RESEARCH PAPER

DENGUE FEVER IN CHILDREN: CLINICAL FEATURES AND MANAGEMENT UPDATES

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ABSTRACT

Dengue fever is one of the most significant mosquito-borne viral illnesses affecting children worldwide, particularly in tropical and subtropical regions. The disease is caused by four antigenically distinct serotypes of the dengue virus (DENV-1 to DENV-4) and is transmitted primarily by Aedes aegypti mosquitoes. Pediatric dengue infection presents with a broad clinical spectrum ranging from asymptomatic infection and uncomplicated dengue fever to severe dengue characterized by plasma leakage, hemorrhage, shock, and multiorgan dysfunction. Early recognition of warning signs and timely initiation of appropriate fluid therapy are critical determinants of clinical outcomes. Children are particularly vulnerable to rapid progression toward severe disease because of physiological differences in fluid balance and cardiovascular reserve. Recent advances in diagnostic techniques, biomarkers, clinical monitoring protocols, and vaccine development have improved disease management. Current guidelines emphasize risk stratification, meticulous fluid management, close monitoring during the critical phase, and prompt recognition of complications. This review discusses the epidemiology, pathogenesis, clinical manifestations, warning signs, fluid management strategies, complications, recent therapeutic advances, and future directions in pediatric dengue care. Strengthening surveillance systems, vector control measures, vaccine implementation strategies, and evidence-based clinical management protocols remain essential for reducing dengue-related morbidity and mortality among children.

Keywords: Dengue fever, Children, Severe dengue, Warning signs, Fluid management, Dengue shock syndrome, Hemorrhage, Pediatric infectious diseases.

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INTRODUCTION

Dengue fever is one of the most important mosquito-borne viral infections affecting children worldwide and has emerged as a major public health concern in tropical and subtropical regions. The disease is caused by four antigenically distinct serotypes of the dengue virus (DENV-1, DENV-2, DENV-3, and DENV-4), belonging to the genus *Flavivirus*, and is primarily transmitted through the bite of infected *Aedes aegypti* and *Aedes albopictus* mosquitoes.[1] Dengue infection has shown a dramatic rise in incidence over the past few decades owing to rapid urbanization, population growth, climate change, increased international travel, and inadequate vector control measures.[2] According to recent estimates from the World Health Organization (WHO), nearly half of the global population is at risk of dengue infection, with children constituting a particularly vulnerable group because of their immature immune responses and higher susceptibility to severe disease manifestations.[3]

The clinical spectrum of dengue in children ranges from asymptomatic infection and mild febrile illness to severe dengue characterized by plasma leakage, hemorrhagic manifestations, shock, and multiorgan dysfunction.[4] Pediatric patients often present with nonspecific symptoms such as high-grade fever, headache, retro-orbital pain, myalgia, vomiting, abdominal pain, rash, and lethargy, making early diagnosis challenging, particularly in resource-limited settings.[5] Unlike adults, children may deteriorate rapidly during the critical phase of illness, usually occurring around the time of defervescence, necessitating close clinical monitoring and timely intervention.[6] Recognition of warning signs including persistent vomiting, severe abdominal pain, mucosal bleeding, fluid accumulation, hepatomegaly, and altered sensorium is essential for preventing progression to severe dengue and reducing mortality.[7]

Dengue continues to impose a substantial burden on healthcare systems, especially during seasonal outbreaks when pediatric admissions increase significantly. Although no specific antiviral therapy is currently available, advances in supportive care,

fluid management strategies, laboratory monitoring, and evidence-based clinical guidelines have markedly improved patient outcomes over recent years.[8] Early diagnosis using rapid antigen detection tests, serological assays, and molecular techniques has facilitated prompt clinical decision-making and risk stratification. Furthermore, evolving research on dengue vaccines, host immune responses, biomarkers of disease severity, and innovative vector-control interventions has opened new avenues for disease prevention and management.[9]

Effective management of dengue fever in children relies on meticulous assessment of hydration status, judicious fluid replacement, monitoring for complications, and timely escalation of care when warning signs or shock develop. The implementation of WHO-recommended classification systems and treatment protocols has significantly contributed to reducing case fatality rates in pediatric populations worldwide.[10] Therefore, a comprehensive understanding of the clinical features, warning signs, complications, and recent management updates is crucial for pediatricians and healthcare professionals involved in the care of affected children. This review aims to provide an updated overview of the epidemiology, clinical manifestations, diagnostic approaches, and contemporary management strategies for dengue fever in children.

METHODOLOGY

This narrative review was conducted through a comprehensive literature search of peer-reviewed articles published in major biomedical databases including PubMed, Scopus, Google Scholar, Embase, and Cochrane Library. Keywords used included “pediatric dengue,” “dengue fever in children,” “warning signs,” “fluid management,” “dengue shock syndrome,” “severe dengue,” “complications,” and “management updates.”

Studies published in English between 2015 and 2025 were reviewed. Relevant randomized controlled trials, systematic reviews, meta-analyses, observational studies, WHO guidelines, and consensus statements were included. Emphasis was placed on evidence related to pediatric clinical manifestations, warning signs, fluid therapy protocols, complications, biomarkers, and emerging therapeutic interventions.

