

REVIEW ARTICLE

Dengue Virus: A Human Threat: Review of Literature

Lavanya J¹, Swaropprani N.B.², Pooja Rao³, Lohith Kumar R⁴

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ABSTRACT

Most Rapidly spreading arboviral infection across various states of our country is Dengue Fever. It is spread by Aedes aegypti mosquito which harbors Dengue virus, which is a RNA virus belonging to family Flaviviridae. The patient affected by Dengue presents with asymptomatic infection to complications like Dengue haemorrhagic fever and Dengue Shock Syndrome. Most common manifestations include high fever of acute onset, muscle and joint pain, cutaneous rash, myalgia, hemorrhagic episodes and circulatory rash. Early and accurate diagnosis is critical to reduce mortality.

KEYWORDS

• Dengue • Dengue hemorrhagic fever • Dengue shock syndrome • Aedes aegypti
• RNA Virus • Sterile insect technique • Dengvaxia

INTRODUCTION

Dengue virus belongs to Flaviviridae family and is a member of genus Flavivirus, an arthropode-borne virus that includes four serotypes (DEN-1, DEN-2, DEN-3, DEN-4). Recently DEN-5 serotype has been identified. In north, Central and South America and the Caribbean island, more than 11 million cases of dengue have been reported in 2024.

In the United States public health authorities declared an outbreak in March 2024.¹ In India The first reported case of Dengue like illness was in 1780 in Madras.²

CLASSIFICATION

According to WHO, Dengue Fever is classified into two groups: Uncomplicated and Severe.

AUTHOR'S AFFILIATION:

¹ Associate Professor & In-charge Head, Department of Microbiology, Chikkamagaluru Institute of Medical Sciences, Chikkamagaluru, Karnataka, India.

² Professor, Department of Microbiology, Subbaiah Institute of Medical Sciences, Shivamogga, Karnataka, India.

³ Associate Professor, Department of Microbiology, Kasturba Medical College, Mangalore, Karnataka, India.

⁴ Associate Professor & In-charge Head, Department of Forensic Medicine, Chikkamagaluru Institute of Medical Sciences, Chikkamagaluru, Karnataka, India.

CORRESPONDING AUTHOR:

Lavanya J, Associate Professor & In-charge Head, Department of Microbiology, Chikkamagaluru Institute of Medical Sciences, Chikkamagaluru, Karnataka, India.

E-mail: lavanya1126@gmail.com

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Severe cases are those with excessive hemorrhage, organ impairment or severe plasma escape.³

According to 1997 classification, Dengue can be divided into undifferentiated fever, DF, and DHF. DHF was further classified into grades I-IV.

Grade I: Only mild bruising or a positive tourniquet test.

Grade II: Spontaneous bleeding into skin and elsewhere.

Grade III: Clinical sign of shock.

Grade IV: Severe shock-feeble pulse, and blood pressure cannot be recorded. (Here grades III and IV comprise DSS).³

Undifferentiated fever

This stage often remains undiagnosed as it is difficult to differentiate from numerous other viral diseases. It is mostly seen in primary infection but may also occur following secondary infection.

Dengue Fever

Follows both primary and secondary infections and most frequently encountered in adults and older children. Onset is characterized by biphasic fever, high grade fever lasting for 3 days to 1 week. Dengue is also known as breakbone fever because of associated myalgia and pain in joints. During the 1st 1-2 days of fever, transient facial flushing erythema appears as an initial rash, which is the result of capillary dilatation. The second rash appears 3-7 days following fever and presents as maculopapular or morbilliform eruption which is asymptomatic. Sometimes a typical appearance of "white islands in the sea of red" is seen due to merging of individual lesions presenting as widespread confluent erythematous areas with pinpoint bleeding spots and rounded island of sparing.⁴

Dengue haemorrhagic fever

DHF is most frequently seen during a secondary dengue infection.⁵ However, It can also occur during a primary infection in case of Infants due to maternally attained dengue antibodies.⁶ The proposed diagnostic criteria for DHF includes:⁷

Clinical parameters:

a Acute-onset febrile phase - high-grade fever lasting from 2 days to 1 week.

