Etiology, Treatment and Complications of Dengue Fever: A Systematic Analysis

Faiza Saleem[1], Aiman Atiq[2], Sidra Altaf[3*], Mubashra Habib[4] and Tasawar Iqbal[5]

ABSTRACT

Dengue fever, a viral illness transmitted by mosquitoes, presents a major health concern worldwide, especially in warm and humid areas. This comprehensive examination delves into the important aspects of Dengue Fever, such as its causes, methods of treatment, and potential negative effects. The Dengue virus, which has four different serotypes, is primarily transmitted through the bite of Aedes mosquitoes that are infected. Comprehensive knowledge of the numerous underlying causes is essential for creating successful measures to prevent and manage the issue. The primary approach to treating Dengue Fever is providing support by relieving symptoms and preventing further complications. Managing pain and fever can be achieved with analgesics such as acetaminophen, and it is crucial to carefully monitor fluid intake to avoid dehydration. In serious instances, hospitalization, blood transfusions, and careful monitoring may be required to reduce the likelihood of developing complications like Dengue Hemorrhagic Fever and Dengue Shock Syndrome. These serious symptoms include bleeding, fluid escaping from blood vessels, and, occasionally, damage to organs, underscoring the necessity of identifying and addressing the problem early. Preventive measures include controlling the mosquito population by getting rid of their breeding sites, using insecticides, and encouraging individuals to use personal protective measures. Furthermore, vaccination initiatives have become a hopeful solution in regions with high disease prevalence. This thorough analysis offers a complete picture of Dengue Fever, highlighting the importance of comprehensive approaches that cover understanding the cause, treatment plans, and strong prevention methods to reduce the impact of this widespread and potentially serious viral illness.

Keyword: Dengue Fever; Etiology; Treatment; Complications; Mosquito-borne

CITATION

Saleem F, Atiq A, Altaf S, Habib M and Iqbal T, 2023. Etiology, treatment and complications of dengue fever: a systematic analysis. In: Aguilar-Marcelino L, Zafar MA, Abbas RZ and Khan A (eds), Zoonosis, Unique Scientific Publishers, Faisalabad, Pakistan, Vol 3: 551-560. https://doi.org/10.47278/book.zoon/2023.123

CHAPTER HISTORY Received: 15-Jan-2023 Revised: 24-Feb-2023 Accepted: 21-May-2023

[1]School of biological Sciences, The University of Edinburgh, United Kingdom
[2]Department of Pharmaceutical Chemistry, Faculty of Pharmaceutical Sciences Govt. College University, Faisalabad-38000 Pakistan.
[3]Department of Pharmacy, University of Agriculture Faisalabad.
[4]School of Biochemistry and Biotechnology, University of the Punjab Lahore.
[5]Institute of Physiology and Pharmacology, University of Agriculture Faisalabad
***Corresponding author:** sidra.altaf@uaf.edu.pk

1. INTRODUCTION

A famous quote from Jill Lepore, a Historian states that "Epidemiologists study patterns to combat infections, but it's important to remember that stories about outbreaks also follow patterns. While stories may not be physically deadly, they possess a different kind of power. They can spread rapidly, weaken resistance, and wreak havoc on our perception of reality".(Uwishema et al. 2021).

Dengue Fever (DF) is a widespread viral infection that affects millions of people worldwide each year. Itis a mosquito-borne viral infection caused by the dengue virus, which is transmitted primarily by the *Aedes* mosquito. Usually, dengue symptoms appear 5 to 7 days after a healthy person is bitten by a mosquito carrying the virus. Due to the existence of the distinct virus kinds, an individual may suffer numerous infections. During the DF stage, the patient develops symptoms including headaches, muscular soreness, and itching as well as an increase in body temperature each day. The patient may also have slight bleeding from the nose, gums, or skin during the dengue hemorrhagic fever (DHF) stage, as well as a drop in body temperature. The body temperature fluctuates as the patient approaches the stage of dengue shock syndrome (DSS), and vomiting may occur along with the presence of trace amounts of blood (Murhekar et al. 2019; Rastogi et al. 2019; Dourjoy et al. 2021).

