REVIEW ARTICLE

Guillain-Barré Syndrome following Dengue Fever: An Emerging Neurological Sequela in Endemic Regions – A Review Article

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Abstract

Objective: To review the association between dengue virus infection and Guillain-Barré Syndrome (GBS), exploring clinical features, diagnosis, pathogenesis, and management in endemic regions.

Material and Methods: This narrative review discusses current literature focusing on dengue-associated GBS (D-GBS), including pathophysiological mechanisms, clinical manifestations, diagnostic approach, therapeutic modalities, and prognosis.

Results: Guillain-Barré Syndrome (GBS) is increasingly recognized as a post-infectious complication of dengue fever. Pathogenesis is immune-mediated, typically presenting with symmetrical ascending weakness and autonomic dysfunction. Diagnosis relies on clinical criteria, electrophysiological studies, and cerebrospinal fluid analysis. Immunotherapy with IVIG or plasmapheresis remains the mainstay of treatment.

Conclusion: Early identification and intervention for D-GBS are essential to reduce morbidity. Heightened clinical awareness and public health preparedness are necessary in dengue-endemic areas.

Keywords: Dengue fever, Guillain-Barré Syndrome (GBS), neurological complications, dengue-associated neuropathy, immune-mediated paralysis

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Introduction:

Dengue virus infection, caused by four antigenically distinct serotypes (DENV-1 to DENV-4) of the Flaviviridae family, has emerged as one of the most prevalent and rapidly spreading mosquito-borne illnesses worldwide. According to the World Health Organization, approximately half of the global population is at risk of dengue, with an estimated 390 million infections annually, of which nearly 100 million manifest clinically. Countries in South and Southeast Asia, Latin America, and the Western Pacific regions bear the brunt of disease burden, with Pakistan experiencing recurrent outbreaks and rising complication rates in recent years.[1,2]

Classically, dengue presents with acute febrile illness, retro-orbital pain, myalgias, arthralgias, rash, thrombocytopenia, and, in severe cases, hemorrhagic manifestations or plasma leakage leading to shock. However, in the last two decades, its neurological manifestations have gained increased recognition. These include encephalitis, meningitis, myelitis, optic neuritis, and peripheral neuropathies such as Guillain-Barré Syndrome (GBS).[3,4]

Guillain-Barré Syndrome is an acute immune-mediated polyradiculoneuropathy that often follows bacterial or viral infections. It presents with rapidly progressive, symmetrical limb weakness, areflexia, sensory disturbances, and varying degrees of autonomic dysfunction.[5] The link between dengue and GBS, although historically considered rare, is now increasingly supported by both clinical observations and

epidemiological studies, particularly in endemic regions.[6,7] Understanding the pathophysiology, clinical presentation, and management of dengue-associated GBS (D-GBS) is vital for timely diagnosis, therapeutic intervention, and prevention of long-term morbidity.

Pathophysiology:
The association between dengue fever and Guillain-Barré Syndrome (GBS) is predominantly immune-mediated. The primary proposed mechanism is molecular mimicry, where antibodies generated against dengue virus cross-react with peripheral nerve gangliosides, resulting in demyelination or axonal degeneration. This response leads to the characteristic motor and sensory findings of Guillain-Barré Syndrome.

The time interval between dengue infection and Guillain-Barré Syndrome onset typically ranges from a few days to two weeks, consistent with a post-infectious immunological process. Additionally, dengue-induced cytokine dysregulation and blood-brain barrier compromise may further facilitate peripheral nerve involvement.

Clinical Presentation:
Dengue-associated Guillain-Barré Syndrome (D-GBS) typically manifests during the convalescent phase of dengue, around 5–14 days after fever resolution. Patients present with symmetrical, ascending weakness, starting in the lower limbs and progressing proximally. Cranial nerve involvement, especially bilateral facial nerve palsy, is common. Deep tendon reflexes are usually reduced or absent. Sensory symptoms, though less pronounced, may include paresthesias and loss of vibration sense. Autonomic dysfunction - seen in up to 60% - can lead to labile blood pressure, arrhythmias, and urinary retention. Severe cases progress to respiratory failure. Atypical variants, including Miller Fisher Syndrome and AMAN, are reported more frequently in dengue-endemic areas. Misdiagnosis with dengue-associated hypokalemic paralysis is possible but can be differentiated based on clinical progression and laboratory findings.

Diagnosis:
Diagnosis is primarily clinical, confirmed by nerve conduction studies that show demyelinating or axonal patterns. CSF typically reveals albuminocytologic dissociation (high protein, normal WBC count) after the first week. Dengue confirmation is done via serology (IgM, NS1 antigen) or PCR. It is important to distinguish D-GBS from other causes of acute flaccid paralysis such as transverse myelitis or hypokalemia, to ensure appropriate management.

