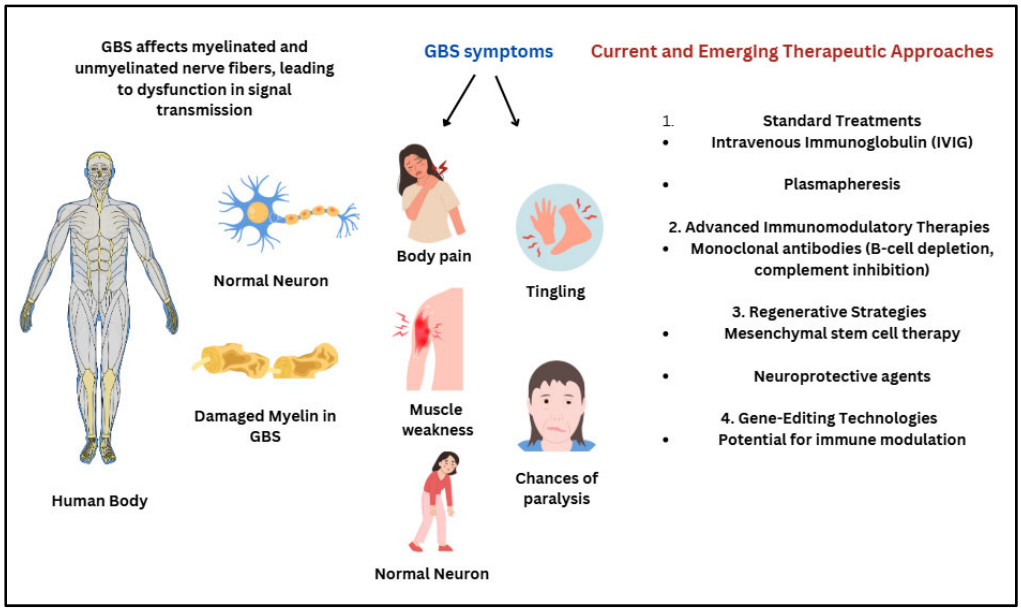

Graphical Abstract

intensive care. Diagnosis is mainly clinical, supported by electrophysiological studies and cerebrospinal fluid (CSF) analysis showing albuminocytologic dissociation, while neuroimaging helps exclude other conditions. Early recognition is vital for timely intervention and improved prognosis. Current treatment relies on immunomodulatory approaches, primarily intravenous immunoglobulin (IVIG) and plasmapheresis. IVIG acts by neutralizing pathogenic antibodies and modulating immune responses, whereas plasmapheresis removes circulating autoantibodies and immune complexes. Although these therapies can shorten disease duration and enhance recovery, variability in patient response and incomplete recovery rates highlight the need for early diagnosis, individualized therapy, and further exploration of novel treatment modalities to improve long-term outcomes in patients with GBS[2].

Although IVIG and plasmapheresis have proven effective in hastening recovery and reducing the severity of GBS, they often fail to prevent lasting neurological complications, especially in cases involving extensive axonal injury. Moreover, patient responses to these treatments vary considerably, highlighting the need for innovative and individualized therapeutic approaches. Recent research has focused on advanced immunomodulatory strategies that target specific components of the immune system. Monoclonal antibodies such as rituximab, which depletes B cells, have demonstrated potential in reducing autoimmune activity, while complement inhibitors like eculizumab aim to block the formation of the membrane attack complex, thereby limiting nerve destruction and promoting recovery. Other agents targeting inflammatory cytokines are also under investigation. Collectively, these emerging therapies signify a move toward precision medicine in GBS, aiming to improve clinical outcomes through targeted and mechanism-based interventions[4].

