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A Review of dengue fever treatment protocol during outbreak

Shahd Ahmed [1], Amal Fadlelsid [2], Isra Muzamil [3], Zainab Elhasan [4], Mohamed Mustafa [5], Rania Siddig [6], Ahmed O Ali [7], Sara Mohamed [8], Rasha Omer [9], Hager Ahmed [10], Tagwa Kalool [11,*] and Sara Ahmed Adam Musa [12]

[1] *Department of medicine, University of Khartoum, khartoum Sudan.*
[2] *Faculty of Medicine Ahfad University for women, Omdurman, Sudan.*
[3] *Department of medicine, University of Juba Khartoum – Sudan.*
[4] *Ahfad university for women - school of medicine Khartoum-Sudan.*
[5] *Medical doctor, NHS UK.*
[6] *NOWDOC family practice CO. Donegal Ireland.*
[7] *Department of Population Health Tropical Medicine, Royal College of Surgeons in Ireland (RCSI), Dublin, Ireland.*
[8] *Ahfad University for Women, Khartoum, Sudan.*
[9] *Clincial Fellow Trauma and Orthopedic Nobles Hospital, Douglas, Isle of Man.*
[10] *Pediatric surgery, Hull Royal Infirmary Hull, United Kingdom.*
[11] *Department of medicine, Ahfad university for women, omdurman, Sudan.*
[12] *Nursing Program coordinator in Almadar college.*

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Abstract

Dengue fever is an acute viral illness transmitted by mosquitoes and caused by one of four distinct dengue virus serotypes (DENV-1, DENV-2, DENV-3, DENV-4), all of which belong to the *Flavivirus* genus. The main carriers are *Aedes aegypti* and *Aedes albopictus* mosquitoes, commonly found in tropical and subtropical regions. Globally, dengue is the most widespread mosquito-borne viral disease, with an estimated 400 million infections each year, including over 100 million symptomatic cases. It is endemic in more than 100 countries, particularly across Asia, the Americas, and Africa.

The illness can range from asymptomatic or mild fever to more severe forms such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Severe cases are characterized by increased vascular permeability, plasma leakage, and, in some cases, life-threatening shock. Individuals who experience a second infection with a different serotype are at greater risk of severe disease due to immune responses like antibody-dependent enhancement.

To improve clinical management, the World Health Organization (WHO) revised its classification in 2009, categorizing dengue into three groups: dengue without warning signs, dengue with warning signs, and severe dengue. There is currently no specific antiviral treatment; management is mainly supportive, focusing on careful fluid replacement and monitoring for complications. Prevention depends on mosquito control efforts and, in certain regions, vaccination as advised by the Advisory Committee on Immunization Practices.

This review aims to examine available treatments and management strategies for dengue fever during outbreak situations.

Keywords: Dengue Fever; Dengue Hemorrhagic Fever; Dengue Outbreak; Dengue Fever Management

* Corresponding author: Tagwa Kalool

1. Introduction

Dengue is a contagious illness caused by any of the four dengue virus serotypes: DENV-1 to DENV-4. It is a mosquito-borne viral infection mainly transmitted to humans through the bite of female *Aedes* mosquitoes. The disease is predominantly found in tropical and subtropical regions, placing nearly one-third of the global population at risk of infection. Dengue has emerged as one of the most rapidly spreading mosquito-borne diseases worldwide, with its incidence increasing thirtyfold over the past five decades [1].

Vector Dengue viruses are transmitted to humans primarily by female Aedes (Ae.) mosquitoes of the Stegomyia subgenus. Ae. aegyptiis the most significant vector responsible for major epidemics in tropical and subtropical regions. Other mosquito species, including Ae. albopictus, Ae. polynesiensis, members of the Ae. scutellariscomplex, and Ae. niveus, also serve as secondary vectors, though Ae. niveusis primarily a sylvatic vector. The Aedes mosquito life cycle spans about 8–10 days at room temperature and includes two stages: the aquatic phase (larvae and pupae) and the terrestrial phase (eggs and adults). Currently, Ae. albopictus has gained importance as a vector because of its adaptability to new environments, including temperate areas. Its expansion into regions lacking Ae. aegypti has facilitated the spread of dengue viruses into new territories [1].

Clinically, dengue virus infection presents in three main forms: Classical Dengue Fever (DF), Dengue Hemorrhagic Fever (DHF), and Dengue Shock Syndrome (DSS). DF is marked by high fever, severe muscle and joint pain, retro-orbital headaches, and a morbilliform rash. The presence of hemorrhagic symptoms in addition to classic DF indicates DHF, while DSS is characterized by low blood pressure, altered mental status, and delayed capillary refill. Differential diagnoses for DF include other viral illnesses such as Chikungunya, as well as bacterial, rickettsial, and parasitic infections presenting with similar symptoms. Mild dengue infections cannot be diagnosed based solely on clinical signs; confirmation requires virus isolation or serological testing. In a study by Wilder-Smith et al., multivariate analysis revealed three laboratory markers highly predictive of dengue: platelet count $<140 \times 10^9$/L, white blood cell count $<5 \times 10^9$/L, and aspartate aminotransferase (AST) levels >34 IU/L. This combination demonstrated 75% sensitivity and 100% specificity. Many cases during the epidemic met these criteria and were negative for malaria and typhoid, although molecular tests were unavailable and IgM antibodies may not have been detectable in early infection [2].