Due to the disease's high rates of morbidity and mortality, which are endemic in many tropical and subtropical countries, it presents a serious public health concern. According to World Health Organisation (WHO) the DENV affects about 50 million individuals each year, killing over 15,000 people. In Pakistan, the months of September to November are very crucial for DF, having a big influence on population. In Pakistan, an alarming 34.75% of patients who suffer from an acute febrile illness are reported to have DF. In addition, a thorough retrospective investigation of Dengue infection during pregnancy in the Pakistani population found a significant maternal death incidence of 7%. These data demonstrate the seriousness of the situation and the pressing need for its solutions (Ahmed and Aman 2022).

2. ETIOLOGY OF DF

The DENV is a member of the Flaviviridae family and categorized into four different serotypes called DENV-1, DENV-2, DENV-3 and DENV-4 (Gulati et al. 2020). These serotypes are further separated into several genotypes with minute genetic variances. Infected female *Aedes* mosquitoes, especially *Aedes aegypti* and, to a lesser extent, *Aedes albopictus*, bite victims to spread the virus. These mosquitoes are generally found in cities and semi-urban settings, where they thrive in stagnant water sources including flowerpots, waste tires, and water storage containers (Saha et al. 2019; Adnan et al. 2021).

People who are infected with the DENV may suddenly develop a high fever, a strong headache, retro-orbital discomfort, muscle and joint pain (myalgia and arthralgia), rash, and minor bleeding symptoms such as petechial haemorrhage and gum bleeding after an incubation period of 4 to 10 days(Gulati et al. 2020). The DENV targets the skin's immune cells, such as dendritic cells and monocytes, after infecting a person through a mosquito bite. After that, it multiplies within these cells before spreading throughout the circulation and lymph nodes. A major component in the severity of DF is the virus capacity to sabotage and regulate the host's immune response (Brar et al. 2021; Uwishema et al. 2021).

3. PATHOGENESIS AND CLINICAL MANIFESTATIONS

The full understanding of dengue's illness, which is characterized by a complicated interplay between virus and host factors, is still inadequate. DF can present in a spectrum of clinical manifestations, ranging from mild DF to severe DHF and DSS (Mulik et al. 2021).The major contributor to fatalities caused by this

infectious disease in severe cases are plasma leakage and thrombocytopenia, a condition characterized by low platelet count. By modifying the bone marrow environment, the DENV affects the platelet count of the host directly or indirectly, altering several components involved in platelet synthesis, shattering, and reproducing inside platelets, and finally causing a reduction in the number of circulating platelets (Bandara and Herath 2020).

The infection of DENV is initiated when the virus binds to host cell receptors. The virus then gets inside the cell via clathrin-mediated endocytosis and the acidic environment within the endosome triggers the fusion of the viral membrane. The viral genome is translated into a polyprotein after membrane fusion and removal of the protective protein coat, and this polyprotein is then cleaved into seven non-structural (NS) proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5) and three structural proteins(S)(Capsid, Membrane, and E). The NS proteins aid RNA replication, resulting in the formation of positive (blue) and negative (green) sense single-stranded RNA copies. The (S) envelope (E) and pre-membrane (prM) are transported to the endoplasmic reticulum (ER). The genomic RNA (blue) is packaged by capsid proteins, and the resulting nucleocapsid buds into the ER lumen, forming an immature virion. The prM protein is subsequently broken down to create the M protein as the immature virions are then transported along the secretory route. Exocytosis is ultimately responsible for the discharge of mature virus particles from the cell(Troost and Smit 2020).

When the immune system is activated by dengue infection, chemokines and cytokines are released, endothelium cells undergo autophagy and apoptosis in T cells. These elements work together to cause endothelial cell dysfunction, which in turn causes fluid loss in the third space, intravascular volume contraction, and plasma leakage. A cascade of hypoxic damage occurs across numerous organ systems as a result of poor organ perfusion and shock-like symptoms brought on by intravascular volume reduction. When the virus triggers the immune response, it causes increased permeability in the blood vessels and leads to plasma leaking into tissues, resulting in shock and organ failure. A common outcome of this chain of events is shock and multi-organ dysfunction, which accounts for a significant cause of fatalities in dengue cases(Islam et al. 2020; Schaefer et al. 2022).

4. MANAGEMENT OF DF

The patient's understanding of their participation in dengue management, especially the identification of warning signals demand rapid hospitalisation, has been recognised as a weak area. This delay in treatment has been a substantial contributor to higher death. Since there is no specific antiviral medication for DF, supportive care and the early identification of severe cases are the main management of DF. In order to properly manage dengue and lower its death rate, early diagnosis is essential. The prompt identification of warning signs is crucial to prevent progression to severe disease and reduce mortality rates. Medical professionals can only alleviate the symptoms associated with the disease. Several suggestions should be followed to control dengue such as bed rest, controlling temperature by using antipyretics or sponging methods, relieving discomfort with light sedatives, and ensuring adequate hydration with fluid or electrolyte treatment(Ksularatnam et al. 2019;Jayawickreme et al. 2021).

In situations of severe dengue, it is necessary to carefully evaluate and cope with organ involvement. It's crucial to recognise secondary hemophagocytic lymphohistiocytosis, a dengue complication that might be fatal. By identifying this ailment, healthcare professionals may put into practise certain treatment plans such as giving intravenous immunoglobulin or steroids, which may improve patient outcomes. However, there is no evidence to support any of these claims. There have been talks about the function of corticosteroids in DSS and the potential to stop the development to severe disease if taken early in

the course (Singh et al. 2019; Dhooria et al. 2021).Reduced blood flow, hemolysis, rhabdomyolysis, the direct effects of the dengue virus, and immune-mediated damage can all contribute to renal impairment in dengue. Careful fluid administration is required for a urine output of greater than 0.5 ml/kg/h, and when necessary, early initiation of renal replacement treatment is required. The preferable method is continuous veno-venous hemofiltration (CVVH) (Tayal et al. 2023).

Myocarditis and cardiogenic shock in dengue patients necessitate highly careful fluid resuscitation and prompt use of inotropic drugs. These people have an increased likelihood of getting pulmonary edema and congestive heart failure (Gupta et al. 2021; Teysseyre et al. 2021; Wijaya and Krisnawati 2022).

Both direct invasion and antibody-dependent enhancement by the dengue virus can result in neural damage. Supportive care includes required protection of airways, keeping track of consciousness levels, hydration, and giving anti-seizure drugs as necessary, and when clinically necessary taking steps to lower excessive intracranial pressure. Post-dengue Guillain-Barré syndrome (acute or severe polyradiculoneuropathy a rare case in DF) can be managed by the use of intravenous immunoglobulin (IVIg) (Kulkarni et al. 2021).

A serious health risk is the co-infections of dengue virus and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The prospect of a more serious course of sickness in such circumstances has given rise to speculation. Patients who have co-infection of both viruses frequently have a more severe illness, a greater risk of ICU admission, and a higher fatality rate. This is caused by the two viruses' same pathophysiology, which results in capillary leakage, cytokine storms, coagulopathy, and thrombocytopenia. The two viruses in a co-infection can harm a number of organs either jointly or separately (Omame et al. 2022; Dutta et al. 2023; Prapty et al. 2023).

Identification of particular symptoms such as plasma leakage, erratic hemostasis, and increased vascular permeability is necessary to differentiate between DHF and DF. According to World Health Organisation (WHO) standards, patients with severe syndromes should be given isotonic crystalloid solutions, such as 0.9% normal saline, Ringer's lactate, or Hartmann's solution. Patients can recover quickly once they have passed the crucial stage of their sickness. The restoration of appetite and the reabsorption of extravascular fluids are indicators of improvement and the general health of the patient(Wang et al. 2020).

To stop the spread of dengue, vector control measures are essential. Populations of *Aedes* mosquitoes have been successfully reduced using integrated methods that combine environmental management, source reduction, and the application of pesticides. The importance of community involvement and educsation programmes in spreading knowledge about dengue preventative measures and control strategies are vital to raise awareness (Selvarajoo et al., 2020; Radhika et al. 2019; Yoshikawa et al. 2019; Chng et al. 2022).

5. ADVANCEMENTS IN RESEARCH

The development of new antiviral medications and vaccines, along with the improvements to diagnostic techniques and understanding of virus interaction with its host, have all been the major areas of attention in dengue research. Understanding the pathophysiology of DF has advanced significantly in recent years, offering important new information on potential therapeutic targets (Halstead 2019).

The development of host-directed medicines, which focus on the host immune system rather than the virus itself, is one promising field of research. Several host factors including the type I interferon response and the inflammasome pathway are two host variables that have been recognized as crucial players in the immune response to DENV infection. Host-directed therapies have shown promising results in preclinical studies, suggesting their potential for treating DF(Shrivastava et al. 2020; Duncan et al. 2021).

The use of monoclonal antibodies as a treatment for DF is another area of study that has attracted a lot of interest. Highly specialized monoclonal antibodies can attack either the S or NS proteins of the virus. In *in-vitro* and animal models, a number of monoclonal antibodies that target the DENV envelope protein, have demonstrated strong antiviral activity, suggesting their potential therapy for DF (Pecetta et al. 2020;Dussupt et al. 2021; Kotaki et al. 2021).

In addition to therapeutic treatments, research has also concentrated on creating more accurate and focussed DF diagnostic techniques. The sensitivity and specificity of current diagnostic techniques, such as enzyme-linked immunosorbent assays (ELISA) and polymerase chain reactions (PCR), are limited. To enhance early identification and management of DF, the development of innovative diagnostic techniques, including biosensors and point-of-care analysis, is essential (Luo et al. 2019; Wilder-Smith et al. 2019; Wang et al. 2020).

6. CURRENT TREATMENT OPTIONS

6.1. SUPPORTIVE CARE

The treatment of DF largely focuses on treating the symptoms, although identifying those who are at risk of developing DHF or DSS is an important step and require hospitalisation and strict monitoring. There isn't a particular antiviral medication for DF as of now. The cornerstone of therapy is supportive care, which emphasizes symptom relief and hydration maintenance. To avoid issues like significant plasma loss and shock, adequate fluid replacement either orally or intravenously is crucial. The increased risk of bleeding makes non-steroidal anti-inflammatory medications (NSAIDs) typically contraindicated (Guarner and Hale 2019).

6.2. ANTIVIRAL THERAPIES

6.2.1. DIRECT ANTI-VIRAL AGENTS (DAA)

Numerous studies have been done so far in developing antiviral treatments for DENV that target both the structural and NS proteins. Given its critical function in promoting virus entrance into host cells, the E protein, one of the (S), has received substantial research as a possible antiviral target. In terms of NS proteins, the NS5 and NS3 proteins have been the most studied. NS5, being the largest and highly conserved NS protein in DENV, serves as the viral RNA-dependent RNA polymerase (RdRP) and possesses methyltransferase (MTase) activity. In preclinical and early clinical trials, several antiviral medications show promising results, nevertheless, this treatment is more likely to develop resistance. Balapiravir, a nucleoside derivative that prevents DENV replication, is one such medication. In vitro and in vivo studies have proven the antiviral efficacy of balapiravir. However, further research is required to assess its effectiveness and safety in humans (Do and Reau 2020).

Moreover, a wide range of naturally occurring substances, including mangiferin-punicalagin, alpha-mangostin, geraniin, curcumin-flavonoids, and quercetin derived from various plant sources have shown activity against DENV (Clain et al. 2018; Fitmawati et al. 2021; Kowalczyk et al. 2021; Santhi et al. 2021; Patil et al. 2021; Dhiman et al. 2022) .

6.2.2. HOST DIRECTED AGENTS (HDA)

HDA has the potential to effectively treat a variety of infections. Additionally, HDA offers a lesser chance of resistance, increasing their efficacy. However, it is important to note that due to their tendency to

interfere with cell homeostasis, HDA often have a limited range of safe and effective doses compared to DAA. There are several HDA antivirals that have been identified, and these all focus on various phases of viral propagation. The α-glucosidase, essential for proper protein folding and maturation, is one widely studied cellular target. Research is being done on blocking the cellular inosine monophosphate dehydrogenase, which is essential for viral replication and nucleotide production (Bhushan et al. 2020; Troost and Smit 2020; Karade et al. 2023).

