EDITORIAL

10.5005/pid-6-3-iv

Dengue Prevention: Our Responsibility for a Safer Tomorrow

The march of dengue, unlike other ancient infectious disease scourges of mankind that have abated of late, has expanded relentlessly for the past several decades, and it currently affects over 120 countries, placing over four billion people at risk of dengue infection. The forces that sustain this expansion include rapid globalization, unplanned urbanization, and poor mosquito control. The vast majority of dengue infections are clinically inapparent. Among the approximately 25% of those infected who have clinical manifestations, symptoms are often mild, but they may be moderate or severe in a small proportion, leading to death in 0.1–2.5% of all cases depending on host factors and access to care.

Global Overview: Current Situation

As of 30th April 2024, over 7.6 million dengue cases have been reported to the WHO in 2024, including 3.4 million confirmed cases, over 16,000 severe cases, and over 3,000 deaths. While a substantial increase in dengue cases has been reported globally in the last five years, this increase has been particularly pronounced in the Region of the Americas, where the number of cases has already exceeded seven million by the end of April 2024, surpassing the annual high of 4.6 million cases in 2023. Furthermore, this is three times what was reported during the same period in 2023, highlighting the acceleration of this health problem. Dengue virus is transmitted to humans through the bite of infected mosquitoes. Cases are most commonly asymptomatic or result in mild febrile illness. However, some cases develop severe dengue, which may involve shock, severe bleeding or severe organ impairment.

The risk of dengue is similar across regions, countries, and within countries. Factors associated with an increasing risk of dengue epidemics and spread to new countries include:

- Early start and longer duration of dengue transmission seasons in endemic areas;
- Changing distribution and increasing abundance of the vectors (*Aedes aegypti and Aedes albopictus*);
- Consequences of climate change and periodic weather phenomena leading to heavy precipitation, humidity, and rising temperatures favoring vector reproduction and virus transmission;
- Changes in the circulating serotypes within a country affecting population immunity;
- Fragile health systems amid political and financial instability in countries facing complex humanitarian crises and large-scale population movements impairing the public health response;
- Movement of people who are infected and goods that could carry the mosquito vectors.

Currently, 90 countries have known active dengue transmission in 2024, not all of which have been captured in formal reporting. In addition, many endemic countries do not have strong detection and reporting mechanisms, so the true burden of dengue globally is underestimated. In order to control transmission more effectively, real-time robust dengue surveillance is needed to address concerns about potential undetected cases, cocirculation and misdiagnosis as other arboviruses, and unrecorded travel movements. These factors could contribute to unrecognized disease spread and establish a potential risk for local transmission in non-endemic countries. Given the current scale of the dengue outbreaks, the potential risk of further international spread and the complexity of factors impacting transmission, the overall risk at the global level is still assessed as high and thus dengue remains a global threat to public health. Dengue epidemics tend to have seasonal patterns, with transmission often peaking during and after rainy season. There are several factors contributing to this increase, and they include high mosquito population levels, susceptibility to circulating serotypes, favorable air temperatures, precipitation and humidity, all of which affect the reproduction and feeding patterns of mosquito populations, as well as the dengue virus incubation period.

Dengue virus is transmitted to humans through the bite of infected mosquitoes typically in tropical and subtropical climates worldwide, mostly in urban and semiurban areas. The primary vectors that transmit the disease are *Aedes aegypti* and, to a lesser extent, *Aedes albopictus* mosquitoes, though in some regions such as Europe and North America, this latter vector is more widespread. DENV has four serotypes (DENV-1, DENV-2, DENV-3, DENV-4). Infection with one serotype provides long-term immunity to the same serotype and only transient immunity to the other serotypes, after which secondary infections with a different serotype increase the risk for severe dengue. Dengue cases are most commonly asymptomatic or result in mild febrile illness. However, some cases will develop severe dengue, which may involve shock, severe bleeding or severe organ impairment. This stage often starts after the fever has gone away and it is preceded by warning signs such as intense abdominal pain, persistent vomiting, bleeding gums, fluid accumulation, lethargy or restlessness, and liver enlargement.

Dengue is primarily an urban disease of the tropics and the viruses that cause it are maintained in a cycle that involves humans and *Aedes aegypti* mosquitoes. The same mosquitoes transmit chikungunya and Zika viruses. The proximity of mosquito vector breeding sites to human habitation is a significant risk factor for DENV infection. *Aedes* species mosquitoes can become infected with the virus after biting individuals infected with DENV and then transmit the virus to others in the vicinity. This cycle, therefore, makes the infective mosquito capable of spreading the dengue virus within households and in the neighborhoods of cases, leading to clusters.

