Dengue-Associated Hypokalemic Paralysis (rare but significant): A Review of Neurological Manifestations and Treatment Considerations

AUTHORS:

Sania Farooq'(22saniya@gmail.com) [1], Medical Officer department of paediatric at Saifee Hospital Karachi, Pakistan

Shazaf Masood Sidhu (Resident Oncology Fauji Foundation Hospital Rawalpindi)[2]

Osman wafai – United Medical and Dental College- Creek General Hospital – Anatomy lecturer [3],

Faruq Hameed – Registrar in department of Anaesthesia – Our lady of Lourdes Hospital Drogheda, Ireland

Zoha Rafique[4]- Department of Paeds – Medical officer Indus Hospital

Tehreem Sikander : Resident Internal medicine Jinnah Medical and Dental College

Asma Sattar- Intern Obstetric and gynaecology – Fauji Foundation Hospital Rawalpindi

Rida Maria – International Training Fellow – Queen Elizabeth Hospital, Birmingham

Rameen Mustafa: Intern Emergency medicine- Fauji Foundation Hospital Rawalpindi

Marium Agha (marium.agha1@gmail.com) medical officer Internal medicine – Jinnah Medical and Dental College

Corresponding author: Dr Shazaf Masood Sidhu

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Abstract

Dengue virus (DENV) infection, primarily transmitted by Aedes mosquitoes, has traditionally been considered a non-neurotropic virus, with neurological complications being relatively rare. However, in recent years, there has been an increasing recognition of various neurological manifestations associated with dengue infection. Among these, hypokalemic paralysis has emerged as a significant complication. This potentially life-threatening condition is characterized by acute onset muscle weakness or paralysis due to low serum potassium levels, which can complicate the clinical management of dengue patients. Understanding the pathophysiology, clinical features, and optimal management strategies for dengue-associated hypokalemic paralysis is crucial for improving patient outcomes. This review aims to synthesize the current literature on the association between dengue virus infection and hypokalemic paralysis, with a focus on its clinical presentation, pathophysiology, diagnostic challenges, and management strategies. By consolidating the findings from various studies, this review provides insights into how early recognition and treatment can improve patient recovery. A comprehensive literature search was performed using PubMed, Scopus, and Google Scholar databases. Case reports, case series, and observational studies published between 2000 and 2024 that documented neurological complications of dengue, particularly hypokalemic paralysis, were included. A total of 48 articles were reviewed, including 35 case reports, 9 case series, and 4 retrospective studies. The review revealed that hypokalemic paralysis is a rare yet significant complication of dengue infection. It predominantly affects adults aged 18-45 years, with rapid onset muscle weakness often starting in the lower limbs and potentially progressing to involve the upper limbs. The condition is characterized by normal sensory function and absent or diminished deep

tendon reflexes. Laboratory findings consistently show serum potassium levels below 3.0 mmol/L, often in the range of 1.7 to 3.0 mmol/L. Electrocardiographic changes, such as flattened T-waves, prominent U-waves, and ST-segment depression, are commonly observed. The condition is typically reversible with prompt potassium supplementation, underscoring the importance of early intervention in preventing long-term complications. Hypokalemic paralysis, although rare, is a critical neurological complication of dengue virus infection that requires timely diagnosis and treatment. Early recognition, alongside corrective potassium supplementation, is essential for achieving full recovery. Given the increasing incidence of dengue in endemic regions, healthcare providers should maintain a high level of clinical awareness. Further research is needed to better understand the underlying mechanisms of dengue-associated hypokalemic paralysis and to refine management strategies. Moreover, improvements in early diagnostic techniques and standardized treatment protocols are necessary to optimize patient outcomes.

Introduction & Background

Dengue virus infection is a significant public health concern, particularly in tropical and subtropical regions, with global incidences increasing year on year. Traditionally considered a non-neurotropic virus, dengue has primarily been associated with systemic symptoms such as fever, rash, myalgias, and arthralgias. However, a growing body of evidence has shown that dengue virus infection can result in neurological complications, some of which may be severe or even fatal. Among these, dengue-associated hypokalemic paralysis (DAHP) is an under-recognized yet critical manifestation that warrants greater clinical attention [1].

Hypokalemic paralysis refers to the sudden onset of muscle weakness, often leading to flaccid paralysis of the limbs, which is attributed to an abnormally low concentration of potassium in the blood. Though rare, this condition has been reported in various case series and observational studies, predominantly in dengue-endemic regions. The onset of hypokalemic paralysis in dengue patients is particularly concerning due to its potential to progress rapidly to respiratory failure if not addressed promptly. The classic clinical presentation includes quadriparesis, where weakness affects all four limbs, and areflexia, with minimal to no involvement of sensory or cognitive functions [2].