7. TACKLING VECTOR CONTROL

Due to lack of antiviral medications, vector control management methods are crucial for the prevention of DF. Insecticides, mosquito repellents, and community participation are just a few of the integrated vector management strategies that have shown effective in lowering mosquito populations and, consequently, dengue transmission. Concerns about continuing to use current techniques to control these mosquitoes are being mounted. Due to their high costs, low acceptability in communities, slow implementation procedures, and widespread development of pesticide resistance in *Aedes* mosquitoes, larviciding methods such as dieldrin and DDT, mosquito fogging with 5% malathion, or Pyrethrin, are now challenged (Jones et al. 2021;Saha and Samanta 2022).

8. VACCINES

It has long been difficult for scientists to develop a dengue vaccination that is effective. In recent years the first dengue vaccine, Dengvaxia, has been approved in several countries. But it delivers partial defence against DENV serotypes 1-4, and its usage is restricted because of questions about its efficacy and safety. The goal of ongoing research is to create vaccines of the next generation with enhanced safety and effectiveness characteristics. To meet the demand for a secure and efficient dengue vaccine, currently, attempts are being made to create dengue vaccines in five main categories: inactivated virus vaccines, live attenuated virus vaccines, DNA vaccines, recombinant subunit vaccines, and viral-vector vaccines. TAK-003, CYD-TDV, and TV003/005, are the most advanced vaccine candidates which are currently under development. The genetic backbone for all four vaccine viruses is provided by TAK-003, a candidate for a tetravalent dengue vaccine that is based on a live, attenuated dengue serotype 2 virus. Phase 3 studies for TAK-003 are presently in progress, and effectiveness has been shown independent of serostatus prior to vaccination (Wilder-Smith 2020; Laydon et al. 2021; Hou et al. 2022). The NIH's National Institute of Allergy and Infectious Diseases (NIAID) developed the live, attenuated tetravalent vaccination TV003/TV005 by utilizing recombinant DNA technology. Phase 2 studies are now being conducted on it. There are also varying phases of development for other vaccination candidates from diverse classifications (Yoshimura et al. 2017; Halstead and Dans 2019; Halstead et al. 2020; Girard et al. 2020; Shukla et al. 2020; Park et al. 2022; Torres-Flores et al. 2022).

9. COMPLICATIONS OF DF

9.1. NEUROLOGICAL COMPLICATIONS

When acute febrile infections exhibit neurological signs, particularly altered sensorium, the complexity of diagnostic difficulties rises. Differentiating between dengue-associated encephalopathy and dengue encephalitis becomes challenging when people with febrile illness have altered sensorium and test positively for dengue through serology. Similar alterations may be seen in several different viral

infections that impact the central nervous system (CNS), but a positive brain neuroimaging study typically be indicative of other viral infections of the CNS and may also exhibit comparable alterations. Alterations to the sensorium in DENV seropositive patients may possibly be the result of a stroke involving an intracerebral haemorrhage or an enlarging infarct. Therefore, in suspected dengue-related cases, caution should be exercised while doing the standard procedure of analysing cerebrospinal fluid (CSF) in ill patients with altered sensorium to rule out underlying CNS illnesses (Rastogi et al. 2019;Kulkarni et al. 2021; Trivedi and Chakravarty 2022).

10. ACUTE PANCREATITIS

Pancreatitis caused by dengue is a largely unexplored complication. The onset of acute pancreatitis complicates the clinical spectrum even further and has an impact on prognosis and therapy. The risk of death and morbidity is considerably reduced when DF accompanied by acute pancreatitis is promptly identified and managed. Healthcare workers must be knowledgeable of these potentially lethal consequences that might develop alongside instances of DF that first appear to be benign. Uncertainty exists regarding the precise underlying processes of pancreatic involvement in DF. Two possibilities have been put forth. One theory is that the virus directly attacks the pancreas, inflaming it and harming its acinar cells. The second hypothesis contends that the shock from DSS might damage the pancreas, triggering either an acute infection or an autoimmune reaction against the islet cells of the pancreas. This reaction can cause the ampulla of Vater to swell, preventing the pancreatic secretions from draining. It is essential to identify pancreatitis as soon as possible using abdominal ultrasonography to avoid serious and perhaps deadly consequences (Naik et al. 2021).