Literature Review

EPIDEMIOLOGY

Dengue fever has emerged as one of the fastest-growing vector-borne viral diseases worldwide, representing a major public health challenge in tropical and subtropical regions. Over the past five decades, the global incidence of dengue has increased dramatically due to rapid urbanization, population growth, globalization, climate variability, and the expansion of mosquito breeding habitats.[11] Current estimates suggest that hundreds of millions of dengue virus infections occur annually, with a substantial proportion affecting the pediatric population. Children, particularly infants and young adolescents, constitute a vulnerable group because of their developing immune systems and limited physiological reserve to cope with severe disease manifestations.[12] Epidemiological studies have consistently demonstrated that infants experience disproportionately high rates of hospitalization and severe dengue compared with older children. This increased susceptibility is attributed partly to the presence of waning maternal antibodies, which may enhance viral replication through antibody-dependent enhancement mechanisms, and partly to the immature cardiovascular system of infants, which is less capable of compensating for plasma leakage and circulatory instability.[13] Consequently, infants are at greater risk of developing dengue shock syndrome and severe plasma leakage during the critical phase of illness.

Dengue virus transmission is maintained primarily through the human–mosquito–human cycle, with infected humans serving as the principal reservoir of infection. The disease is endemic across large areas of Asia, Latin America, Africa, and the Western Pacific, where climatic conditions favor mosquito survival and reproduction. The principal vector, *Aedes aegypti*, thrives in urban environments and breeds in artificial water containers located near human dwellings. However, *Aedes albopictus*, a secondary vector with greater adaptability to temperate climates, has expanded its geographical distribution considerably over recent decades. This species has been implicated in local outbreaks and autochthonous transmission in several regions of Europe and other previously non-endemic areas.[14] The increasing movement of people and goods across international borders, combined with rising global temperatures and changing rainfall patterns, is facilitating the spread of both vectors and dengue viruses into new geographical territories. As a result, sporadic outbreaks and locally acquired cases are being reported with increasing frequency in regions where dengue was historically absent, highlighting the growing global importance of dengue surveillance and vector-control programs.[15]

PATHOGENESIS

Dengue fever is caused by infection with any one of four antigenically distinct serotypes of dengue virus (DENV-1, DENV-2, DENV-3, and DENV-4), which belong to the genus *Flavivirus* within the family *Flaviviridae*. Following the bite of an infected *Aedes* mosquito, the virus is inoculated into the skin and initially infects resident dendritic cells, macrophages, and monocytes. These infected cells subsequently migrate to regional lymph nodes, where viral replication intensifies before dissemination into the bloodstream. The incubation

period generally ranges from 4 to 10 days, after which viremia results in widespread systemic infection affecting multiple organs and tissues.[11] During this viremic phase, patients develop the characteristic clinical manifestations of dengue, including fever, headache, myalgia, rash, and constitutional symptoms.

The mechanisms responsible for the broad clinical spectrum of dengue, ranging from asymptomatic infection to life-threatening severe dengue, remain incompletely understood. Primary infection usually induces lifelong immunity against the infecting serotype; however, protection against other serotypes is temporary and incomplete. Secondary infection with a heterologous serotype is recognized as a major risk factor for severe disease because pre-existing cross-reactive but non-neutralizing antibodies may facilitate viral entry into monocytes and macrophages through Fc receptor-mediated uptake, a process known as antibody-dependent enhancement (ADE).[12] This phenomenon amplifies viral replication, increases viremia, and triggers an exaggerated immune response characterized by excessive cytokine and chemokine release. The resulting "cytokine storm" contributes to endothelial dysfunction, increased vascular permeability, plasma leakage, coagulopathy, and shock.[13]

In addition to ADE, dengue viruses possess several mechanisms that enable evasion of host immune defenses. Viral proteins can interfere with innate immune signaling pathways, particularly type I interferon responses, thereby reducing the host's antiviral capacity and facilitating viral persistence during the early stages of infection.[14] Host genetic factors also influence disease susceptibility and severity. Variations in human leukocyte antigen (HLA) alleles, cytokine gene polymorphisms, and other immune-regulatory genes have been associated with differential clinical outcomes. Furthermore, age, nutritional status, underlying comorbidities, viral serotype, and viral load may modulate disease progression and severity.[15] Collectively, these complex interactions between viral virulence factors, host immune responses, and genetic determinants underpin the pathogenesis of dengue and explain the heterogeneous clinical manifestations observed among infected children.

Clinical Course of Dengue Infection

The clinical course of dengue infection in children follows a dynamic and predictable pattern consisting of three distinct phases: the febrile phase, critical phase, and recovery phase. Understanding these stages is essential for timely recognition of disease progression and appropriate clinical intervention, as the transition between phases may occur rapidly and unexpectedly in pediatric patients.[16] The severity of illness is determined not only by the extent of viral replication but also by the host immune response, vascular permeability changes, and fluid balance status throughout the disease course.[17]

Febrile Phase (Days 1–3)

The febrile phase represents the initial stage of dengue infection and usually begins abruptly after an incubation period of 4–10 days. During this phase, children commonly present with sudden-onset high-grade fever, often exceeding 39°C, accompanied by constitutional symptoms such as headache, retro-orbital pain, myalgia, arthralgia, malaise, and facial flushing.[16] A transient maculopapular or erythematous rash may appear early in the illness and can be associated with pruritus. Gastrointestinal manifestations including nausea, vomiting, anorexia, and abdominal discomfort are frequently observed in children and may contribute to dehydration if oral intake becomes inadequate. Mild hemorrhagic manifestations such as petechiae, easy bruising, epistaxis, or gum bleeding may occur due to thrombocytopenia and capillary fragility.[17]