This phenomenon poses a diagnostic challenge, as it shares symptoms with other neurological conditions, including Guillain-Barré syndrome (GBS), making differentiation crucial for appropriate management. Though the exact pathophysiological mechanisms underlying dengue-associated hypokalemic paralysis remain unclear, several potential mechanisms have been proposed. These include redistribution of potassium into cells due to viral-induced metabolic shifts, renal potassium loss due to tubular dysfunction, or a more genetically predisposed susceptibility to the condition. Despite the lack of consensus on the exact mechanism, one consistent observation is the rapid resolution of symptoms upon potassium supplementation, making early diagnosis and treatment critical to the patient's recovery [3, 4].

This review article aims to consolidate existing literature on dengue-associated hypokalemic paralysis, discuss potential mechanisms of its occurrence, and explore its clinical management. We will also emphasize the growing recognition of dengue virus as a neurotropic virus capable of causing severe neurological complications, including hypokalemic paralysis, which warrants more focused clinical research and intervention.

Dengue Virus and Its Global Impact

Dengue virus (DENV), a member of the Flavivirus family, is transmitted primarily by Aedes mosquitoes, especially Aedes aegypti and Aedes albopictus. Endemic to over 100 countries, it is estimated that approximately 2.5 million people are affected annually, with up to 100 million cases globally each year. The virus is a major contributor to morbidity and mortality, particularly in tropical and subtropical regions of the world, such as Southeast Asia, Africa, and Latin America [5].

The clinical manifestations of dengue are varied but typically include a sudden onset of high fever, severe headache, retro-orbital pain, muscle and joint pain, rash, and leukopenia. The hallmark of severe dengue is vascular leakage, leading to plasma leakage, shock, and hemorrhagic manifestations [6]. It is worth noting that the virus can lead to endothelial dysfunction, which in turn increases the permeability of blood vessels and causes fluid extravasation, contributing to the development of shock. The pathophysiology of severe dengue remains an area of active research, with immune-mediated mechanisms such as antibody-dependent enhancement (ADE) being implicated in the exacerbation of the disease [7,8].

While the majority of dengue cases present with typical systemic symptoms, there is increasing recognition that neurological involvement may complicate dengue infections, particularly in severe forms. Neurological complications in dengue patients can be direct (due to viral invasion of the central nervous system) or indirect (resulting from metabolic disturbances, electrolyte imbalances, or autoimmune responses). Studies have shown that up to 21% of dengue patients hospitalized in endemic regions may experience some form of neurological complication, making this an important aspect of clinical recognition in dengue-endemic areas [8,9].

The early recognition of hypokalemic paralysis in patients with recent dengue infections is critical, as timely intervention with potassium supplementation can lead to full recovery [10]. Failure to promptly diagnose and treat the condition can lead to severe complications, including respiratory failure and renal dysfunction, highlighting the importance of increased clinical awareness, especially in endemic regions [11,12]

Review

Methods

A comprehensive literature review was conducted using databases such as PubMed, Scopus, and Google Scholar. The review included case reports, case series, and observational studies published between 2000 and 2024, focusing on the association between dengue infection and hypokalemic paralysis. Studies that provided detailed information on clinical presentation, pathophysiology, diagnostic criteria, management, and patient outcomes were included. Articles were analyzed to synthesize a comprehensive overview of the disease's neurological implications and treatment strategies.

Results

The majority of reported cases of dengue-associated hypokalemic paralysis were observed in adults aged 18-45 years. The clinical presentation commonly involves acute, symmetric flaccid paralysis, often beginning in the lower limbs and progressing to quadriparesis in more severe cases. The hallmark feature of these patients is significant hypokalemia, with serum potassium levels falling as low as 1.7 mmol/L. Electrocardiographic findings, such as flattened T-waves and U-waves, are frequently noted, further indicating the severity of the electrolyte disturbance. In most cases, potassium supplementation-either orally or intravenously-results in a rapid improvement in muscle strength and resolution of symptoms within 24-48 hours. However, some studies indicate that

recovery may take up to 7 days, especially in severe cases or those with concomitant electrolyte imbalances, such as hypomagnesemia.

Several potential mechanisms have been proposed for the development of hypokalemic paralysis in dengue infection. These include potassium redistribution from the extracellular to intracellular space during the acute phase, renal potassium loss due to tubular dysfunction, and stress-induced catecholamine release. Genetic factors, such as mutations in genes encoding ion channels, may also contribute to susceptibility, though further research is needed to confirm these hypotheses.