11. OTHER COMPLICATIONS

DF may affect several organs in addition to plasma leakage, which can result in problems such as liver damage, myocarditis, subacute thyroiditis, gallbladder wall thickness (GWT), ascites, Isolated subdural hematoma, encephalopathy, and renal impairment. These issues call for prompt identification and adequate care since they have a major impact on patient health outcomes (Vyas et al. 2020; Mangaraj 2020; Sivanesan Uthraraj et al. 2022; Ashraf et al. 2022).

12. CONCLUSION

Millions of individuals worldwide suffer from DF a common viral infection spread by *Aedes* mosquitoes, each year. The clinical symptoms caused by the dengue virus (DENV) infection include mild DF, severe DHF, and DSS. Since DF does not currently have a particular antiviral medication, supportive care is essential for illness management. Research is mainly focused on the development of antiviral drugs, vaccines, and better diagnostic methods.A host-directed therapy and monoclonal antibodies are promising treatments for DF, while research is ongoing to develop safe and effective vaccines. Potential treatment targets have been revealed by better understanding of the pathophysiology of dengue disease.DF remains a significant public health challenge, particularly in tropical and subtropical regions. Despite the lack of specific antiviral therapy, advances in research have provided valuable insights into the virus-host interaction and potential therapeutic targets. Developing safe and effective vaccines, host-directed therapies, and monoclonal antibodies, along with effective vector control strategies, are crucial in preventing and controlling DF. The approval of Dengvaxia has been a significant breakthrough in dengue vaccination, although further research is needed to develop more effective vaccines. Continued research efforts in understanding the pathogenesis of DF, early recognition of complications

and developing novel interventions are essential to reduce the morbidity and mortality associated with this disease.

REFERENCES

Adnan RA et al., 2021. The Impact of Sociological and Environmental Factors for Dengue Infection in Kuala Lumpur, Malaysia. Acta Tropica 216: 105834.

Ahmed U and Aman A, 2022. Intraoperative Post Partum Hemorrhage in a Patient with Dengue Fever. Pakistan Journal of Medical Sciences 38: 326.

Ashraf M et al., 2022. Isolated subdural hematoma due to dengue hemorrhagic fever: Surgical intervention and review of the literature. Surgical Neurology International 13: 244.

Bandara SMR and Herath HM, 2020. Corticosteroid actions on dengue immune pathology; A review article. Clinical Epidemiology and Global Health 8: 486–494.

Chng JWQ et al., 2022. Knowledge, attitudes and practices of dengue prevention between dengue sustained hotspots and non-sustained hotspots in Singapore: a cross-sectional study. Scientific Reports 12: 1–10.

Clain E et al., 2018. Extract from Aphloia theiformis, an edible indigenous plant from Reunion Island, impairs Zika virus attachment to the host cell surface. Scientific Reports 8: 1–12.

Dhiman M et al., 2022. Traditional Knowledge to Contemporary Medication in the Treatment of Infectious Disease Dengue: A Review. Frontiers in Pharmacology 13: 750494.

Dhooria GS et al., 2021. Comparison of Clinical Features and Outcome of Dengue Fever and Multisystem Inflammatory Syndrome in Children Associated With COVID-19 (MIS-C). Indian Pediatrics 58: 951–954.

Do A and Reau NS, 2020. Chronic Viral Hepatitis: Current Management and Future Directions. Hepatology Communications 4: 329–341.

Duncan CJA et al., 2021. Genetic Lesions of Type I Interferon Signalling in Human Antiviral Immunity. Trends in Genetics 37: 46–58.

