

# Dengue: A global health concern

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Dengue is a mosquito-borne, acute febrile illness also known as breakbone fever that has now become a major public health concern in the tropics and subtropics worldwide. According to the World Health Organization (WHO) and the Centers for Disease Control and Prevention, dengue is now endemic in more than 100 countries. Each year, an estimated 400 million people have been infected with dengue virus, 100 million become ill with dengue, and 21,000 deaths have been reported.<sup>[1]</sup> Dengue infection is prevalent in regions having tropical and subtropical climates typically in urban and semi-urban areas; however, due to the effects of climate change impacting on the rainfall rate and intensity of hurricanes and typhoons, the global incidence of dengue has been increasing exponentially and now nearly, half of the world's population is at risk of this infection.<sup>[2]</sup> In 2023, and as of 9 March, 380,171 dengue cases and 113 deaths have been registered, most of the dengue cases and their associated death have been registered from Brazil, Bolivia, Peru, Columbia, Nicaragua, Sudan, and Bangladesh.<sup>[3]</sup> Dengue infection is caused by dengue virus, which is a febrile illness with clinical manifestations vacillating from asymptomatic infection to severe systemic manifestations and multiorgan failure proceeding to lethal consequences.<sup>[4]</sup> The virus is transmitted to humans by the bite of an infected *Aedes aegypti* mosquito (also known as yellow fever mosquito). Other species within the *Aedes* genus can also serve as vectors, but their contribution is secondary to *A. aegypti*.<sup>[2]</sup> After being bitten by an infected mosquito, initial viral replication take place in subdermal dendritic cells after which the virus migrates to regional lymph nodes and viremia occurs through circulating monocytes and macrophages which can infect the solid organs as well as bone marrow.<sup>[5,6]</sup> Similar to various viral infections, dengue presents as a self-limiting infection called dengue fever, from which the majority of patients recover without suffering from any serious complication. On the contrary, dengue hemorrhagic fever is the severe form of disease that occurs due to an abnormal immune response with cytokine production termed as a cytokine storm, in which there is increased vascular permeability that leads to leaking of plasma into the pleural cavity, peritoneal space, and tissue plains and leads to altered thromboregulatory mechanisms.<sup>[7]</sup> The clinical symptoms are divided into three main phases which are febrile, critical, and recovery phase. The febrile phase lasts for 2 to 7 days and is marked by high-grade

fever associated with skin erythema, facial flushing, myalgias, arthralgias, headache, anorexia, nausea, and vomiting along with maculopapular rash.<sup>[8]</sup> The onset of the critical phase is signaled by a rapid waning of platelet count and rise in hematocrit and it can advance to shock, organ dysfunction, disseminated intravascular coagulation, and hemorrhage and the recovery phase entails the gradual decline in fever and an increase in platelet count toward normal.<sup>[7-9]</sup> The clinical diagnosis of dengue is challenging as numerous other illnesses can exist similarly early in the disease course such as influenza, Zika, malaria, chikungunya, and yellow fever.<sup>[10,11]</sup> Obtaining a detailed history of immunizations, travel, and contact exposure can aid in sorting out the disease, followed by the laboratory diagnosis, and the timeline of clinical presentation; all play a crucial role in the diagnosis of dengue infection. The WHO guideline on the management of dengue divides the patients into three groups: A, B, or C regarding treating a patient at home or in hospital. Those who meet the criteria of Groups A and B could be managed at home under supervision; however, Group C needs hospital admission.<sup>[12]</sup> There are various measures that can be undertaken to avoid contracting dengue.<sup>[13-17]</sup> These methods include certain biological control methods to eradicate the vector for this disease such as use of viviparous species of larvicidal fish, and *Poecilia reticulata* can be used in confined water bodies such as large water tanks and open freshwater wells, which will help in eliminating the larvae of *A. aegypti*.<sup>[17]</sup> Several chemical control methods can also be used to eliminate larvae that flourish in breeding containers such as environmental protective agency approved insecticidal sprays composed of organophosphorus compounds (fenitrothion and malathion) and pyrethroids (bioresmethrin and cypermethrin) can be used and applied as thermal fogs and cold aerosols.<sup>[18]</sup> Moreover, oil-based formulations are favored as they impede evaporation.<sup>[19]</sup> Other than these, taking general precautionary which measures in endemic areas can also play an important role in reducing the chance of being infected, these protective measures include using of bed nets, application of mosquito repellent creams that contain DEET or picaridin, use of mosquito coils, and wearing full-sleeve shirts and pants.<sup>[20]</sup>

A vaccine against dengue infection (CYD-TDV, Dengvaxia®) is licensed and available in more than 20 countries for individuals of 9–45 years old.<sup>[21]</sup> This vaccine is based on

a live recombinant tetravalent dengue vaccine formulation using recombinant DNA technology by replacing the PrM (pre-membrane) and E (envelope) structural genes of the yellow fever attenuated 17D strain vaccine with those from the four dengue serotypes but evidence indicates that this vaccine leads to a higher risk of severe dengue infection in those who have not been previously infected.<sup>[22,23]</sup> Therefore, the WHO recommends that this vaccine Dengvaxia® only should be given to individuals with confirmed prior dengue infection.<sup>[21]</sup> Now, Dengvaxia® is frequently given to those individuals living in an area with endemic dengue with laboratory confirmed prior dengue virus infection.

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