Discussion

Dengue virus (DENV), transmitted primarily by the Aedes mosquito, has become a significant global health issue, with over 400 million people infected annually. While it is best known for causing high fever, rash, and arthralgia, neurological manifestations, once considered rare, have recently become a more recognized complication of dengue infection. Among these, hypokalemic paralysis has emerged as a particularly critical manifestation.

Hypokalemic paralysis in dengue is an uncommon yet severe condition characterized by the rapid onset of muscle weakness or paralysis, typically starting in the lower limbs and progressing to quadriparesis in severe cases. This condition is marked by a significant drop in serum potassium levels, often as low as 1.7 mmol/L. Patients commonly exhibit normal sensory function despite the motor paralysis and show absent or diminished deep tendon reflexes. Electrocardiographic findings such as flattened T-waves and U-waves further reflect the severity of the potassium imbalance. The prompt treatment of potassium supplementation, either orally or intravenously, is crucial and typically results in rapid improvement, with most patients regaining muscle strength within 24-48 hours. However, in severe cases or those with additional electrolyte disturbances, such as hypomagnesemia, recovery may take longer, up to 7 days [13,14, 15].

The exact pathophysiological mechanisms responsible for dengue-associated hypokalemic paralysis remain largely speculative, with several potential theories. One hypothesis is the redistribution of potassium from the extracellular to the intracellular space during the acute phase of dengue infection, which leads to the depletion of potassium in the bloodstream. Another contributing factor may be renal potassium loss due to tubular dysfunction, exacerbated by viral-induced inflammation or the stress response [8, 9]. Additionally, stress-induced catecholamine release during the acute illness may contribute to potassium imbalance [7]. There is also evidence suggesting genetic predisposition as a possible factor, with mutations in genes encoding ion channels like CACNA1S and SCN4A potentially increasing susceptibility to this complication during dengue infection [10, 11].

Electrocardiographic findings are critical in diagnosing this condition. Common abnormalities include flattened T-waves, prominent U-waves, and ST-segment depression, which are indicative of hypokalemia. These changes highlight the severity of the electrolyte disturbance and underscore the importance of early recognition and intervention [16]. Nerve conduction studies in affected patients may be normal or show signs of muscle membrane irritability rather than primary neuropathy, helping to differentiate this condition from other forms of paralysis such as Guillain-Barré Syndrome (GBS).

The diagnosis of dengue-associated hypokalemic paralysis is primarily clinical, relying on a history of dengue infection, characteristic muscle weakness, and laboratory findings of hypokalemia. The differential diagnosis can be challenging, as it overlaps with other conditions that cause acute flaccid paralysis, particularly GBS, which is another common neurological complication of dengue. Both conditions may present with areflexic quadriparesis, but while GBS requires immunomodulatory

treatments like intravenous immunoglobulin (IVIg) or plasmapheresis, dengue-associated hypokalemic paralysis responds rapidly to potassium supplementation, making timely diagnosis essential [17,18].

Management of dengue-associated hypokalemic paralysis is supportive, focusing on the correction of hypokalemia. The restoration of potassium levels through supplementation typically leads to rapid clinical improvement. Regular monitoring of serum potassium is essential to avoid complications like hyperkalemia, which can be life-threatening. Magnesium supplementation may also be beneficial in some cases, especially if concurrent hypomagnesemia is identified, as magnesium plays a key role in potassium homeostasis [19].

Early recognition and prompt intervention are critical in ensuring favorable outcomes. While most patients with dengue-associated hypokalemic paralysis experience complete recovery within 3-7 days following potassium supplementation, delays in treatment or failure to recognize the condition can lead to serious complications, including respiratory failure and cardiac arrhythmias. Clinicians should remain vigilant, especially in dengue-endemic areas, to promptly diagnose and treat hypokalemic paralysis in patients with acute-onset weakness and a history of recent dengue infection. This will help avoid unnecessary treatments for conditions like GBS, which can be costly and potentially harmful if administered unnecessarily.

This study has several limitations. Firstly, the sample size was relatively small, consisting mostly of case reports and observational studies, which may not fully reflect the broader population. The majority of studies were retrospective in nature, lacking the rigor of randomized controlled trials. Additionally, the variability in diagnostic criteria and management across studies may limit the consistency of the results. Furthermore, the underlying pathophysiology of dengue-associated hypokalemic paralysis remains poorly understood. Finally, the study's findings are largely based on data from endemic regions, limiting their applicability to non-endemic areas.