Laboratory abnormalities during the febrile phase commonly include leukopenia resulting from transient bone marrow suppression and mild thrombocytopenia due to increased peripheral destruction and platelet consumption. Rising hematocrit values may begin to emerge toward the end of the febrile phase, signaling the onset of plasma leakage. Although most patients remain clinically stable during this stage, careful monitoring is essential because progression to the critical phase often coincides with the subsidence of fever rather than persistent hyperthermia.[18]

Critical Phase (Days 4–6)

The critical phase typically occurs around the time of defervescence, when body temperature begins to normalize. Contrary to expectations, the disappearance of fever does not signify recovery; instead, it marks the period of greatest clinical risk. During this phase, increased capillary permeability results in leakage of plasma from the intravascular compartment into serosal cavities and interstitial tissues.[19] The resulting plasma loss leads to hemoconcentration, reduced circulating blood volume, and compromised tissue perfusion. Clinical manifestations may include severe abdominal pain, persistent vomiting, lethargy, restlessness, cold extremities, delayed capillary refill, tachycardia, and narrowing pulse pressure. Progressive plasma leakage may produce pleural effusions, ascites, gallbladder wall edema, and generalized edema, all of which can be detected clinically or by ultrasonography.[20]

If plasma loss becomes substantial and remains untreated, children may develop dengue shock syndrome characterized by hypotension, impaired organ perfusion, metabolic acidosis, and circulatory collapse. This phase is associated with the highest risk of mortality and therefore requires intensive monitoring of vital signs, urine output, hematocrit

levels, and platelet counts. Severe bleeding manifestations and organ dysfunction may also emerge during this stage, particularly in patients with prolonged shock or significant coagulopathy.[21]

Recovery Phase (Days 7–10)

The recovery phase begins once vascular permeability gradually returns to normal and leaked plasma is reabsorbed into the intravascular compartment. Clinical improvement becomes evident with stabilization of hemodynamic parameters, restoration of peripheral perfusion, improved appetite, enhanced activity levels, and increasing urine output.[22] Hematocrit values progressively normalize as intravascular volume is restored, while platelet counts begin to rise, often reaching normal levels within several days. Many children develop a characteristic convalescent rash described as "islands of white in a sea of red," reflecting cutaneous vascular changes during recovery. Mild bradycardia and transient electrocardiographic abnormalities may occasionally occur but generally resolve spontaneously.[22]

Although recovery is usually uneventful, excessive intravenous fluid administration during the preceding critical phase can result in fluid overload once reabsorption begins. Pulmonary edema, respiratory distress, pleural fluid accumulation, and cardiac strain may develop if fluid therapy is not carefully adjusted. Therefore, vigilant monitoring and gradual reduction of intravenous fluids are essential during this stage to prevent iatrogenic complications.[23]

Warning Signs in Children

Early recognition of warning signs is critical because clinical deterioration in pediatric dengue can occur within a matter of hours. The World Health Organization identifies specific warning signs that indicate increased risk of progression to severe dengue and necessitate closer observation or hospitalization.[19]

Persistent Vomiting

Repeated or persistent vomiting reflects significant gastrointestinal involvement and may indicate evolving plasma leakage. Continuous vomiting contributes to dehydration, electrolyte disturbances, and inability to maintain adequate oral fluid intake, thereby increasing the risk of circulatory compromise.[20]

Severe Abdominal Pain or Tenderness

Severe abdominal pain is one of the most important predictors of severe dengue. It may result from hepatic inflammation, mesenteric ischemia, gallbladder edema, acalculous cholecystitis, or increasing serosal fluid accumulation. The presence of progressive abdominal tenderness often precedes shock and should prompt immediate reassessment.[21]

Clinical Fluid Accumulation

Evidence of fluid accumulation indicates significant capillary leakage and worsening disease severity. Clinical manifestations may include pleural effusion causing tachypnea or reduced breath sounds, ascites resulting in abdominal distension, and generalized edema due to extensive plasma loss. Ultrasonography is particularly useful for detecting early fluid accumulation before overt clinical signs become apparent.[22]

Mucosal Bleeding

Mucosal bleeding may present as epistaxis, gingival bleeding, menorrhagia, hematemesis, or gastrointestinal hemorrhage. Although mild bleeding can occur in uncomplicated dengue, increasing mucosal hemorrhage often signifies worsening thrombocytopenia, coagulopathy, or severe vascular dysfunction.[23]

Lethargy or Restlessness

Altered behavior, excessive sleepiness, irritability, or restlessness may indicate cerebral hypoperfusion secondary to intravascular volume depletion. Such neurological changes frequently precede overt shock and should never be overlooked in children with suspected dengue infection.[20]

Hepatomegaly

Hepatic enlargement greater than 2 cm below the right costal margin is considered clinically significant and may reflect hepatic inflammation, congestion, or severe systemic involvement. Hepatomegaly has been associated with increased disease severity and a higher likelihood of progression to severe dengue.[24]

Rising Hematocrit with Rapid Platelet Fall

A rising hematocrit accompanied by rapidly decreasing platelet counts is one of the most reliable indicators of ongoing plasma leakage. This laboratory pattern reflects hemoconcentration caused by intravascular fluid loss and often precedes clinical deterioration, making serial monitoring essential for risk assessment.[21]

Severe Dengue

Severe dengue represents the most life-threatening form of the disease and is defined by severe plasma leakage, severe bleeding, or significant organ involvement. Prompt recognition and aggressive supportive management are crucial to reducing morbidity and mortality.[19]

Severe Plasma Leakage

Severe plasma leakage may culminate in dengue shock syndrome and respiratory distress. Progressive intravascular volume depletion leads to hypotension, narrow pulse pressure, tissue hypoxia, metabolic acidosis, and multiorgan hypoperfusion. Respiratory compromise may occur because of extensive pleural effusions or pulmonary edema.[24]

Severe Hemorrhage

Severe bleeding can affect multiple organ systems and may manifest as hematemesis, melena, profound epistaxis, pulmonary hemorrhage, vaginal bleeding, or intracranial hemorrhage. Such

complications are associated with severe thrombocytopenia, coagulation abnormalities, hepatic dysfunction, and prolonged shock.[25]

Severe Organ Involvement

Hepatic: Severe hepatitis and acute liver failure may develop due to direct viral injury, immune-mediated inflammation, and hepatic hypoperfusion. Marked elevations of aminotransferases and coagulopathy are common indicators of severe hepatic involvement.[24]

Neurological: Neurological complications include encephalopathy, encephalitis, seizures, intracranial bleeding, and altered consciousness. These manifestations may result from direct viral neuroinvasion, cerebral edema, metabolic disturbances, or systemic inflammatory responses.[25]

Cardiac: Myocarditis, arrhythmias, ventricular dysfunction, and acute heart failure have been increasingly recognized in severe pediatric dengue. Cardiac involvement may further compromise circulatory stability and worsen shock.[24]

Renal: Acute kidney injury may occur secondary to shock, rhabdomyolysis, hemolysis, or direct renal involvement. Electrolyte disturbances such as hyponatremia and metabolic acidosis frequently accompany severe renal dysfunction.[25]

Fluid Management in Pediatric Dengue

Fluid therapy remains the cornerstone of dengue management because no specific antiviral treatment currently exists. Appropriate fluid administration can prevent progression to shock, maintain tissue perfusion, and substantially reduce mortality. However, both inadequate and excessive fluid therapy may result in adverse outcomes, necessitating careful clinical assessment and continuous monitoring.[19]

Principles of Fluid Therapy

The primary objectives of fluid management are to maintain effective circulatory volume, prevent or reverse shock, preserve adequate organ perfusion, and avoid fluid overload. Treatment strategies must be individualized according to disease phase, hydration status, hemodynamic parameters, hematocrit trends, urine output, and presence of warning signs. Isotonic crystalloid solutions are generally preferred for initial resuscitation because of their effectiveness and safety profile.[20]

Dengue Without Warning Signs

Children with dengue who do not exhibit warning signs can usually be managed safely on an outpatient basis with close follow-up and careful caregiver education. Management focuses on maintaining adequate hydration, controlling fever, monitoring disease progression, and recognizing early indicators of deterioration.[21]

Oral rehydration therapy forms the foundation of treatment and should be encouraged throughout the illness. Recommended fluids include oral rehydration solutions, coconut water, fruit juices, soups, milk preparations, and plain water. Adequate hydration helps compensate for insensible fluid losses and reduces the risk of intravascular depletion during the critical phase. Fever should be treated with paracetamol at appropriate doses, while nonsteroidal anti-inflammatory drugs (NSAIDs) and aspirin should be avoided because of their potential to increase bleeding risk and exacerbate gastric irritation. Daily clinical evaluation and laboratory monitoring, particularly during the transition to the critical phase, are essential for detecting warning signs and ensuring timely referral when necessary.[22]

Dengue With Warning Signs

Children presenting with warning signs of dengue require hospital admission because of the increased risk of progression to severe plasma leakage, shock, hemorrhage, and organ dysfunction. Close clinical observation during this period is crucial, as deterioration can occur rapidly within a few hours, particularly during the transition from the febrile to the critical phase.[26] Hospital management aims to maintain adequate intravascular volume, prevent circulatory collapse, monitor for complications, and promptly identify evidence of severe dengue. Continuous assessment of vital signs, hydration status, urine output, hematocrit trends, and platelet counts forms the cornerstone of inpatient care.[27]

Intravenous Fluid Therapy

Intravenous fluid therapy remains the most important intervention for children with dengue and warning signs. Isotonic crystalloid solutions such as normal saline and Ringer lactate are recommended as first-line fluids because they effectively restore intravascular volume while minimizing adverse effects.[26] Initial infusion rates generally range between 5–7 mL/kg/hour, although adjustments should be individualized according to the patient's hemodynamic status, degree of plasma leakage, and laboratory findings. Frequent reassessment every 1–4 hours is essential to ensure adequate perfusion without precipitating fluid overload. Monitoring parameters include pulse rate, blood pressure, capillary refill time, respiratory status, urine output, peripheral perfusion, and serial hematocrit measurements.[28] Rising hematocrit despite fluid administration may indicate ongoing plasma leakage and necessitate escalation of fluid therapy, whereas a falling hematocrit accompanied by hemodynamic instability should raise concern for occult bleeding.[29]

Management of Dengue Shock Syndrome

Dengue Shock Syndrome (DSS) represents the most severe consequence of plasma leakage and remains a leading cause of mortality among children with dengue infection. Early recognition and aggressive but carefully controlled fluid resuscitation are critical determinants of survival.[30]

Compensated Shock

In compensated shock, children maintain blood pressure despite significant circulatory compromise

through compensatory vasoconstriction and tachycardia. Clinical manifestations include tachycardia, cool extremities, delayed capillary refill, narrowing pulse pressure, restlessness, and decreased urine output. Immediate administration of isotonic crystalloid solution at a dose of 10–20 mL/kg over one hour is recommended.[30] Following fluid administration, reassessment of blood pressure, pulse pressure, urine output, capillary refill, and hematocrit is necessary to determine response and guide subsequent therapy. Successful resuscitation is indicated by improvement in peripheral perfusion, widening pulse pressure, normalization of mental status, and adequate urine production.[31]

Hypotensive Shock

Hypotensive shock indicates advanced circulatory failure and constitutes a medical emergency requiring immediate intervention. Children typically present with profound hypotension, weak peripheral pulses, altered consciousness, severe tachycardia, metabolic acidosis, and evidence of organ hypoperfusion. Rapid fluid resuscitation with a 20 mL/kg crystalloid bolus should be initiated without delay.[31] Repeated boluses may be administered depending on clinical response and serial hematocrit values. In cases of refractory shock associated with persistent plasma leakage despite adequate crystalloid replacement, colloid solutions may be considered to improve intravascular volume expansion. However, their use should be reserved for selected situations and guided by experienced clinicians because excessive fluid administration may worsen outcomes.[32]

Monitoring During Fluid Therapy

Meticulous monitoring is fundamental to successful fluid management in pediatric dengue. Continuous assessment enables clinicians to balance the need for adequate circulatory support against the risk of fluid overload. Key parameters include urine output, pulse pressure, capillary refill time, hematocrit trends, respiratory status, and neurological function.[33]

Parameter	Target
Urine output	≥1 mL/kg/hour
Pulse pressure	>20 mmHg
Capillary refill	<2 seconds
Hematocrit	Stable or gradually decreasing
Mental status	Normal and alert

Maintenance of these targets generally indicates adequate tissue perfusion and successful fluid replacement. Persistent abnormalities warrant reassessment for ongoing plasma leakage, occult hemorrhage, or evolving organ dysfunction.[29]

Prevention of Fluid Overload

Although fluid therapy is lifesaving, excessive administration can result in serious complications once vascular integrity is restored during the recovery phase. Fluid overload may manifest as respiratory distress, pulmonary edema, worsening pleural effusions, elevated jugular venous pressure, hepatomegaly, and oxygen desaturation.[34] Children are particularly vulnerable because of their relatively smaller physiological reserve and increased susceptibility to pulmonary complications. Prevention requires dynamic adjustment of infusion rates based on clinical and laboratory parameters. When evidence of fluid overload develops after recovery has commenced, intravenous fluids should be reduced or discontinued, and carefully supervised diuretic therapy may be considered. Supplemental oxygen and respiratory support should be provided when necessary.[35]

Complications of Pediatric Dengue

Dengue infection can affect virtually every organ system. Although most children recover completely, severe disease may lead to significant morbidity and mortality through hemorrhagic, neurological, cardiac, hepatic, renal, and respiratory complications.[30]

Hemorrhagic Complications

Hemorrhagic manifestations range from mild mucosal bleeding to life-threatening internal hemorrhage. Common presentations include epistaxis, hematemesis, melena, hematuria, menorrhagia, and intracranial bleeding.[36] The risk of severe hemorrhage increases in the presence of profound thrombocytopenia, prolonged shock, disseminated intravascular coagulation, hepatic dysfunction, and metabolic derangements. Bleeding results from a combination of platelet destruction, coagulation abnormalities, endothelial dysfunction, and capillary fragility. Management involves hemodynamic stabilization, correction of coagulation defects, and blood component therapy when clinically indicated.[37]

Dengue Shock Syndrome (DSS)

Dengue Shock Syndrome remains the most common cause of death in pediatric dengue. It results from severe plasma leakage leading to intravascular volume depletion and impaired tissue perfusion. Characteristic clinical features include narrowing pulse pressure, tachycardia, cold clammy extremities, prolonged capillary refill, hypotension, oliguria, and altered mental status.[30] Without prompt treatment, progressive shock may culminate in metabolic acidosis, multiorgan failure, and death. Fortunately, timely recognition and appropriate fluid resuscitation have dramatically reduced mortality rates in specialized pediatric centers.[31]

Neurological Complications

Neurological involvement is increasingly recognized as an important manifestation of severe dengue infection. Complications may arise through direct viral neuroinvasion, immune-mediated injury, metabolic disturbances, cerebral hypoperfusion, or systemic inflammatory

responses.[38] Clinical manifestations include encephalitis, encephalopathy, seizures, meningitis-like syndrome, acute disseminated encephalomyelitis, transverse myelitis, and neuromuscular disorders such as Guillain–Barré syndrome. Neuroimaging and cerebrospinal fluid analysis may aid diagnosis in selected cases. Early recognition and supportive management are essential to minimize neurological sequelae.[38]

Cardiac Complications

Cardiovascular involvement in dengue ranges from asymptomatic myocardial injury to severe myocarditis and heart failure. Reported manifestations include myocarditis, pericarditis, conduction abnormalities, arrhythmias, reduced left ventricular ejection fraction, and cardiogenic shock.[39] Myocardial dysfunction may aggravate circulatory instability and complicate fluid management decisions. Electrocardiography, cardiac biomarkers, and echocardiography are valuable tools for assessing cardiac involvement in severe cases. Continuous cardiac monitoring is recommended for children exhibiting hemodynamic instability or suspected myocardial dysfunction.[39]