Haemorrhagic episodes (at least one of the following forms): Petechiae, purpura, epistaxis, gingival and mucosal bleeding, GIT or injection site, hematemesis and/or malena Positive tourniquet and hepatomegaly.

b Laboratory parameters: Thrombocytopenia (platelet count <100,000/cu mm).

The haemorrhagic episodes in DHF are associated with multifactorial pathogenesis. Vasculopathy, deficiency and dysfunction of platelets and defects in the blood coagulation pathways are the attributed factors. Decreased production of platelets and increased destruction of platelets may result in thrombocytopenia in DHF. Haemorrhage results due to impaired platelet function causing the blood vessels to become fragile.

The clinical course of DHF is characterized by three phases: Febrile phase, plasma leakage phase, and convalescent phase. characterizes the commencement of the febrile phase is characterised by acute onset of high-grade fever along with constitutional signs and facial erythema. The initial febrile illness is marked by a morbilliform rash and haemorrhagic tendencies. The fever persists for 2 days to 1 week and then drops to normal or subnormal levels when the patient either convalesces or advances to the plasma leakage phase. Plasma leakage phase is characterised by frank shock with low pulse pressure, cyanosis, hepatomegaly, pleural and pericardial effusions, and ascites. Severe ecchymosis and gastrointestinal bleeding followed by epistaxis may also be noted in a few cases. Bradycardia, confluent petechial rashes, erythema, and pallor are seen during this phase.

Dengue shock syndrome

DSS is defined as DHF accompanied by a unstable pulse, narrow pulse pressure (<20 mmHg), restlessness, cold, clammy skin, and circumoral cyanosis. Progressively worsening shock, multiorgan damage, and disseminated intravascular coagulation account for a high mortality rate associated with DSS. The shock persists for a short span of time and the patient promptly recovers with supportive therapy.^{8,9}

Diagnosis

Clinicians should initiate appropriate management for all suspected dengue cases without delay, monitoring for signs of shock

and complications related to plasma leakage and organ damage. Clinical samples can be sent to state health departments or commercial laboratories for diagnostic testing.

The following laboratory tests should be performed:

- Complete blood cell (CBC) count
- Metabolic panel
- Serum protein and albumin levels
- Liver panel
- Coagulation profile and disseminated intravascular coagulation (DIC) panel

Characteristic findings in dengue fever are thrombocytopenia (platelet count $<100 \times 10^9/L$), leukopenia, and mild-to-moderate elevation of liver enzymes like aspartate aminotransferase and alanine aminotransferase values. Enzyme levels begin to rise during the early stage and peak during the second week.¹³

A haematocrit level increase greater than 20% is a sign of haemoconcentration and precedes shock. Monitoring of haematocrit level should be done at least every 24 hours to help in early identification of dengue haemorrhagic fever and every 3-4 hours in case of severe dengue haemorrhagic fever or dengue shock syndrome.

In patients with dengue haemorrhagic fever, the following may be present:

- Increased haematocrit level secondary to plasma extravasation and/or third-space fluid loss
- Hypoproteinemia
- Prolonged prothrombin time
- Prolonged activated partial thromboplastin time
- Decreased fibrinogen
- Increased amount of fibrin split products

Signs of early coagulopathy may be as subtle as a guaiac test that is positive for occult blood in the stool. Guaiac testing for occult blood in stool should be performed on all patients in whom dengue virus infection is suspected.

In cases of severe dengue haemorrhagic fever or dengue shock syndrome, typing and crossmatching of blood should be performed because blood products may be required.

Urinalysis identifies hematuria. Cultures of blood, urine, CSF, and other body fluids

should be performed as necessary to exclude or confirm other potential causes of the patient's condition.

Arterial blood gas should be assessed in patients with severe cases to assess pH, oxygenation, and ventilation.

Electrocardiography may demonstrate nonspecific changes as a result of fever, electrolyte disturbances, tachycardia, or medications.

Biopsy of the skin lesions in patients with nonfatal, uncomplicated dengue fever reveals an abnormality of the small blood vessels. Endothelial swelling, perivascular edema, and mononuclear cell infiltration are the primary histologic findings.

Perform chest radiography to look for pleural effusions and bronchopneumonia. Right-sided pleural effusion is typical. Bilateral pleural effusions are common in patients with dengue shock syndrome. Head computed tomography without contrast may be indicated in patients with altered level of consciousness, to detect intracranial bleeding or cerebral edema from dengue hemorrhagic fever.