Beyond immunotherapy, regenerative medicine is emerging as a promising approach to enhance nerve healing and functional recovery in GBS. Mesenchymal stem cell (MSC) therapy, in particular, has shown encouraging neuroprotective, anti-inflammatory, and remyelination effects in experimental studies, suggesting its potential role in restoring peripheral nerve function. These findings suggest a promising avenue for translational research, potentially transforming the long-term management of GBS by promoting endogenous repair mechanisms. In addition to pharmacological advancements, neurorehabilitation plays a pivotal role in improving patient outcomes post-GBS. Comprehensive rehabilitation programs encompassing physical therapy, occupational therapy, and psychological support are essential for restoring motor function, preventing complications such as contractures and muscle atrophy, and addressing the profound psychological impact of the disease. Cognitive-behavioral therapy (CBT) and counselling interventions further aid in mitigating the anxiety, depression, and post-traumatic stress disorder (PTSD) frequently observed in GBS survivors[5].

Although the progress in therapeutic interventions, GBS continues to exert a significant burden on patients lives, impacting their physical abilities, mental well-being, and socioeconomic stability. Persistent residual weakness, chronic neuropathic pain, and fatigue often limit patients reintegration into daily activities and professional life, leading to long-term disability. Furthermore, the financial burden associated with prolonged hospitalization, intensive care requirements, and rehabilitation services underscores the need for healthcare policies aimed at optimizing patient care and support systems. Future research directions in GBS should focus on biomarker-driven approaches for early disease detection, stratification of treatment responses, and the development of targeted immunotherapies. Large-scale, multicentre clinical trials are essential to validate emerging therapies and refine current treatment guidelines to achieve optimal patient outcomes. Likewise, the exploration of gene-editing technologies, such as CRISPR-Cas9, for precise modulation of immune responses presents an exciting frontier in GBS therapeutics[6].

This review aims to provide a comprehensive analysis of advanced treatment modalities for GBS, delving into the latest advancements in immunotherapies, regenerative medicine, and rehabilitation strategies. Furthermore, we highlight the profound impact of GBS on normal human life, encompassing physical, psychological, and socioeconomic dimensions. By bridging the gap between current knowledge and future perspectives, this discussion seeks to enhance clinical decision-making and improve the overall quality of life for individuals affected by this debilitating disorder.

Immunomodulatory therapies in Guillain-barré syndrome

Guillain-Barré Syndrome (GBS) is a severe autoimmune disorder affecting the peripheral nervous system, primarily mediated by aberrant immune responses directed against neuronal components. The pathogenesis of GBS involves immune dysregulation, autoantibody production, and complement activation, leading to demyelination and axonal degeneration. Immunomodulatory therapies serve as the cornerstone of treatment, aiming to attenuate the dysregulated immune response, prevent further neuronal damage, and facilitate recovery. The primary modalities of immunomodulatory intervention include Intravenous Immunoglobulin (IVIG), Plasma Exchange (Plasmapheresis), and emerging Monoclonal Antibody therapies, each demonstrating distinct mechanistic pathways and therapeutic efficacies[7].

Intravenous immunoglobulin (IVIG)

Intravenous Immunoglobulin (IVIG) constitutes a frontline therapeutic intervention for GBS, widely recognized for its ability to modulate immune responses. The mechanistic underpinnings of IVIG therapy are multifaceted, encompassing Fc receptor blockade on macrophages, inhibition of pro-inflammatory cytokines, suppression of autoreactive T-cell responses, and modulation of complement activation. A standard IVIG regimen involves administration at 0.4 g/kg/day over five consecutive days, significantly ameliorating disease progression in both demyelinating and axonal subtypes of GBS[8].

The efficacy of IVIG is attributed to several key immunological mechanisms. Firstly, Fc receptor blockade on antigen-presenting cells (APCs) prevents excessive phagocytosis of myelin debris, mitigating further neuronal injury. Secondly, IVIG exerts anti-inflammatory effects through direct sequestration of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interferon-gamma (IFN-γ), thereby attenuating the inflammatory cascade. Likewise, IVIG enhances the expression of regulatory T-cells (Tregs), shifting the immune system toward an anti-inflammatory state[9].