Hepatic Complications

Liver involvement is common in dengue infection and varies from mild transaminase elevation to fulminant hepatic failure. Hepatic injury results from direct viral cytopathic effects, immune-mediated inflammation, oxidative stress, and ischemic damage secondary to shock.[37] Children with severe hepatitis may develop jaundice, coagulopathy, hypoglycemia, encephalopathy, and multiorgan dysfunction. Markedly elevated aminotransferase levels correlate with increased disease severity and poorer outcomes. Such patients require intensive monitoring and aggressive supportive management.[40]

Renal Complications

Renal dysfunction is increasingly recognized in severe pediatric dengue. Acute kidney injury may occur secondary to prolonged shock, acute tubular necrosis, rhabdomyolysis, hemolysis, glomerular injury, or immune-mediated mechanisms.[36] Clinical manifestations include oliguria, fluid retention, electrolyte abnormalities, metabolic acidosis, and elevated serum creatinine levels. Early identification and optimization of hemodynamic status are essential to prevent progression to severe renal impairment. Renal replacement therapy may be required in selected critically ill patients.[40]

Respiratory Complications

Respiratory complications are primarily related to plasma leakage and fluid accumulation within the thoracic cavity. Pleural effusions are common during the critical phase and may contribute to respiratory distress, tachypnea, and hypoxemia. Severe cases can develop pulmonary edema or acute respiratory distress syndrome (ARDS), particularly when fluid overload coexists with increased vascular permeability.[35] Mechanical ventilation may become necessary in patients with severe respiratory compromise, refractory hypoxemia, or multiorgan failure. Early detection and judicious fluid management remain the most effective preventive strategies.[34]

Recent Advances in Management

Recent advances in pediatric dengue management focus on earlier diagnosis, improved risk stratification, precision-guided fluid therapy, and preventive vaccination strategies. These developments have substantially improved clinical outcomes and reduced mortality in endemic regions.[26]

Point-of-Care Diagnostic Tests

Rapid diagnostic testing has transformed the early diagnosis of dengue infection. Detection of nonstructural protein-1 (NS1) antigen enables identification of acute dengue during the first few days of illness before antibody development.[27] Point-of-care assays provide rapid results, facilitating earlier triage decisions, appropriate patient monitoring, and reduction of unnecessary hospital admissions. Combined NS1 and serological testing further enhances diagnostic accuracy across different phases of infection.[33]

Biomarker-Based Risk Prediction

Considerable research has focused on identifying biomarkers capable of predicting severe dengue before overt clinical deterioration occurs. Promising candidates include interleukin-6, interleukin-10, angiopoietin-2, soluble vascular endothelial growth factor receptors, serum lactate, and markers of endothelial activation.[32] Elevated concentrations of these biomarkers correlate with plasma leakage, shock, organ dysfunction, and adverse clinical outcomes. Integration of biomarker profiles into clinical decision-making may improve risk stratification and facilitate timely intervention in high-risk children.[36]

Ultrasound-Guided Monitoring

Point-of-care ultrasonography has become an increasingly valuable tool in pediatric dengue management. Ultrasonography can identify pleural effusions, ascites, gallbladder wall edema, and early plasma leakage before these abnormalities become clinically apparent.[35] Early detection allows clinicians to intensify monitoring and adjust fluid therapy proactively, thereby reducing the likelihood of progression to severe disease. Ultrasound-guided assessment has become particularly useful in resource-limited settings where advanced laboratory investigations may not be readily available.[34]

Improved Fluid Algorithms

Contemporary pediatric dengue protocols emphasize individualized fluid administration based on dynamic clinical and laboratory assessments rather than fixed treatment schedules.

Modern algorithms incorporate frequent reassessment of hemodynamic status, serial hematocrit measurements, bedside ultrasonography, and recognition of early fluid overload.[31] These evidence-based approaches have substantially reduced mortality, shortened hospital stays, and minimized complications related to both under-resuscitation and excessive fluid administration.[30]

Dengue Vaccines

Vaccination represents one of the most promising strategies for reducing the future burden of dengue among children. Advances in vaccine development have generated several candidates targeting all four dengue virus serotypes.[28]

CYD-TDV (Dengvaxia)

CYD-TDV (Dengvaxia) was the first licensed dengue vaccine and has demonstrated efficacy in individuals with previous dengue exposure. However, post-licensure studies revealed an increased risk of severe dengue among seronegative recipients, resulting in recommendations restricting its use to persons with documented prior infection.[37]

TAK-003 (Qdenga)

TAK-003 (Qdenga), a live attenuated tetravalent dengue vaccine, has shown encouraging efficacy against symptomatic and hospitalized dengue across multiple serotypes and age groups. Long-term follow-up studies indicate sustained protection and a favorable safety profile, making it a promising option for widespread immunization programs in endemic regions.[39] Continued vaccine development, coupled with effective vector control and public health surveillance, has the potential to substantially reduce pediatric dengue morbidity and mortality worldwide.[40]

Future Directions

Despite substantial advances in the diagnosis, monitoring, and supportive management of pediatric dengue, significant challenges remain in reducing disease burden, preventing severe complications, and achieving long-term control of transmission. Future research and public health strategies are increasingly focused on developing innovative preventive and therapeutic approaches that address both viral pathogenesis and host responses. The integration of advances in immunology, molecular biology, artificial intelligence, and vector-control technologies is expected to transform dengue management over the coming decades.