Since January 2010, dengue has been a reportable illness in all states in the United States. Report known or suspected cases of dengue fever, dengue hemorrhagic fever, or dengue shock syndrome to public health authorities. Such reports should include the following:

- Patient demographics and recent travel history
- Case classification
- Date of onset of illness
- Whether hospitalization was necessary
- Outcome

When multiple patients are involved, reports should include the number of cases of dengue fever and severe dengue stratified by age, number of confirmed cases and serotypes, and number of hospitalizations and deaths.

Pregnant woman exhibiting symptoms, and residing in or has traveling to a region where Zika is a risk, molecular tests for Zika along with dengue testing must be performed.^{14,15}

Differential Diagnosis

There are many other illnesses which can present similar to Dengue fever in the

early course of disease making the clinical diagnosis of Dengue fever challenging. Other differential diagnoses include Measles, Influenza, Zika virus disease, West Nile Infection, Chikungunya, Malaria, Yellow fever, Arenaviruses, Chikungunya Virus, Ebola Virus Infection, Hemorrhagic Fever Viruses, Immune Thrombocytopenia (ITP) in Emergency Medicine, Leptospirosis, Mayaro Fever, Meningitis, Orbivirus, Rickettsial Infection, Rocky Mountain Spotted Fever (RMSF), Roseola Infantum, Ross River Fever, Scarlet Fever, Sinbis Virus, Typhus, Viral Hepatitis, West Nile Virus (WNV) Infection and Encephalitis (WNE).¹⁰

Because the signs and symptoms of dengue fever are nonspecific, attempting laboratory confirmation of dengue infection is important.

Acute Phase (0-7 Days Post Symptom Onset)

1. During acute phase i.e. 0-7 days after symptom onset, laboratory diagnosis of dengue should be performed using serum samples with one of the following combinations: a nucleic acid amplification test (NAAT), such as RT-PCR, paired with an IgM antibody test, or a NS1 ELISA test combined with an IgM detection test. NAAT can detect dengue virus RNA in blood, serum, and plasma, and it typically identifies the specific serotype of the infecting virus. A positive NAAT result is definitive and does not require further confirmation. The presence of the dengue virus non-structural protein 1 (NS1) in serum during acute phase is indicative of current or recent infection. But most importantly, a negative result from either RT-PCR or NS1 ELISA does not rule out dengue infection, while a positive result fulfills the diagnostic criteria set by the National Notifiable Diseases Surveillance System (NNDSS).¹¹

Convalescent Phase (>7 Days Post Symptom Onset)

If the acute sample is negative or unavailable, a convalescent serum sample can be collected for testing. After day 7, IgM ELISA is the recommended primary test, although some patients may still test positive on NAAT or NS1 ELISA. IgM antibodies can remain detectable for three months or longer following infection.

Interpreting Test Results

A positive NAAT or NS1 ELISA confirms

an acute dengue virus infection. The presence of IgM antibodies in a single sample suggests a presumptive recent infection, while a change from negative to positive IgM in paired samples indicates a current infection. Single specimen IgG testing is not recommended for diagnosing acute dengue due to potential cross-reactivity with past infections; however, a change from negative to positive IgG in paired samples can signify a current infection.

Recommended Tests

Molecular tests are effective for detecting dengue virus RNA in symptomatic patients during the first week, while NS1 ELISA tests are similarly sensitive during this acute phase but may lose sensitivity afterward. IgM antibody testing is reliable after day 3, especially when NS1 and PCR results are negative, though interpretation can be complicated by cross-reactivity with other flaviviruses. Plaque Reduction Neutralization Tests (PRNT) can help clarify false-positive IgM results but may not confirm a significant proportion of IgM positives in regions with high prevalence of dengue and Zika virus antibodies.¹²

PREVENTION AND CONTROL STRATEGIES

Three types of dengue prevention and control methods may be distinguished: chemical, biological, and physical control.

In order to prevent and control dengue, physical control entails surveillance to determine risk, assess programs, and give prompt actions. Vectors' behavioral characteristics are essential for identifying and lowering their population density. Community based control initiatives raise awareness and educate the public about mosquito breeding grounds. Genetic techniques like paratransgenesis, which use genetically altered symbiotic bacteria to colonize the vector population and reduce disease transmission, are part of biological control.