A significant aspect of IVIG therapy involves its impact on complement activation, which plays a pivotal role in neuronal injury. The deposition of C3b and membrane attack complexes (MAC) on Schwann cells and axonal membranes exacerbates nerve damage in GBS. IVIG neutralizes complement activity by inhibiting C1q and reducing classical pathway activation, thus preventing further neuronal degeneration. In addition, IVIG enhances the expression of inhibitory FcγRIIb receptors on B-cells, dampening autoreactive B-cell activity and reducing autoantibody production against gangliosides (*e.g.*, GM1, GD1a, and GQ1b). Although its broad-spectrum immunomodulatory effects, IVIG therapy is not devoid of limitations. Clinical variability exists in patient responsiveness, and adverse effects such as aseptic meningitis, transient haemolysis, and thromboembolic events have been reported. Likewise, IVIG resistance in certain GBS subtypes, particularly in severe axonal variants, necessitates alternative or adjunctive treatment strategies[10].

Plasma exchange (Plasmapheresis)

Plasmapheresis (PE) is an important first-line therapy in Guillain-Barré Syndrome (GBS), working by removing harmful autoantibodies, immune complexes, and inflammatory substances from the blood that cause nerve damage. In this process, the patient's blood is filtered to separate plasma, which holds these harmful components. The removed plasma is then replaced with albumin or fresh frozen plasma to restore blood volume. Studies show that 4–5 sessions of PE over two weeks can significantly improve muscle strength and lower disability levels, similar to intravenous immunoglobulin (IVIG)[11]. PE effectively eliminates pathogenic IgG and IgM antibodies and complement proteins that contribute to nerve injury. Starting PE early (within 2 weeks of symptom onset) leads to better outcomes, especially in severe and fast-progressing cases. However, the procedure involves risks like low blood pressure, electrolyte imbalances, infections, and requires specialized equipment and skilled staff, making it less accessible in some healthcare settings[12].

Monoclonal antibody therapies

The emergence of monoclonal antibodies (mAbs) has introduced novel targeted strategies in the immunotherapeutic landscape of GBS. These agents allow precise modulation of immune mechanisms implicated in disease pathogenesis, minimizing systemic immunosuppression.

Rituximab, a chimeric monoclonal antibody against CD20, depletes pathogenic B-cell clones responsible for anti-ganglioside autoantibody production. This B-cell depletion is particularly advantageous in GBS subtypes where humoral immunity plays a central role, such as Miller-Fisher Syndrome (MFS) and CIDP-associated variants[13]. By reducing circulating autoantibody levels, rituximab may attenuate ongoing nerve damage and support recovery. Eculizumab, a humanized monoclonal antibody targeting complement protein C5, inhibits terminal complement activation, preventing formation of the membrane attack complex (MAC). This mechanism offers neuroprotection by limiting complement-mediated axonal injury, especially in patients with excessive complement activation.

Despite their promise, both agents remain under clinical investigation. High cost, immunosuppression risks, and the potential for opportunistic infections necessitate careful patient selection. Presently, IVIG and plasmapheresis remain first-line therapies, while mAbs represent emerging adjunctive options pending further clinical validation[14].

Emerging experimental therapies

Stem cell therapy: Pioneering a regenerative approach

Mesenchymal stem cell (MSC) therapy has emerged as an innovative approach to counteract the neuropathological consequences of Guillain-Barré Syndrome (GBS), primarily focusing on the repair of demyelinated nerve fibres and damaged axons. Preclinical investigations have illuminated the intrinsic immunomodulatory properties of MSCs, which play a pivotal role in suppressing excessive autoimmune responses. The deployment of MSCs, derived from autologous or allogeneic sources such as bone marrow, adipose tissue, or umbilical cord-derived progenitor cells, has shown promising outcomes in experimental models of inflammatory neuropathies. The secretome of MSCs, enriched with neurotrophic factors such as nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), and glial cell-derived neurotrophic factor (GDNF), is critical for mitigating neuroinflammation and fostering neuronal regeneration[15].