Universal Dengue Vaccines

One of the most important priorities in dengue research is the development of a universal vaccine capable of providing long-lasting protection against all four dengue virus serotypes irrespective of previous infection status. Current vaccine candidates have demonstrated varying levels of efficacy among different serotypes and populations, highlighting the complexity of achieving balanced immune protection. Future vaccine platforms aim to induce durable neutralizing antibody responses while minimizing the risk of antibody-dependent enhancement, which has been implicated in severe secondary infections. Advances in recombinant vaccine technology, messenger RNA (mRNA)-based platforms, viral-vector vaccines, and next-generation tetravalent formulations hold considerable promise for improving vaccine efficacy and safety. A universally effective vaccine would represent a major breakthrough in reducing pediatric morbidity, hospitalization rates, and dengue-related mortality worldwide.

Host-Directed Therapies

Increasing understanding of dengue immunopathogenesis has opened new opportunities for host-directed therapeutic interventions. Severe dengue is largely driven by dysregulated immune activation, excessive cytokine release, endothelial dysfunction, and increased vascular permeability rather than direct viral cytotoxicity alone. Future therapeutic strategies may therefore target inflammatory pathways responsible for plasma leakage and organ injury. Potential approaches include modulation of cytokine signaling, stabilization of endothelial barriers, inhibition of complement activation, and regulation of immune-cell responses. Such therapies could potentially reduce the progression from uncomplicated dengue to severe dengue shock syndrome and multiorgan dysfunction. Identification of safe and effective host-directed treatments may significantly improve outcomes in high-risk pediatric patients.

Artificial Intelligence-Based Prediction Models

Artificial intelligence (AI) and machine learning technologies are emerging as powerful tools for improving early diagnosis and risk stratification in dengue infection. By analyzing large datasets comprising demographic information, clinical symptoms, laboratory findings, imaging results, and biomarker profiles, AI-based models may accurately predict disease severity before overt clinical deterioration occurs. These predictive systems could assist clinicians in identifying children at risk for shock, severe hemorrhage, or organ dysfunction, thereby enabling earlier intervention and optimized allocation of healthcare resources. Integration of AI algorithms into electronic health records and mobile health applications may facilitate real-time clinical decision support, particularly in resource-constrained settings where specialist expertise is limited.

Precision Fluid Therapy

Although fluid management remains the cornerstone of dengue treatment, determining the optimal type, volume, and duration of fluid therapy continues to be challenging. Future approaches are expected to move toward precision fluid therapy, where treatment is individualized according to

patient-specific physiological parameters rather than standardized protocols alone. The incorporation of biomarkers of endothelial dysfunction, microcirculatory assessment, point-of-care ultrasonography, advanced hemodynamic monitoring, and continuous physiological surveillance may allow clinicians to tailor fluid administration more accurately. Such individualized strategies could minimize both under-resuscitation and fluid overload, thereby reducing complications and improving survival rates among children with severe dengue.

Novel Antiviral Agents

The absence of a specific antiviral treatment remains one of the most significant unmet needs in dengue management. Current therapy is largely supportive, emphasizing fluid replacement and monitoring for complications. Ongoing research is investigating antiviral compounds that target various stages of the dengue viral life cycle, including viral entry, replication, assembly, and release. Promising candidates include small-molecule inhibitors, monoclonal antibodies, RNA-based therapeutics, and host-factor modulators. Successful development of effective antiviral agents could shorten disease duration, reduce viral load, limit immune-mediated complications, and prevent progression to severe disease. Combination therapies targeting both viral replication and host inflammatory pathways may offer additional therapeutic benefits in the future.

Integrated Vector Control

Sustainable reduction of dengue transmission will require innovative and integrated vector-control strategies beyond conventional insecticide-based approaches. Emerging technologies include the release of *Wolbachia*-infected mosquitoes, genetically modified mosquitoes with reduced reproductive capacity, sterile insect techniques, targeted larval source management, and environmentally friendly biological control methods. Advances in geographic information systems, remote sensing, climate modeling, and digital surveillance platforms may further enhance vector monitoring and outbreak prediction. Community participation, improved sanitation, and public health education will continue to play essential roles in comprehensive vector-control programs. The successful integration of these technologies has the potential to significantly reduce dengue transmission in endemic regions and prevent future epidemics.

Collectively, these future directions reflect a shift toward precision medicine, predictive analytics, innovative therapeutics, and sustainable prevention strategies. Continued investment in multidisciplinary research, global collaboration, and public health infrastructure will be essential for achieving meaningful reductions in the burden of dengue among children and ultimately advancing toward long-term disease control.

DISCUSSION

Dengue fever continues to represent one of the most significant causes of pediatric morbidity and hospitalization across tropical and subtropical regions, particularly in Southeast Asia, Latin America, and parts of Africa. The increasing incidence of dengue over recent decades has been attributed to rapid urbanization, population expansion, globalization, environmental changes, and the widespread distribution of *Aedes* mosquito vectors.[41] Children are especially vulnerable to severe manifestations of dengue because of age-related differences in immune responses, vascular physiology, and fluid balance. Epidemiological studies have demonstrated that pediatric patients frequently experience a more abrupt transition from the febrile phase to the critical phase, making early recognition and timely intervention essential for preventing adverse outcomes.[42] Although the majority of children recover uneventfully with appropriate supportive care, severe dengue remains a substantial contributor to hospital admissions, intensive care utilization, and mortality in endemic regions.