In order to reduce vector density and spread vector-borne illnesses in urban areas, the Sterile Insect Technique (SIT) releases male mosquitoes that have been laboratory sterilized. Insecticides, which have been used for decades in chemical control, can have adverse effects on the environment and have caused resistance in the target vector population. By preventing growth and development, insect growth

regulators (IGRs) cause alterations that kill the insect before it reaches adulthood. IGRs, which have been used to combat viral infections carried by *A. aegypti*, include diflubenzuron, endotoxins, and Methoprene.¹⁶⁻¹⁹

DENGUE VACCINE

Dengue virus poses a global health threat, with approximately 390 million dengue infections occurring annually. This rapid spread is attributed to transportation and travel worldwide, increased urbanization, and climate changes that support the proliferation of *Aedes* mosquitoes. Currently, there are no efficient vaccines available to prevent dengue fever. In this study, we report a brief summary of recent advancements in dengue vaccine development.^{20,21}

Cross-immunity across distinct serotypes produces antibodies that aid in viral invasion rather than neutralizing virions. The term “antibody-dependent enhancement” (ADE) describes this hypothesis. In addition to signaling greater viral entry, antiviral responses, both innate and adaptive, are aided by ADE, which promotes viral replication. There is currently no specific antiviral treatment for dengue; instead, supportive care is the mainstay of treatment. In theory, immunization is the best way to avoid contracting dengue fever.²²

Stable efficacy, dependable safety, and cross-protective qualities for all four serotypes are desirable qualities in a dengue vaccine. Nevertheless, the development of dengue vaccines is hampered by the impact of ADE during infections with other serotypes and the absence of appropriate animal models. Investigations have been conducted on five different forms of dengue vaccines: DNA vaccines, recombinant subunit vaccines, live-modified vaccinations, and inactivated vaccines.²³

The development and application of a secure and reliable dengue vaccine may considerably contribute to lowering the incidence of dengue illness worldwide. A few decades later, the first dengue vaccine received a license. Sanofi Pasteur created the Dengvaxia® chimeric live-modified yellow fever/dengue vaccine, which has received approval in a number of nations, including Mexico, Thailand, Brazil, El Salvador, and Costa Rica. The efficacy of

two more vaccine candidates, DENVax and TV003/TV005, has been investigated in Asia and Latin America.^{24,25}

The four dengue virus serotypes (DENV) constituted a threat to control and provided impetus for vaccine research in 2019, as they resulted in 56 million cases of illness and 5000–40,000 deaths over a range of tropical and subtropical countries. The molecular and immunological characteristics of DENV in humans inevitably impact the outcomes of clinical studies for dengue vaccines. Infection with any DENV serotype in the first place usually causes mild to moderate feverish symptoms that last for a short while in people who have never been infected. Lifelong defense against reinfection with the same immunological DENV serotype is offered by these initial infections. A large portion of the severe dengue disease spectrum seen worldwide is caused by secondary infections. Rarely can severe dengue fever develop during the third or fourth DENV infection. The immunological state that protects against secondary infections plays a role in the development of dengue vaccines.^{26,23}

Live-modified dengue virus vaccines are a type of vaccine that protects against dengue fever. These vaccines contain a weakened form of the dengue virus that can stimulate an immune response without causing severe disease. Currently, some live-modified dengue vaccines available include Dengvaxia TV, Dengvaxia® (CYD-TDV), Tetravax (TV003/TV005), TAK-003, TDEN F17/F19 vaccine, Dengue with host range (HR) mutation, KD382, DENVax, and Butantan-DV.²⁷⁻³⁰

Vaccines against the inactivated or dead dengue virus can stimulate the immune system but cannot spread illness. Inactivated vaccines are usually administered in multiple doses. Some inactivated or killed dengue virus vaccines include TDEV PIV and purified psoralen-inactivated virus.³¹ Subunit vaccines comprise particular dengue virus proteins or components that are immunogenic and able to trigger an immune response. These vaccines can target specific proteins, such as envelope (E) proteins and non-structural proteins. Some of the most notable subunit vaccines include V180 (DEN-80E), which often requires multiple doses. Viral vector vaccines utilize harmless viruses, such as adenoviruses or chimeric viruses, to deliver dengue virus

proteins and genes into the body. These viral vectors stimulate an immune response against dengue virus, such as the VEE-Dengue VRPs vaccine.