Furthermore, exosome-mediated paracrine signalling mechanisms associated with MSCs have demonstrated potential in modulating microglial activity, thereby reducing oxidative stress-induced neuronal apoptosis. By releasing extracellular vesicles containing anti-inflammatory cytokines (*e.g.*, IL-10 and TGF-β), MSCs downregulate pro-inflammatory mediators such as TNF-α, IL-6, and IFN-γ. The immunosuppressive milieu established by MSCs facilitates the reprogramming of autoreactive T cells and the attenuation of Th1 and Th17 pathways, which are implicated in the aberrant immune response characteristic of GBS. The transplantation of MSCs has also been linked to enhanced Schwann cell proliferation, which is essential for the remyelination of peripheral nerves[16].

Although these encouraging findings, the clinical translation of MSC therapy faces challenges such as immune rejection, potential oncogenic transformation, and the variability in differentiation potential across donor sources. Recent advancements in gene-edited MSCs, utilizing CRISPR-based modifications to enhance immunotolerance and regenerative efficacy, are being explored to overcome these barriers. Further randomized controlled trials are required to establish the long-term safety and efficacy of MSC transplantation in GBS patients[31] (Mechanism action of monoclonal antibodies in GBS, Fig. 1).

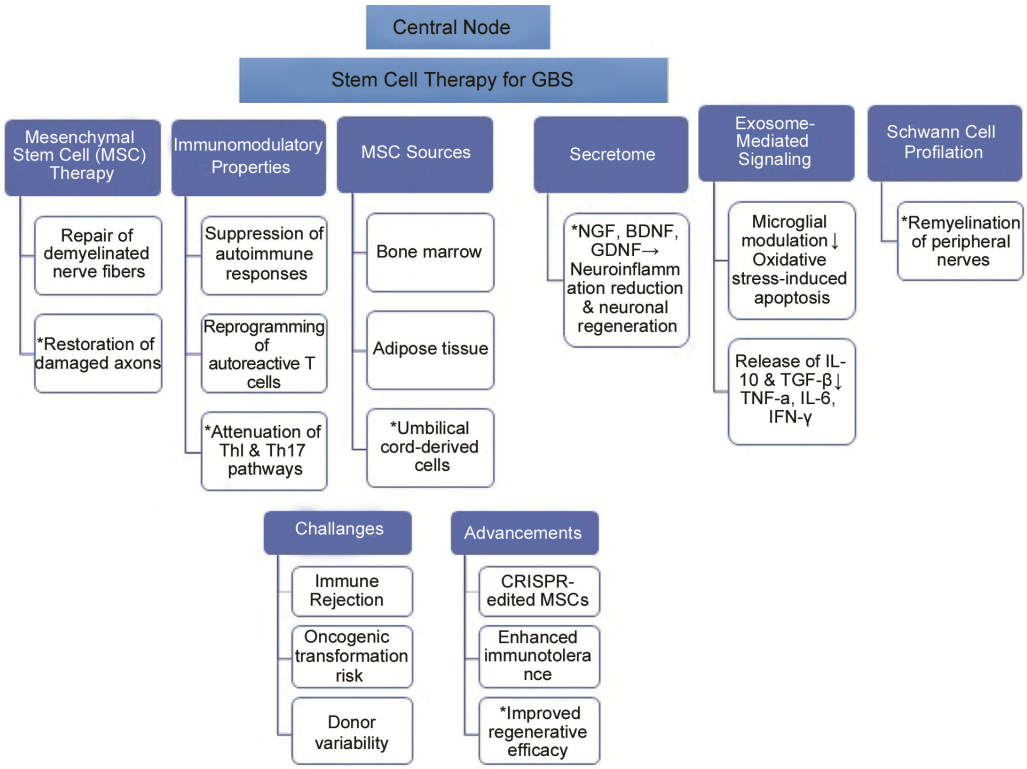

Fig. 1 — Mechanism of action of monoclonal antibodies in GBS

Neuroprotective agents: Targeting neuroinflammation and axonal integrity

The pathogenesis of GBS is characterized by a cascade of inflammatory insults that lead to the destruction of the myelin sheath, oxidative stress-mediated neuronal damage, and apoptotic degeneration of motor and sensory axons. Neuroprotective agents such as erythropoietin (EPO) and minocycline have garnered significant attention for their ability to mitigate neuroinflammation and promote neural regeneration. Erythropoietin, a glycoprotein hormone with neurotrophic properties, has been shown to exert anti-apoptotic effects on neuronal cells by activating the JAK2/STAT5 signalling cascade. This pathway plays a crucial role in reducing oxidative stress-induced neuronal degeneration by upregulating endogenous antioxidant enzymes such as superoxide dismutase (SOD) and catalase (CAT). Minocycline, a tetracycline-class antibiotic with profound anti-inflammatory and neuroprotective properties, has been investigated for its role in attenuating microglia-mediated neuroinflammation[17].

By inhibiting the activation of nuclear factor-kappa B (NF-κB) and reducing the expression of matrix metalloproteinases (MMPs), minocycline prevents the disruption of the blood-nerve barrier, thereby limiting immune cell infiltration into the peripheral nervous system. The modulation of mitochondrial dysfunction and the inhibition of cytochrome c release further contribute to the neuroprotective effects of minocycline. Recent advances in targeted drug delivery systems have enabled the encapsulation of neuroprotective agents within liposomal or nanoparticle-based carriers to enhance bioavailability and therapeutic efficacy. The incorporation of ligand-mediated targeting strategies has allowed for site-specific drug delivery, minimizing off-target effects and maximizing neuronal uptake. Ongoing clinical trials aim to establish the optimal dosing regimens and combinatory potential of neuroprotective agents with existing immunomodulatory therapies such as intravenous immunoglobulin (IVIG) and plasma exchange[18].

Gene therapy: Precision medicine for immune modulation

The development of gene-editing technologies, particularly CRISPR-Cas9, has transformed experimental therapeutics in autoimmune neuropathies like Guillain-Barré Syndrome (GBS). Gene therapy targets immune dysregulation by modifying autoreactive immune cells to prevent attacks on peripheral nerves[19]. CRISPR-mediated deletion of pathogenic T-cell receptors (TCRs) offers a selective strategy to suppress autoimmunity while

preserving general immune function. A key focus is the enhancement of regulatory T cells (Tregs) by upregulating FOXP3, the transcription factor critical for Treg development and function, which restores immune tolerance by suppressing autoreactive T cell activity. Similarly, increasing IL-2 receptor α-chain (CD25) expression stabilizes and expands Treg populations, offering sustained immunosuppressive effects[20].

Another promising approach involves silencing pro-inflammatory cytokine genes, such as IL-17, TNF-α, and IFN-γ, using RNA interference (RNAi) and antisense oligonucleotides (ASOs). This cytokine downregulation reduces neuroinflammation and myelin damage in preclinical models. Advances in lipid nanoparticle (LNP) vectors have enhanced delivery efficiency and targeting accuracy, improving the potential for clinical translation. Despite these advances, gene therapy still faces challenges, including immune responses to viral vectors, off-target effects, and ensuring long-term therapeutic stability. Ongoing research is focused on developing safer non-viral delivery systems and conducting robust clinical trials[21].

In parallel, regenerative therapies such as stem cell transplantation show promise in repairing demyelinated axons and restoring neurological function. Neuroprotective agents are being integrated into therapeutic regimens to prevent neuronal loss and promote recovery. As gene-editing and regenerative medicine technologies advance, GBS treatment is shifting from symptomatic management toward curative, disease-modifying strategies. Future progress will depend on interdisciplinary collaboration and carefully designed clinical studies to establish safety, efficacy, and long-term benefits[22].

Rehabilitation and supportive care in Guillain-Barré Syndrome

Physical rehabilitation

The cornerstone of recovery for individuals affected by Guillain-Barré Syndrome (GBS) lies in early and comprehensive physical rehabilitation. Initiating physical therapy at the earliest feasible stage is vital to prevent muscle atrophy and to maintain joint flexibility, thereby reducing the risk of long-term functional impairment. A tailored program typically includes passive and active range-of-motion exercises, progressing to resistive training as muscle strength returns. Neuromuscular re-education strategies are also employed to enhance motor control and coordination. Evidence suggests that integrating aquatic therapy can alleviate discomfort while facilitating limb movement, which is particularly beneficial in cases of severe weakness[23]. Advanced techniques, such as functional electrical stimulation (FES), have shown promise in accelerating muscle re-innervation and strength recovery. Physical rehabilitation also focuses on respiratory muscle training, vital for those who have experienced prolonged mechanical ventilation, thereby enhancing pulmonary function and endurance. The ultimate objective of physical rehabilitation is to enable patients to achieve optimal functional independence, minimizing residual deficits and improving quality of life[23].

Occupational therapy

Occupational therapy plays an equally pivotal role in the holistic recovery of GBS patients, emphasizing the restoration of autonomy in daily activities. When occupational therapists get involved early, they carefully look at the patient's physical limits and create individualized treatment plans to help them improve their self-care, work, and leisure activities. Innovative strategies together with the use of devices that help such as adapted utensils, dressing aids, and mobility supports, serve as essential in helping patients find self-reliance. Cognitive rehabilitation may also be considered, especially in situations when exhaustion and cognitive impairment are severe. Therapists frequently use energy-saving techniques and work simplification tactics to effectively treat these symptoms.Home modifications, including grab bars, wheelchair ramps, and accessible shower facilities, are recommended to ensure a safe and supportive living environment. Continuous monitoring and adjustment of the rehabilitation plan are essential, based on periodic reassessment of functional gains and evolving patient goals. The integration of virtual reality-based rehabilitation exercises has also been explored, offering engaging and innovative ways to facilitate motor and cognitive recovery. The overarching aim of occupational therapy is not only to restore function but to empower patients to reintegrate into their social and occupational roles, thereby enhancing overall well-being[24].

Psychological and social support

The psychological impact of GBS is profound, necessitating comprehensive mental health support as a core component of the rehabilitation process. Patients frequently experience anxiety, depression, and in some cases, post-traumatic stress disorder (PTSD) due to the abrupt onset and severity of the illness. Early psychological intervention is critical,

beginning with thorough psychosocial assessments to identify individual needs and challenges. Cognitive-behavioral therapy (CBT) is widely employed to address maladaptive thoughts and behaviors, promoting resilience and adaptive coping strategies[25]. Group therapy sessions provide a platform for shared experiences, fostering a sense of community and mutual support. Family involvement is encouraged, with educational sessions aimed at enhancing understanding and providing caregivers with coping tools. Pharmacological treatments, including antidepressants and anxiolytics, may be indicated for severe psychological symptoms. Likewise, mindfulness-based stress reduction (MBSR) programs have been beneficial in managing anxiety and improving quality of life. Social support networks are crucial, facilitating connections with patient advocacy groups and community resources. Vocational rehabilitation services are also integral, offering job retraining and skill development to aid patients in returning to the workforce. The goal of psychological and social support interventions is to address the multifaceted impact of GBS on mental health, ensuring comprehensive care that encompasses both physical and emotional recovery[26].

Adverse effects of Guillain-barré syndrome (gbs) on normal human life

Physical limitations

Guillain-Barré Syndrome (GBS) is a severe autoimmune disorder affecting the peripheral nervous system, leading to a cascade of neuromuscular impairments that significantly diminish physical function. The pathological hallmark of GBS is |the immune-mediated demyelination or axonal degeneration, which disrupts nerve conduction and results in progressive muscle weakness, paralysis, and sensory deficits. Patients frequently report profound fatigue, which persists even after partial neurological recovery. This fatigue is not merely a consequence of muscle weakness but is also linked to aberrant neuromuscular junction transmission and dysautonomia, where autonomic nerve dysfunction impairs cardiovascular and thermoregulatory homeostasis[27].

Muscle atrophy and persistent weakness, particularly in the lower limbs, lead to a substantial reduction in ambulatory capacity.Although many individuals recover their basic ability to move, ongoing problems often make it hard to perform daily tasks such as climbing stairs, standing for extended periods, or walking short distances. Difficulties with small hand movements also worsen functional challenges, making activities like writing, gripping objects, or using tools more difficult[23].

Similarly, abnormal sensations are a common issue. Many people feel tingling, numbness, or unusual sensations, which can affect their sense of body position and coordination. This loss of sensation often causes problems with walking, sometimes requiring the use of support devices like canes or walkers to avoid falls. In severe cases, GBS can cause long-lasting pain, including nerve pain caused by ongoing nerve damage and changes in how the central nervous system processes signals. As a result, the effects of GBS go beyond temporary paralysis, leading to long-term issues with muscles and nerve function[28].

Psychological and emotional impact

GBS causes deep psychological and emotional stress because it starts suddenly and often has an uncertain and lengthy recovery. The rapid shift from being fully able to move and function normally to being mostly paralyzed causes intense mental distress.Patients frequently experience intense anxiety during the acute phase, particularly due to respiratory failure and ventilator dependence in severe cases. The inability to communicate effectively due to facial or bulbar muscle involvement exacerbates feelings of helplessness and fear.

Post-traumatic stress disorder (PTSD) is a common sequela in GBS survivors, arising from the distressing nature of prolonged hospitalization, intensive care unit (ICU) stays, and invasive procedures such as tracheostomies or mechanical ventilation. The persistent uncertainty regarding functional recovery further fuels emotional distress. Many individuals struggle with depression due to prolonged disability, social isolation, and the perceived loss of independence. The interplay between chronic pain and depressive symptoms compounds emotional suffering, as neuropathic pain is inherently linked to mood disturbances through shared neurobiological pathways involving serotonin and norepinephrine dysregulation[27].

Cognitive impairments, although less commonly discussed, also play a role in the emotional burden of GBS. Research indicates that extended hospital stays, widespread inflammation, and severe nerve-related illnesses can lead to problems with thinking, memory, concentration, and decision-making. These mental changes, along with ongoing emotional stress, often

require long-term psychological treatments such as therapy, medications like antidepressants, and counseling support[28].

Socioeconomic burden

The financial effect of GBS went beyond acute medical treatment costs. It includes continuous charges associated with long-term incapacity, reduced job productivity, and the high expectations imposed on caretakers. Long hospital stays in critical care, breathing help, treatments such as IVIG or plasmapheresis, and considerable rehabilitation are frequently required for treatment. These combined expenditures might be prohibitively expensive, especially for people who do not have comprehensive health insurance[29].

Many people recovering from GBS face challenges with work because they often need to take extended time off. This is due to ongoing physical problems, tiredness, or remaining neurological issues that affect their ability to perform daily job tasks. In cases where full functional recovery is not achieved, individuals may be forced into early retirement or undergo vocational retraining to accommodate residual disabilities. The financial strain resulting from loss of income, combined with ongoing medical expenses, creates an economic hardship that extends beyond the affected individual to their entire family unit[29].

Caregivers, often family members, experience substantial emotional, physical, and financial strain while providing long-term support. Many caregivers are required to modify their professional commitments, reducing work hours or exiting the workforce entirely to care for their loved one. The increased dependency on social welfare programs, disability benefits, and rehabilitative services highlights the broader societal impact of GBS, necessitating the development of comprehensive support structures for affected individuals and their families[30].

Impact on quality of life and social functioning

The long-term repercussions of GBS extend beyond physical and economic constraints, deeply influencing the overall quality of life and social engagement of affected individuals. Many survivors experience significant alterations in their social roles, often struggling to reintegrate into their pre-illness lifestyles. The progressive nature of recovery, coupled with persistent physical limitations, restricts participation in recreational and social activities. Individuals who were previously active in sports, travel, or community engagement often find themselves limited by residual fatigue and motor deficits[30,31].

Social isolation becomes a prevalent issue, as mobility restrictions and emotional distress deter individuals from participating in group activities or social gatherings. The stigma associated with visible disabilities further exacerbates this isolation, as many individuals experience self-consciousness regarding their physical impairments. The intersection of social withdrawal and psychological distress often culminates in reduced life satisfaction, highlighting the need for holistic rehabilitation programs that address not only physical recovery but also social reintegration and emotional well-being[31].

Long-term neurological consequences

Although many patients with GBS achieve substantial neurological recovery, a significant proportion exhibit residual deficits that persist indefinitely. Chronic neuropathic pain, muscle weakness, and sensory abnormalities remain prevalent long after the resolution of the acute phase[66]. Demyelinating variants of GBS, such as acute inflammatory demyelinating polyneuropathy (AIDP), often lead to prolonged nerve conduction abnormalities, resulting in persistent motor and sensory impairments. Axonal subtypes, including acute motor axonal neuropathy (AMAN) and acute motor and sensory axonal neuropathy (AMSAN), are associated with more severe long-term disability due to direct axonal degeneration and slower regenerative capacity[32].

Dysautonomia, another common feature of GBS, may persist beyond the acute phase, manifesting as orthostatic hypotension, cardiac arrhythmias, thermoregulatory dysfunction, and gastrointestinal motility disorders. These autonomic complications further complicate functional recovery and necessitate multidisciplinary management strategies involving neurologists, physiotherapists, and cardiologists[33,34].

The adverse effects of GBS on normal human life are profound and multifaceted, affecting physical function, emotional well-being, socioeconomic stability, and overall quality of life. While advancements in medical interventions have improved survival rates and recovery outcomes, long-term rehabilitation and support systems remain essential for optimizing functional independence and social reintegration in affected individuals. Ongoing research efforts are crucial in refining therapeutic strategies to mitigate these adverse effects and enhance the overall prognosis of GBS survivors[35].

Future directions and challenges

Despite notable advances in Guillain-Barré Syndrome (GBS) research and treatment, substantial challenges remain in delivering patient-specific, effective interventions. The heterogeneity of GBS sub types such as AIDP, AMAN, and AMSAN necessitates precision medicine informed by immunological, genetic, and multi-omics profiling to identify predictive biomarkers and tailor therapies. Current diagnostic limitations, particularly in differentiating variants and monitoring disease progression, highlight the need for reliable CSF, metabolomic, and lipidomic biomarkers[36]. While IVIg and plasma exchange remain standard, emerging treatments including monoclonal antibodies (*e.g.*, eculizumab, rozanolixizumab), Treg and CAR-T cell therapies, and neuroprotective agents targeting oxidative stress and mitochondrial dysfunction show promise. Stem cell-based regenerative strategies, especially with MSCs and iPSC-derived neural cells, offer potential for remyelination, though clinical translation faces hurdles in cell viability and integration. Enhancing rehabilitation through neuromodulation, BCI technologies, and exoskeleton-assisted training is crucial, alongside addressing disparities in global access to advanced therapies[37]. Artificial intelligence and machine learning could transform diagnostics, treatment planning, and robotic rehabilitation, while growing interest in the gut microbiome and long-term neuropsychiatric outcomes calls for multidisciplinary, longitudinal research[38]. Ultimately, global collaboration, standardized protocols, and equitable access are essential for translating scientific progress into improved patient care and quality of life[39,40].

Conclusion

Guillain-Barré Syndrome remains a complex autoimmune neuropathy with significant implications for affected individuals and healthcare systems worldwide. While current therapeutic strategies have improved survival and functional outcomes, ongoing research into immunopathogenesis, neuroprotection, and regenerative medicine holds promise for enhancing disease management. A multidisciplinary approach integrating neurology, immunology, and rehabilitation medicine is essential for optimizing patient recovery and minimizing long-term disability. By advancing scientific knowledge and fostering innovation in treatment modalities, the medical community can continue to improve the prognosis and quality of life for individuals affected by this debilitating disorder.

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Conflict of interests

All authors declare no conflict of interests.

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