The surge in dengue incidence is likely triggered by various factors, including shifts in the circulating serotype and climate change. At least five countries (Bangladesh, India, Myanmar, Nepal and Thailand) are currently grappling with the initiation of monsoon season, which creates suitable conditions for *Aedes* mosquito breeding and survival. Additionally, urbanization and population movements have played a pivotal role in the increasing burden in the region. Changes in the predominant circulating serotype increase not only the incidence but also the population risk of subsequent exposure to a heterologous DENV serotype, which in turn increases the risk of higher rates of severe dengue and deaths.

There is no specific treatment for dengue, but the timely diagnosis of dengue cases, identification of warning signs for severe dengue, and appropriate clinical management are key elements of care to prevent the progression to severe dengue and deaths. The 1997 clinical classification of dengue that was later modified in 2009 highlighted the importance of recognizing 'warning signs' with the potential to turn nonsevere dengue into severe dengue; this had real practical value for triaging and clinical management of dengue (World Health Organization, 2009). Early access to health care is critical, and appropriate management includes close monitoring for thrombocytopenia and disease progression and supportive care for shock, hemorrhage, and organ failure. Careful and precise replacement of fluid losses can be life-saving. Early detection and access to appropriate health care for case management reduces mortality, as can rapid detection of dengue cases with warning signs and timely referrals of severe cases to tertiary healthcare facilities. Case surveillance should continue to be enhanced in all affected countries and globally. Where feasible, resources should be allocated for the strengthening of case referral mechanisms and for the confirmation and serotyping of the dengue viruses.

Effective vector control interventions are key to the prevention and control of dengue. Vector control activities should target all areas where there is a risk of human-vector contact, such as residences, workplaces, schools, and hospitals. WHO promotes Integrated Vector Management (IVM) to control *Aedes* species. IVM should include removing potential breeding sites, reducing vector populations, and minimizing individual exposure. This should involve vector control strategies for larvae and adults (i.e., environmental management and source reduction), especially monitoring water storage practices, draining and cleaning household water storage containers weekly, larvicide in non-potable water using WHO-prequalified larvicides at correct dosages, distribution of insecticide-treated nets (ITNs) for fever/dengue in patients to contain spread of the virus from health facilities. Indoor space spraying for rapidly containing dengue-infected mosquitoes may be challenging to deliver in densely populated areas.

Personal protective measures during outdoor activities include topical repellents to exposed skin or the treatment of clothing and using long-sleeved shirts and pants. Additionally, indoor protection can include the use of household insecticide aerosol products, or mosquito coils during the day; window and door screens can reduce the chances of mosquitoes entering the house and insecticide-treated nets offer good protection to people against mosquito bites while sleeping during the day. Personal protective measures are recommended from dawn to dusk due to the diurnal *Aedes aegypti*. These measures and mosquito control should also cover workplaces and schools since the vectors are day-biting mosquitoes. Entomological surveillance should be undertaken to assess the breeding potential of *Aedes* mosquitoes in containers to target vector control activities and monitor insecticide resistance to help select the most effective insecticide-based interventions.

Vaccination against dengue should be viewed as part of an integrated strategy to control the disease, including vector control, proper case management, community education, and community engagement. WHO recommends the use of TAK-003 (only available vaccine) in children aged 6–16 years in settings with high dengue transmission intensity. The first dengue vaccine to be licensed (CYD-TDV) is a recombinant tetravalent live-attenuated product with target dengue proteins expressed on a yellow fever virus backbone. Early data from large carefully conducted dengue vaccine trials in Asia and Latin America showed favorable safety and efficacy results. However, when these results were re-evaluated with baseline serological status at the time of immunization, it was found that vaccinated seronegative children of any age were at higher risk of hospitalization for severe dengue compared to age-matched and serostatus-matched controls (non-recipients of the vaccine). These observations suggest that the vaccine can be given safely only to individuals who have had one or more dengue infections in their lifetime. Taking into consideration these new data, and recognizing the potential public health benefit of even a partially efficacious dengue vaccine, the WHO in September 2018 recommended that individuals 9–45 years of age living in dengue-endemic areas may receive the vaccine as long as the individual shows evidence of a past dengue infection (World Health Organization, 2018). However, the quest for an appropriate point-of-care serological test for pre-vaccination screening is still in progress.

The way forward in dengue control is to obtain full commitment from global stakeholders in addressing a complex disease with solutions that include integrating disease surveillance, clinical management, vector control, and vaccination methods. For India, complete support from all aspects of the government, including health, science, infrastructure, sanitation, and regulatory agencies will be critical to achieving the WHO dengue control targets. An important research gap is the establishment of prospective cohorts and systematic serosurveillance to study viral patterns and immune epidemiological phenomena that can inform scientists, funders, and policy-makers on appropriate dengue control strategies

Vijay N Yewale
Editor-in-Chief

Bhaskar Shenoy
Managing Editor