Management:
The mainstay of D-GBS treatment is immunomodulatory therapy—IVIG or plasmapheresis. IVIG (0.4 g/kg/day for 5 days) is preferred due to ease of use and effectiveness. Plasmapheresis is equally effective but less available in resource-limited settings. Combining both is not beneficial. Supportive care includes respiratory support, cardiovascular monitoring for autonomic dysfunction, pain control with gabapentinoids, thromboprophylaxis, nutritional support, and pressure sore prevention. Rehabilitation therapy is crucial for long-term functional recovery, especially in axonal variants like AMAN. Public health education and clinician awareness are key for early identification and intervention.

Prognosis:
Prognosis is generally favorable with early treatment. Most patients recover in weeks to months. Axonal variants and delayed treatment are associated with poorer outcomes. Long-term sequelae include persistent weakness, fatigue, or neuropathic pain.

Discussion:
The increasing incidence of Guillain-Barré Syndrome (GBS) following dengue outbreaks is a concerning trend that underscores the need for enhanced clinical vigilance and public health preparedness. GBS is a well-established post-infectious autoimmune neuropathy, traditionally associated with pathogens such as Campylobacter jejuni, cytomegalovirus, Epstein-Barr virus, and more recently, Zika virus.[5,8] The growing number of case reports and observational

studies linking dengue virus (DENV) to GBS supports a possible causal association.[6,7]

Multiple studies have reported clusters of GBS cases coinciding with dengue epidemics in South Asia, Southeast Asia, and South America.[4,6] These observations suggest that DENV may act as a potent immunological trigger for peripheral nerve autoimmunity. Although the exact pathogenesis remains incompletely understood, immune-mediated mechanisms including molecular mimicry, antibody cross-reactivity with gangliosides, and cytokine-induced inflammation have been proposed.[7,9]

Differentiating dengue-associated GBS (D-GBS) from other neuromuscular complications, such as dengue-associated hypokalemic paralysis (DAHP), is crucial. While both conditions may present with acute flaccid paralysis, DAHP is due to transient potassium depletion and typically responds quickly to potassium replacement therapy.[10] In contrast, D-GBS involves immune-mediated nerve damage and requires immunotherapy, such as intravenous immunoglobulin (IVIG) or plasmapheresis.[5,6] Failure to recognize and treat D-GBS promptly may lead to respiratory failure, severe autonomic instability, and prolonged disability.

Furthermore, D-GBS may present in atypical forms, including Miller Fisher syndrome (ophthalmoplegia, ataxia, areflexia), acute motor axonal neuropathy (AMAN), and pure motor or sensory variants.[6,8] In resource-constrained settings, the lack of access to nerve conduction studies or cerebrospinal fluid analysis may delay diagnosis and compromise outcomes. Thus, the development of pragmatic clinical algorithms and point-of-care diagnostic tools for early detection in endemic regions is imperative.[7,11]

From a public health perspective, incorporating neurological surveillance into national dengue response strategies is critical. Training frontline healthcare workers to recognize signs of neuromuscular complications, ensuring availability of IVIG in tertiary centers, and launching awareness campaigns can enhance early referral and treatment.[6,9] Early ICU admission for patients with bulbar or respiratory involvement is essential to reduce mortality.[5]

In addition, further research is required to understand the individual risk factors that predispose patients with dengue to develop GBS. These may include host genetics, immune response to specific DENV serotypes, viral load, co-infections, and the presence of pre-existing autoimmune susceptibilities.[7,9] Longitudinal studies focusing on rehabilitation outcomes, relapse rates, and long-term neurological sequelae are also necessary.

In summary, D-GBS is a serious and increasingly reported complication of dengue fever. With growing awareness of its occurrence, especially in endemic regions, the need for multidisciplinary approaches involving neurology, infectious disease, public health, and critical care becomes apparent. Early recognition, prompt initiation of immunotherapy, and comprehensive supportive care are crucial to optimize patient outcomes and reduce long-term disability.

Conclusion:
Guillain-Barré Syndrome is a rare but serious neurological consequence of dengue. With increasing incidence and the potential for severe disability or death, it is essential that healthcare providers in endemic areas remain vigilant. Early recognition, timely treatment, and comprehensive care are vital for improving outcomes. Further research is needed to better understand pathogenesis, identify risk factors, and optimize treatment strategies in low-resource settings.

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Dawood Sohail, collected the data, references and did the initial writeup.

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