Dussupt VK et al., 2021. Landscape of Monoclonal Antibodies Targeting Zika and Dengue: Therapeutic Solutions and Critical Insights for Vaccine Development. Frontiers in Immunology 11: 3687.

Dutta D et al., 2023. Cross-reactivity of SARS-CoV-2 with other pathogens, especially dengue virus: A historical perspective. Journal of Medical Virology 95: e28557.

Fitmawati et al., 2021. Mangifera foetida L. (Macang) Source of Potent Antiviral Activity of Against Dengue Virus Serotype 2 (Anti DENV2). Journal of Physics: Conference Series 2049: 012018.

Girard M et al., 2020. Arboviruses: A global public health threat. Vaccine 38: 3989-3994.

Guarner J and Hale GL, 2019. Four human diseases with significant public health impact caused by mosquito-borne flaviviruses: West Nile, Zika, dengue and yellow fever. Seminars in Diagnostic Pathology 36: 170-176.

Gulati K et al., 2020. Dengue fever presenting with severe myositis—An unusual presentation. Journal of Family Medicine and Primary Care 9: 6285.

Gupta S et al., 2021. Insights Into the Emerging Role of Myocarditis in Dengue Fever. Current Tropical Medicine Reports 8: 239-245.

Halstead S, 2019. Recent advances in understanding dengue. F1000 Research 8.

Halstead SB and Dans LF, 2019. Dengue infection and advances in dengue vaccines for children. The Lancet Child and Adolescent Health 3: 734–741.

Hou J et al., 2022. Current Development and Challenges of Tetravalent Live-Attenuated Dengue Vaccines. Frontiers in Immunology 13: 840104.

Jayawickreme KP et al., 2021. A study on knowledge, attitudes and practices regarding dengue fever, its prevention and management among dengue patients presenting to a tertiary care hospital in Sri Lanka. BMC Infectious Diseases 21: 1–14.

Jones RT et al., 2021. Novel control strategies for mosquito-borne diseases. Philosophical Transactions of the Royal Society B 376: 20190802.

Karade SS et al., 2023. Structure-Based Design of Potent Iminosugar Inhibitors of Endoplasmic Reticulum α-Glucosidase I with Anti-SARS-CoV-2 Activity. Journal of Medicinal Chemistry 66(4): 2744-2760.

Kotaki T et al., 2021. An affinity-matured human monoclonal antibody targeting fusion loop epitope of dengue

virus with in vivo therapeutic potency. Scientific Reports 11: 1–14.
Kowalczyk M et al., 2021. Drug Design Strategies for the Treatment of Viral Disease. Plant Phenolic Compounds and Their Derivatives. Frontiers in Pharmacology 12: 709104.
Ksularatnam GAM et al., 2019. Evaluation of biochemical and haematological changes in dengue fever and dengue hemorrhagic fever in Sri Lankan children: A prospective follow up study. BMC Pediatrics 19: 1-9.
Kulkarni R et al., 2021. Neurological Manifestations of Dengue Fever. Annals of Indian Academy of Neurology 24: 693.
Laydon DJ et al., 2021. Efficacy profile of the cyd-tdv dengue vaccine revealed by bayesian survival analysis of individual-level phase III data. Elife 10: e65131.
Luo R et al., 2019. Rapid diagnostic tests for determining dengue serostatus: a systematic review and key informant interviews. Clinical Microbiology and Infection 25: 659-666.
Mulik V et al., 2021. Dengue in pregnancy: Review article. European Journal of Obstetrics and Gynecology and Reproductive Biology 261: 205–210.
Murhekar M et al., 2019. Epidemiology of dengue fever in India, based on laboratory surveillance data, 2014–2017. International Journal of Infectious Diseases 84: S10–S14.
Naik S et al., 2021. Acute Pancreatitis Complicating a Case of Dengue Fever: Double Trouble. Cureus 13(11).
Omame A et al., 2022. Assessing the impact of SARS-CoV-2 infection on the dynamics of dengue and HIV via fractional derivatives. Chaos, Solitons and Fractals 162: 112427.
Park J et al., 2022. Current status and perspectives on vaccine development against dengue virus infection. Journal of Microbiology 60: 247–254.
Patil P et al., 2021. In vitro and in vivo studies reveal α-Mangostin, a xanthonoid from Garcinia mangostana, as a promising natural antiviral compound against chikungunya virus. Virology Journal 18: 1-12.
Prapty CN et al., 2023. SARS-CoV-2 and dengue virus co-infection: Epidemiology, pathogenesis, diagnosis, treatment, and management. Reviews in Medical Virology 33: e2340.
Rastogi N et al., 2019. Dengue fever with acute disseminated encephalomyelitis: sensorium imbroglio. Journal of the Association of Physicians of India 67(10): 80-82.
Saha P et al., 2019. Prevalence of kdr mutations and insecticide susceptibility among natural population of *Aedes aegypti* in West Bengal. PLoS one 14: e0215541.
Saha S and Samanta G, 2022. Analysis of a host–vector dynamics of a dengue disease model with optimal vector control strategy. Mathematics and Computers in Simulation 195: 31-55.
Santhi VP et al., 2021. Therapeutic potential of phytoconstituents of edible fruits in combating emerging viral infections. Journal of Food Biochemistry 45: e13851.
Schaefer TJ et al., 2022. Dengue Fever. BMJ Best Practice 2022: 5-6.
Selvarajoo S et al., 2020. Knowledge, attitude and practice on dengue prevention and dengue seroprevalence in a dengue hotspot in Malaysia: A cross-sectional study. Scientific Reports 10(1): 9534.
Shrivastava G et al., 2020. Inflammasome Fuels Dengue Severity. Frontiers in Cellular and Infection Microbiology 10: 489.
Shukla R et al., 2020. Antibody-Dependent Enhancement: A Challenge for Developing a Safe Dengue Vaccine. Frontiers in Cellular and Infection Microbiology 10: 597.
Singh H et al., 2019. Dengue: Uncommon Neurological Presentations of a Common Tropical Illness. Indian Journal of Critical Care Medicine : Peer-reviewed, Official Publication of Indian Society of Critical Care Medicine 23: 274.
Sivanesan Uthraraj N et al., 2022. Predictive Factors for the Complications of Dengue Fever in Children: A Retrospective Analysis. Cureus 14(12).
Tayal A et al., 2023. Management of Dengue: An Updated Review. Indian Journal of Pediatrics 90: 168-177.
Teysseyre L et al., 2021. Case Report: Refractory Shock due to Fulminant Dengue Myocarditis Treated with Venoarterial Extracorporeal Membrane Oxygenation: A Report of Four Cases. The American Journal of Tropical Medicine and Hygiene 104: 552.
Trivedi S and Chakravarty A, 2022. Neurological Complications of Dengue Fever. Current Neurology and Neuroscience Reports 22: 515–529.
Troost B and Smit JM, 2020. Recent advances in antiviral drug development towards dengue virus. Current Opinion

in Virology 43: 9-21.
Uwishema O et al., 2021. Dengue fever outbreak in Cook Island: A rising concern, efforts, challenges, and future recommendations. Journal of Medical Virology 93: 6073–6076.
Wang WH et al., 2020. Dengue hemorrhagic fever – A systemic literature review of current perspectives on pathogenesis, prevention and control. Journal of Microbiology, Immunology and Infection 53: 963-978.
Wijaya WS and Krisnawati I, 2022. Fulminant myocarditis-associated expanded dengue syndrome in pregnant woman: a case report. Bulletin of the National Research Centre 46: 1–5.
Wilder-Smith A, 2020. Dengue vaccine development by the year 2020: challenges and prospects. Current Opinion in Virology 43: 71–78.
Yoshikawa MJ et al., 2019. An interdisciplinary study: disseminating information on dengue prevention and control in the world-famous travel destination, Bali, Indonesia. Evolutionary and Institutional Economics Review 17: 265-293.
Yoshimura M et al., 2017. Well-balanced immune response and protective efficacy induced by a single dose of live attenuated tetravalent dengue vaccine (KD-382) in monkeys. Heliyon 6(7): e04506