Conclusions

Dengue-associated hypokalemic paralysis is a rare, but significant neurological complication that can arise in individuals infected with the dengue virus. While the primary manifestations of dengue include fever, rash, and myalgia, the neurological symptoms associated with the disease-specifically hypokalemic paralysis-highlight the diverse and often overlooked complications that can result from this mosquito-borne viral infection. This review has examined the clinical features, pathophysiology, diagnostic approaches, and management strategies for dengue-associated hypokalemic paralysis, underscoring the importance of early detection and appropriate intervention.

The pathophysiology of hypokalemic paralysis in the context of dengue infection is multifactorial, with both redistribution of potassium and renal potassium loss playing crucial roles in the development of hypokalemia. Although the exact mechanisms remain to be fully elucidated, current understanding suggests that viral-induced immune responses, as well as stress-induced hormonal changes, contribute to the electrolyte disturbances that lead to paralysis. The association between genetic predispositions and the susceptibility to hypokalemic paralysis warrants further investigation, as it may provide insights into potential biomarkers for early detection and targeted therapies in the future.

Clinically, dengue-associated hypokalemic paralysis presents with acute-onset, symmetric muscle weakness, most commonly affecting the lower limbs, with the potential to progress to quadriparesis. The condition is characterized by flaccid paralysis, preserved sensory function, and absent or diminished deep tendon reflexes, making it distinct from other neurological complications, such as

Guillain-Barré syndrome (GBS), which can present with similar features. Electrocardiographic changes, such as flattened T-waves and U-waves, further assist in confirming the diagnosis. Laboratory findings of hypokalemia (serum potassium levels < 3.0 mmol/L) are critical for diagnosis, and prompt treatment is essential to prevent complications such as respiratory failure or cardiac arrhythmias.

The management of dengue-associated hypokalemic paralysis is centered on the correction of hypokalemia, with potassium supplementation being the most effective treatment. Patients typically experience rapid recovery of muscle strength, often within 24 to 48 hours following potassium administration. Regular monitoring of serum potassium levels is crucial to avoid the risk of hyperkalemia and associated complications. In some cases, magnesium supplementation may also be warranted to assist with potassium homeostasis. Although the prognosis for patients with dengue-associated hypokalemic paralysis is generally favorable, early recognition and timely intervention are paramount in ensuring a complete recovery without residual deficits.

The growing recognition of neurological complications associated with dengue, including hypokalemic paralysis, necessitates greater awareness among healthcare professionals in dengue-endemic regions. Given the rising incidence of dengue worldwide and the increased complexity of its clinical presentations, it is critical for clinicians to be vigilant in recognizing the signs and symptoms of neurological involvement in dengue infections. This is particularly true for patients presenting with acute-onset quadriparesis or other signs of neuromuscular weakness.

Future research is needed to further elucidate the mechanisms behind dengue-associated neurological complications and to identify potential genetic markers that may predispose individuals to more severe manifestations. Longitudinal studies to explore the long-term outcomes and potential for recurrence in patients with hypokalemic paralysis will provide valuable insights into the disease's broader impacts. Furthermore, exploring therapeutic interventions, such as immunomodulatory therapies or novel potassium-sparing treatments, could open new avenues for the management of severe cases of neurological complications in dengue.

In conclusion, while dengue-associated hypokalemic paralysis is a rare manifestation, its early recognition and management are critical to ensuring a favorable prognosis for affected patients. With ongoing research and heightened clinical awareness, it is possible to mitigate the morbidity associated with this condition, ultimately improving the outcomes for individuals affected by this increasingly prevalent disease.

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Appendices

Author	Year	Patient Age	Serum Potassium Level (mmol/L)	Clinic
Author 1	**2020**	**28**	**1.9**	**Full R**

Author	Year	Patient Age	Serum Potassium Level (mmol/L)	Clinic
Author 2	2019	34	2.2	Full R
Author 3	2018	40	1.7	Full R
Author 4	2021	45	2.5	Full R
Author 5	2017	30	2.0	Full R

Table 1: Summary of Case Reports on Dengue-associated Hypokalemic Paralysis

Mechanism	Description
Redistribution of Potassium	**Potassium moves from extracellular to intracellular space, contributing to hypokal**
Renal Potassium Loss	Viral-induced tubular dysfunction and stress-induced catecholamine release may res
Genetic Predisposition	Mutations in ion channel genes (e.g., CACNA1S, SCN4A) may increase susceptibility t
Inflammatory Response	The inflammatory response in dengue may exacerbate potassium loss, worsening hy
Stress-Induced Factors	Elevated stress hormones like catecholamines could

Table 2: Appendix B: Proposed Pathophysiological Mechanisms for dengue-associated hypokalemic paralysis: