



Perspective

Challenges & options in dengue prevention & control: A perspective from the 2015 outbreak

The menace of dengue has reached pandemic proportions and become a major public health concern. It has emerged and re-emerged across the globe to cause larger, more frequent and severe outbreaks involving areas thus far unaffected. As per the World Health Organization (WHO) fact sheet, dengue is endemic in >100 countries with 50 per cent of the world population at risk¹. The true global burden of dengue is still uncertain, and the incidence may be as high as 390 million infections per year as opposed to the WHO estimates of 50-100 million, due to lack of surveillance and under-reporting². The worst affected are the WHO South-East Asia region (SEAR) and Western Pacific regions.

In the SEAR, India accounts for 20 per cent of the cases³. The virus was first isolated in India in 1945, and occurrence of dengue fever was first reported in Vellore, Tamil Nadu in 1956³. From sporadic epidemics in the beginning, the outbreak frequency has increased over the last few decades. The fifth serotype, first reported from the forests of Malaysia in 2013⁴, has not yet been isolated from India. The worldwide spread of disease has been attributed to geographical spread of the vector and the virus, enormous infrastructure development, climate change and increased international trade and travel.

Despite being a self-limiting viral illness, a small proportion of patients develops severe dengue, which is a leading cause of mortality and morbidity associated with the disease¹. The WHO estimates that around 500,000 people every year are hospitalized for severe dengue infection¹. In 2015, India witnessed one of its largest outbreaks with 99,913 cases and 220 deaths⁵. Although the outbreak was relatively mild, the large numbers of cases during the outbreak threw the entire healthcare set-up into disarray, creating a state of panic. Despite media awareness, people with trivial

symptoms thronged medical outpatient departments (OPDs) and emergencies of all public and private hospitals in large numbers. Special screening OPDs were created, dedicated dengue wards were set up and healthcare staff was recalled from sub-specialities to cater to the demand of increased trained workforce. Blood banks too bore the brunt, facing an acute shortage of blood and blood products, which had a bearing on the survival of other sick patients. Some patients had to be denied admission in view of shortage of hospital beds, blood products and/or medicines. This led to the unfortunate eventualities of potentially salvageable lives. Delayed referral of complicated cases to tertiary care centres was identified as a major contributing factor to mortality.

Management of a dengue outbreak has two aspects: preparedness and response. Outbreak preparedness includes stringent larval, viral and vector surveillance, institution of warning systems, supply of sufficient diagnostic kits, development of locally adapted integrated vector control measures and community awareness. Although the frequency and magnitude of dengue outbreaks are hard to predict, knowledge of disease epidemiology and viral cycle can aid in pattern recognition and better outbreak preparedness. With the last spike of cases seen in 2010 and then in 2013, the next spike was expected in 2015 or 2016. Pre-emptive strengthening of preventive measures in this setting could have reduced the magnitude of the outbreak in 2015. Percentage gross domestic product (GDP) allocated to health is dismal in India (1.97% of the public expenditure; 4.1% of the total expenditure) and still below the 'alleged' WHO recommendation of 5 per cent⁶.

Prevention of dengue outbreaks centres around vector control. The current vector control measures in India are restricted primarily to the use of insecticides

and community clean-up/awareness campaigns which have had little impact on dengue control. Several shortcomings in the form of cost, delivery, insecticide resistance, sustainability and environmental safety exist. Several factors impede the effective implementation of the integrated vector management (IVM) strategy advocated by the WHO and the National Vector Borne Diseases Control Programme (NVBDCP). Widespread infrastructural activities without prior health impact assessments, poorly designed irrigation and water systems, improper solid waste management, deforestation, increased international travel and trade and climate change all contribute to vector proliferation and persistence. The multipronged IVM strategy, which emphasizes environmental management and biological control with judicious use of chemical methods, is effective, efficient and sustainable⁷.

The road ahead in vector control includes introduction of novel vector control strategies (population replacement with *Wolbachia*-infected mosquitoes, which is currently in its pilot phase in the United States⁸ and China; sterile insect technique and genetic editing) and scaling up of existing methods of biological control (copepods, larvivorous fishes such as *Gambusia* and *Poecilia*) and community participation. Embryonic introduction of *Wolbachia*, an obligate intracellular bacterium, results in *Aedes aegypti* that are partially resistant to infection with dengue virus. Clustered regularly interspaced short palindromic repeat (CRISPR)-Cas9 gene editing technology induces female embryos to develop male genitalia, thus converting all females to males or killing them⁹. Targeted use of vector control measures after identification of areas at greatest risk through understanding of local vector ecology and patterns of disease transmission is needed. Identification of latex collecting cups in rubber plantations of Kerala as a breeding habitat of *Ae. albopictus* is one such example¹⁰. Interruption of disease transmission by preventing mosquito bite is also important. Besides use of mosquito repellents (diethyltoluamide based) and long-lasting insecticide-treated bed nets (LLINs), novel, insecticide-treated ovitraps are close to commercialization as lure-and-kill devices¹¹. Bottom-up community-based rather than a top-down policy is essential for sustainability. Setting up of geographical information systems (GIS) and simpler entomological survey models/indices may be considered over long term.

The CYD-TDV dengue vaccine has been approved for marketing and use in five countries (Mexico, El Salvador, Costa Rica, Brazil and Philippines) based on the WHO recommendation for its use in high endemic

areas with a seroprevalence >50 per cent (ideally 70%) in the target age group¹². It has not yet been approved by the Indian government in view of concerns regarding its low efficacy against the widely prevalent serotype 2, doubtful safety in children less than nine years and lack of data/trials in the Indian population. The development of an efficacious sustainable vaccine still has a long way to go¹³, and identification of a dengue vaccine cohort in India is a step towards it. From 2016, the Ministry of Health and Family Welfare, Government of India, has declared 16th May as National Dengue Day and July as Anti-Dengue Month to increase public awareness and signal the onset of preparatory activities for the prevention and control, as outbreaks mostly occur in the monsoon-post-monsoon period (July-October)^{14,15}. A National Health Portal, available in six different languages, has been designed as a gateway for dissemination of authentic health-related information¹⁶. A mobile application 'India Fights Dengue' has also been launched in 2016 to carry out the behaviour change communication campaigns¹⁵. Mass clean-up campaigns linked with the 'Swachh Bharat Abhiyan (Clean India Mission)' have been planned¹⁷.

With the development of national guidelines in 2008 and their revision/update in 2014, rapid advances have occurred in the domain of case management³. Lack of competency in case management, especially at the primary and secondary healthcare levels, was identified by the Joint Monitoring Mission (JMM) on vector-borne diseases in March 2014¹⁸. It recommended strengthening the existing capacity of healthcare staff and development of adequate and timely referral mechanisms for sick patients^{18,19}. Triage using previously identified predictors of disease severity needs to be done to identify sick patients and curtail unnecessary hospital admissions so that limited human and material resources can be optimally used. Management-related information needs to be disseminated and reinforced through media for cases being managed at home. Prophylactic platelet transfusion has no role, as shown in a recent randomized control trial (RCT) published in the Lancet²⁰. A tendency to 'chase' the platelet count to >50,000/ μ l with repeated transfusions (dengue panic syndrome) is widely prevalent and needs to be discouraged, as it not only creates a shortage of blood products for sick patients but also exposes the patient to risks of transfusion reactions, transfusion-related infections, post-transfusion purpura and transfusion-associated graft-versus-host disease (GVHD)^{21,22}. Alternative medicines such as papaya extract, goat

milk and *giloy* are being used without any proof of evidence of benefit. The NVBDCP has established 527 Sentinel Surveillance Hospitals with laboratory support for quality-assured laboratory diagnosis free of cost (the cost is borne by the programme)²³. These are linked to 14 Apex Referral Laboratories with advanced diagnostic facilities for back up support²⁴. Despite this, the laboratory support for quality assured testing is still inadequate and needs further strengthening.

Dengue continues to expand and involve newer geographical areas and populations. Although associated with low mortality, financial resources required for dengue control, especially in developing countries like India, is a huge challenge. Advancements in the domain of prevention need to parallel the advancements in case management. We believe that release of *Wolbachia*-infected mosquitoes, the sterile insect technology, use of lure-and-kill devices and piloting of dengue vaccine in India along with better intersectoral coordination to improve implementation of existing preventive measures are a promising solution to the growing menace of dengue in India. A preventive approach to dengue control rather than a reactive one is the key.

Conflicts of Interest: None.

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