Large-scale dengue-like illness outbreaks have been documented across the Americas, southern Europe, North Africa, the eastern Mediterranean, Asia, Australia, and various islands in the Indian and Pacific Oceans and the Caribbean since the late eighteenth century. The first recorded dengue-like epidemic occurred between 1779 and 1780 in Batavia (Jakarta), Cairo, and Philadelphia, showing that dengue has had a global presence for over 200 years. During the eighteenth and early nineteenth centuries, dengue epidemics or regional pandemics recurred roughly every 10 to 40 years in tropical regions [3].

Inadequate management of febrile illnesses—especially the routine use of antimalarial drugs without diagnostic confirmation—has contributed to drug resistance. In West Africa, febrile patients are often treated inappropriately with antimalarials and unnecessary antibiotics, leading to antimicrobial resistance (AMR). AMR, driven by the misuse and overuse of antibiotics, poses a significant global health challenge, with Africa experiencing the highest mortality rates linked to AMR. To improve dengue case management, implementing reliable diagnostic measures is essential. For early detection, NS1 antigen and IgM antibody tests are valuable, while IgG testing identifies past infections. Differentiating between primary and secondary infections is critical, as secondary dengue infections carry a higher risk of severe disease. In endemic regions, individuals are frequently exposed to multiple dengue virus serotypes over time, heightening their vulnerability to severe outcomes [4].

The first clinical form, DF, begins with a sudden high fever without respiratory symptoms, accompanied by intense headaches, hence its nickname “breakbone fever.” It typically lasts three to seven days and is usually mild. The hemorrhagic form (DHF) also presents with sudden fever, nausea, vomiting, and fainting due to hypotension from plasma leakage. This form lasts about two to three days and can be fatal. Secondary infections play a critical role, as they increase the risk of developing severe hemorrhagic disease [5].

Before 1970, dengue hemorrhagic fever outbreaks were reported in only nine countries. By 1995, this number had increased more than fourfold, with around 2.5 billion people now at risk of dengue infection. During dengue epidemics, infection rates among susceptible individuals often range from 40–50%, reaching as high as 80–90% in favorable environmental conditions. Each year, more than 500,000 dengue hemorrhagic fever cases require hospitalization [5].

2. Methodology

This review adopts a retrospective narrative research design focused on treatment protocols for dengue fever in outbreak scenarios. In order to achieve this objective, a comprehensive literature search was done through three major scientific databases, namely PubMed, Google Scholar, and Scopus. The search utilized a combination of controlled vocabulary and free-text terms, including "dengue fever," "outbreak," and "dengue fever treatment."

Only English-language publications with free full-text access were included in this review. Articles published in other languages, lacking full-text accessibility, or studies unrelated to dengue treatment during outbreaks were excluded. The search was conducted from Augst 2025 to October 2025 ensuring that both recent and relevant literature were considered. Moreover, the research process was independently carried out by two reviewers for accuracy and bias reduction.

Data extracted from the eligible studies included details on treatment approaches, supportive care protocols, antiviral therapies, and public health management strategies utilized during dengue outbreaks. All the authors involved in this review participated actively in literature search, data extraction, and manuscript preparation. A methodological quality assessment of all included studies was conducted to evaluate reliability and validity of results. Monitoring was concerned with study design, clarity in treatment description, and appropriateness of conclusions.

3. Discussion

Dengue fever (DF) is a major global public health concern, with frequent outbreaks occurring in tropical regions. The true incidence of DF is often underestimated, as many dengue infections are mild, self-limiting, and go unreported. The silent and continuous transmission of the dengue virus often leads to outbreaks of varying magnitudes, influenced by factors such as human population density, susceptibility, previous exposure to DENV, and the abundance of mosquito vectors. Furthermore, situations involving armed conflict or humanitarian crises increase community vulnerability to infectious diseases, including DF. For example, a yellow fever outbreak was linked to poor living conditions in humanitarian settings that promoted the spread of Aedes aegypti, the same mosquito responsible for transmitting DF [6].

Climate change significantly affects the transmission and incidence of DF. The factors driving dengue outbreaks are complex. An analysis of rainfall and temperature patterns before and after a pipeline explosion found that both rainfall and higher temperatures were strongly correlated with the 2014 dengue outbreak (Spearman correlation analysis; $P < 0.0001$; $r = 0.87$ and 0.78, respectively). These findings suggest that increased rainfall and elevated temperatures enhance mosquito breeding and activity. It was also proposed that the underground gas explosion might have indirectly triggered or contributed to this dengue outbreak [7].

Until safe and effective vaccines are widely available and used in endemic areas, favorable clinical outcomes for symptomatic dengue cases depend on early detection, appropriate case management, and close monitoring to identify and treat severe manifestations promptly. However, since dengue shares symptoms with many other febrile illnesses—especially during the early stages—large numbers of suspected cases are often hospitalized for observation, overwhelming healthcare systems during seasonal outbreaks. Therefore, better clinical diagnostic tools and risk prediction methods for severe dengue are urgently needed, particularly in high-burden areas where effective resource allocation is essential [8].

As previously mentioned, dengue's clinical presentation varies greatly. Most symptomatic cases recover after a short illness, but a small percentage progress to severe disease characterized by plasma leakage and hemorrhagic complications. This plasma leakage can be severe, especially in children, and may lead to life-threatening dengue shock syndrome (DSS). Although less common, other serious complications such as severe liver or neurological involvement can occur. The World Health Organization (WHO) revised its classification in 2009, simplifying the categories into "dengue" and "severe dengue" to replace the earlier, more complex classification of dengue fever and dengue hemorrhagic fever [8].

Most of the 262 documented dengue outbreaks occurred in developing countries such as India, China, and Brazil. These high numbers are likely due to limited laboratory facilities and inadequate vector control measures. Additionally, socioeconomic challenges, high population density, and favorable environmental conditions in these countries promote mosquito survival and disease transmission. After 2010, most dengue outbreaks were reported in the Western Pacific region, particularly in China, Singapore, and Malaysia. Conversely, only a few outbreaks were recorded in Europe,

involving just two countries. The disappearance of Aedes aegypti from the European Basin between the 1950s and 2005 likely contributed to the low prevalence of dengue in that region. It is important to note that there are still many dengue-endemic areas globally [9].

The confirmation of acute dengue infection is most often achieved through serological testing. Recently, commercial tests for detecting viral antigens have become available outside the United States and show promise for early diagnosis. For patients with suspected dengue, if laboratory facilities are available, an acute-phase serum or plasma sample should be collected. The IgM immunoassay (MAC-ELISA or equivalent) is the preferred rapid diagnostic test. However, if the sample is taken within the first six days of illness, the result may be falsely negative. To confirm a positive IgM result—or when the IgM test is negative—a convalescent serum sample should be collected 10 to 14 days after the acute-phase sample. Both samples can then be tested together using hemagglutination inhibition (HI) or enzyme immunoassays to confirm acute infection. If the patient is seen within the first five or six days of illness and has a negative IgM result, testing for the dengue NS1 antigen is recommended [10].

Dengue fever is generally a self-limiting illness with no specific antiviral treatment currently available. Supportive care—including the use of analgesics, adequate fluid replacement, and bed rest—is typically sufficient. No medications have been proven effective in treating dengue or its complications. Acetaminophen may be used to manage fever and discomfort, while aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), and corticosteroids should be avoided. Managing severe dengue involves careful fluid administration and proactive control of bleeding. In a double-blind, placebo-controlled trial, single-dose methylprednisolone showed no benefit in reducing mortality in patients with dengue shock syndrome [11].

Patients experiencing moderate dehydration from fever and vomiting should receive oral rehydration therapy. Platelet counts and hematocrit levels should be checked daily from the third day of illness until one to two days after fever resolution. Those showing clinical signs of dehydration, a rising hematocrit, or a decreasing platelet count should receive intravenous fluid replacement under close supervision [11].

Severe dengue requires meticulous fluid management and prompt treatment of bleeding. Patients with dengue shock syndrome should be admitted to an intensive care unit (ICU). Such patients may require a central venous line for fluid resuscitation and an arterial line for continuous blood pressure monitoring and frequent blood testing. Volume deficits should be corrected using isotonic fluids like Ringer's lactate solution, administered as 10–20 mL/kg boluses over 20 minutes, repeated as needed. If the hematocrit rises despite treatment, plasma expanders such as starch, dextran 40, or 5% albumin (10–20 mL/kg) may be used, with some evidence suggesting that starch is preferable due to fewer hypersensitivity reactions compared to dextran [11].

Dengue–malaria co-infection management has been discussed in only one study, in which 90% (306/357) of healthcare providers recommended hospitalization for patients with both dengue and other concurrent diseases, though specific co-infections were not detailed. Another study found that 29% (4/14) of hospitalized patients who died from severe dengue and 25% (44/179) of those with complicated dengue were co-infected with malaria, although specific treatment strategies for such cases were not reported [12].

4. Conclusion

Dengue is a global health problem, with approximately 2.5 billion of the world's population at risk of infection. The incidence of dengue has risen over the last 50 years at a phenomenal rate for reasons which are as yet poorly explained. Despite being a short-lasting illness without any significant long-term sequelae, a severe infection can be lethal. The pathophysiology of dengue is still obscure, although it is widely accepted that the "severe illness" is due to an interaction between the virus and the over-reacting immune system of the host. There is no specific treatment for the infection, and management is only supportive care with judicious fluid management during the critical phase coupled with continuous monitoring. The advantages of having a vaccine against dengue are immense, but progression in this regard is slow due to many technical difficulties.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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