A DNA vaccine for dengue virus has been developed and is currently undergoing clinical trials. Furthermore, a tetravalent dengue DNA vaccine has been created by mixing equal parts of plasmid DNA that encodes the prM and E genes of each of the four serotypes (1, 2, 3, and 4) that VR1012 simulates. Other nucleic acid-based vaccines include D1ME100 and TVDV (It is significant to remember that different countries may have different dengue vaccination policies and recommendations. Guidelines for the administration of dengue vaccinations and their incorporation into dengue preventive and control tactics are provided by the World Health Organization (WHO). The future outlook for dengue vaccine research and development is promising, with potential advancements in dengue prevention and control.

CONCLUSION

This article provides insight into clinical manifestations, diagnosis, differential diagnosis, prevention and treatment of Dengue.

Conflict of Interest: Nothing to declare

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REFERENCES

1. National Institute of Health. Available at <https://www.niaid.nih.gov/diseases-conditions/dengue-fever>.
2. Gupta N, Srivastava S, Jain A, Chaturvedi UC. Dengue in India. *Indian Journal of Medical Research* 2012; 136; 373-90.
3. Geneva Switzerland: WHO 2009, WHO. Dengue: Guidelines for diagnosis, Treatment, Prevention and Control. Part 1.1.6: Dengue case classification; pp. 10-2.
4. (Waterman SH, Gubler DJ, Dengue fever. *Clinical Dermatology*. 1989; 7;117-22.).
5. (Gubler DJ). Dengue and dengue Hemorrhagic fever. *Clin Microbiol Rev*. 1998;11:480-96.
6. (Ahmed FU, Mahmood CB, Sharma JD, Hoque SM, Zaman R, Hasan MH. Dengue fever and dengue haemorrhagic fever in children the 2000 outbreak in Chittatong, Bangladesh. *Dengue Bulletin*. 2001;25:33-9.
7. (National Institute of Communicable Diseases. Investigation and Control of Outbreaks: Dengue and Dengue Hemorrhagic Fever. 1997.
8. Gurugama P, Garg P, Perera J, Wijewickrama A, Seneviratne SL. Dengue viral infections. *Indian J Dermatol*. 2010;55(1):68-78. doi: 10.4103/0019-5154.60357.
9. Shivpuri A, Shivpuri A. Dengue – An overview. *Dent Med Probl*. 2011;48(2):153-6.
10. Darvin Scott Smith et al, Dengue Differential Diagnoses. *Medscape* Updated: Dec 14, 2024.
11. Chaterji S, Allen JC Jr, Chow A, Leo YS, Ooi EE. Evaluation of the NS1 rapid test and the WHO dengue classification schemes for use as bedside diagnosis of acute dengue fever in adults. *Am J Trop Med Hyg*. 2011 Feb. 84(2):224-8.
12. Potts JA, Rothman AL. Clinical and laboratory features that distinguish dengue from other febrile illnesses in endemic populations. *Trop Med Int Health*. 2008 Nov. 13(11):1328-40.
13. (Bottieau E, Clerinx J, Van den Enden E, Van Esbroeck M, Colebunders R, Van Gompel A. Fever after a stay in the tropics: diagnostic predictors of the leading tropical conditions. *Medicine (Baltimore)*. 2007 Jan. 86(1):18-25.
14. Guideline CDC. Clinical Testing Guidance for Dengue. Centers for Disease Control and Prevention. Available at <https://www.cdc.gov/dengue/hcp/diagnosis-testing>. August 26, 2024; Accessed: December 14, 2024.
15. Malhotra N, Chanana C, Kumar S. Dengue infection in pregnancy. *Int J Gynaecol Obstet*. 2006 Aug. 94(2):131-2.
16. A. Rather, H.A. Parry, J.B. Lone, W.K. Paek, J. Lim, V.K. Bajpai, Y.H. Park Prevention and control strategies to counter dengue virus infection *Front. Cell. Infect. Microbiol.*, 7 (2017), p. 336.
17. W.H. Wang, A.N. Urbina, M.R. Chang, W. Assavalapsakul, P.L. Lu, Y.H. Chen, S.F. Wang. Dengue hemorrhagic fever—a systemic literature review of current perspectives on pathogenesis, prevention and control. *J. Microbiol. Immunol. Infect.*, 53 (6) (2020), pp. 963-978
18. T. Pang, T.K. Mak, D.J. Gubler. Prevention and control of dengue—the light at the end of the