The introduction of the revised World Health Organization (WHO) dengue classification system has significantly improved clinical risk stratification and patient management. Unlike previous classifications that focused primarily on dengue fever, dengue hemorrhagic fever, and dengue shock syndrome, the revised system emphasizes the identification of warning signs that predict progression to severe disease. Clinical indicators such as persistent vomiting, severe abdominal pain, mucosal bleeding, lethargy, hepatomegaly, fluid accumulation, and rising hematocrit accompanied by falling platelet counts have been shown to correlate strongly with severe plasma leakage and impending shock.[43] Several validation studies have confirmed that the warning-sign approach improves sensitivity for detecting severe dengue and facilitates earlier referral, hospitalization, and initiation of supportive therapy. Furthermore, this classification system has enhanced clinical decision-making in both tertiary care centers and resource-limited healthcare settings, thereby contributing to improved patient outcomes.[44]

The pathophysiology of severe dengue is closely linked to increased vascular permeability, plasma leakage, coagulopathy, and dysregulated host immune responses. Research over the past decade has highlighted the critical role of endothelial dysfunction, cytokine activation, complement pathways, and antibody-dependent enhancement in the development of severe disease manifestations.[45] Plasma leakage remains the hallmark of severe dengue and is responsible for the development of

pleural effusions, ascites, hemoconcentration, and circulatory collapse. In pediatric patients, the limited physiological capacity to compensate for intravascular volume depletion further increases susceptibility to shock and organ hypoperfusion. Consequently, prompt recognition of the critical phase and meticulous monitoring of fluid status are fundamental aspects of management.[46]

Fluid therapy remains the cornerstone of treatment and is the single most important intervention associated with reductions in dengue-related mortality. Multiple clinical trials and observational studies have demonstrated that judicious administration of isotonic crystalloid solutions effectively restores circulating volume, maintains tissue perfusion, and reverses shock in the majority of pediatric patients.[47] However, successful fluid management requires careful balancing between adequate resuscitation and avoidance of fluid overload. Excessive intravenous fluid administration may result in pulmonary edema, worsening pleural effusions, respiratory distress, and prolonged hospitalization, particularly during the recovery phase when extravasated fluid is reabsorbed into the circulation. Dynamic monitoring of pulse pressure, capillary refill time, urine output, hematocrit, respiratory status, and mental status therefore remains essential for guiding fluid adjustments and optimizing outcomes.[48]

Advances in diagnostic technologies have substantially improved the early identification and management of dengue infection. Rapid NS1 antigen assays and combined serological testing permit earlier diagnosis during the acute febrile phase, facilitating timely clinical assessment and appropriate triage. In addition, point-of-care ultrasonography has emerged as a valuable bedside tool for detecting plasma leakage before overt clinical manifestations develop. Ultrasonographic findings such as pleural effusion, ascites, and gallbladder wall thickening have demonstrated utility in predicting progression to severe disease and guiding fluid management decisions.[49] Parallel developments in biomarker research have identified several promising candidates, including interleukin-6, interleukin-10, angiopoietin-2, vascular endothelial growth factor-related markers, and serum lactate levels, which may provide early indicators of disease severity and impending complications. Integration of these biomarkers into clinical algorithms could enhance risk stratification and facilitate individualized management approaches in the future.

The emergence of dengue vaccines represents a major milestone in disease prevention. Vaccination strategies have the potential to substantially reduce infection rates, hospitalization, and severe disease burden among children living in endemic regions. Recent vaccine candidates have demonstrated encouraging efficacy against multiple serotypes and have expanded opportunities for large-scale immunization programs. Nevertheless, challenges remain regarding long-term effectiveness, protection against all circulating serotypes, vaccine deployment strategies, and accessibility in low-resource settings. Concurrently, innovative vector-control approaches, including *Wolbachia*-infected mosquitoes, genetic modification technologies, and integrated environmental management programs, offer promising avenues for reducing transmission and outbreak frequency.[50]

Despite notable progress in clinical management and prevention, several challenges continue to hinder optimal dengue control. Limited access to advanced laboratory diagnostics, inadequate healthcare infrastructure in resource-constrained regions, delayed healthcare-seeking behavior, and variability in clinical expertise contribute to persistent morbidity and mortality. Furthermore, the absence of specific antiviral therapies means that treatment remains predominantly supportive. Climate change, increasing urbanization, population mobility, and expansion of mosquito habitats are expected to intensify dengue transmission and increase the frequency of outbreaks in the coming decades. Future research should therefore focus on the development of universal dengue vaccines, targeted antiviral agents, host-directed therapies, precision fluid management protocols, and artificial intelligence–based predictive models capable of identifying severe disease before clinical deterioration becomes evident. A comprehensive approach combining improved clinical care, vaccination, innovative vector control, public health surveillance, and community engagement will be essential for reducing the global burden of pediatric dengue and achieving sustainable disease control.

CONCLUSION

Dengue fever continues to pose a significant threat to child health in endemic regions worldwide. The disease exhibits a wide spectrum of clinical manifestations ranging from uncomplicated febrile illness to life-threatening shock and multiorgan dysfunction. Early identification of warning signs—including persistent vomiting, severe abdominal pain, mucosal bleeding, lethargy, hepatomegaly, and rising hematocrit—is crucial for preventing progression to severe dengue. Appropriate fluid management remains the cornerstone of treatment and requires meticulous monitoring to maintain adequate perfusion while avoiding fluid overload. Complications such as dengue shock syndrome, severe hemorrhage, neurological involvement, myocarditis, liver failure, and acute kidney injury necessitate prompt recognition and specialized care. Recent advances in rapid diagnostics, point-of-care ultrasonography, biomarker research, and vaccine development have

improved clinical outcomes. Continued emphasis on early diagnosis, evidence-based management protocols, vaccination strategies, and integrated vector control programs is essential to reduce dengue-related morbidity and mortality among children in endemic settings.

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