- tunnel. *Lancet Infect. Dis.*, 17 (3) (2017), pp. e79-e87
19. A. Abidemi, N.A. Aziz. Optimal control strategies for dengue fever spread in Johor, Malaysia. *Comput. Methods Prog. Biomed.*, 196 (2020), Article 105585
 20. W.H. Wang, A.N. Urbina, M.R. Chang, W. Assavalapsakul, P.L. Lu, Y.H. Chen, S.F. Wang Dengue hemorrhagic fever—a systemic literature review of current perspectives on pathogenesis, prevention and control *J. Microbiol. Immunol. Infect.*, 53 (6) (2020), pp. 963-978.
 21. H.J. Kuo, K. Lee, J.W. Liu Analyses of clinical and laboratory characteristics of dengue adults at their hospital presentations based on the World Health Organization clinical-phase framework: emphasizing risk of severe dengue in the elderly *J. Microbiol. Immunol. Infect.*, 51 (6) (2018), pp. 740-748
 22. L.C. Katzelnick, L. Gresh, M.E. Halloran, J.C. Mercado, G. Kuan, A. Gordon, A. Balmaseda, E. Harris Antibody-dependent enhancement of severe dengue disease in humans *Science*, 358 (6365) (2017), pp. 929-932
 23. S.B. Halstead, S. Mahalingam, M.A. Marovich, S. Ubol, D.M. Mosser Intrinsic antibody-dependent enhancement of microbial infection in macrophages: disease regulation by immune complexes *Lancet Infect. Dis.*, 10 (10) (2010), pp. 712-722
 24. S.R. Hadinegoro, J.L. ArredondoGarcía, M.R. Capeding, C. Deseda, T. Chotpitayasunondh, R. Dietze, H. Muhammad Ismail, H.I., Reynales, H., Limkittikul, K., Rivera-Medina, D.M. and Tran, H.N. Efficacy and long-term safety of a dengue vaccine in regions of endemic disease *N. Engl. J. Med.*, 373 (13) (2015), pp. 1195-1206.
 25. M. Aguiar, N. Stollenwerk, S.B. Halstead The impact of the newly licensed dengue vaccine in endemic countries *PLoS Negl. Trop. Dis.*, 10 (12) (2016), Article e0005179.
 26. X. Yang, M.B. Quam, T. Zhang, S. Sang Global burden for dengue and the evolving pattern in the past 30 years *J. Travel Med.*, 28 (8) (2021).
 27. A. Wilder-Smith TAK-003 dengue vaccine as a new tool to mitigate dengue in countries with a high disease burden *Lancet Glob. Health*, 12 (2) (2024), pp. e179-e180.
 28. E.G. Kallás, M.A. Cintra, J.A. Moreira, E.G. Patiño, P.E. Braga, J.C. Tenório, V. Infante, R. Palacios, M.V.G. de Lacerda, D. Batista Pereira, A.J. da Fonseca Live, attenuated, tetravalent Butantan-Dengue vaccine in children and adults *New England J. Med.*, 390 (5) (2024), pp. 397-408.
 29. E. Prompetchara, C. Ketloy, S.J. Thomas, K. Ruxrungtham Dengue vaccine: Global development update *Asian Pac. J. Allergy Immunol.*, 38 (3) (2020), pp. 178-185.
 30. C.H. Huang, Y.T. Tsai, S.F. Wang, W.H. Wang, Y.H. Chen Dengue vaccine: an update *Expert Rev. Anti-Infect. Ther.*, 19 (12) (2021), pp. 1495-1502).
 31. W.H.O.I. Dengue Guidelines for diagnosis, treatment *Prev. Control.*, No Title (2009).
 32. V. Kamath, A.B. Aishwarya Dengue vaccines: current status and future perspectives *APIK J. Int. Med.* (2024), pp. 10-4103.

