New Microbes and New Infections 55 (2023) 101183

Contents lists available at ScienceDirect

New Microbes and New Infections

journal homepage: www.journals.elsevier.com/new-microbes-and-new-infections

Letter to the Editor

Countering Dengue infection in Bangladesh in the backdrop of current outbreak

Dear Editor,

Dengue virus outbreak has been reported in Bangladesh since 1960s and has been known as "Dacca fever". Since 2010, dengue cases in Bangladesh coincide with the rainy season from May to September and high temperatures. Excessive rainfall, water logging, flooding, rise in temperature and the unusual shift in the country's traditional seasons have made Bangladesh more favorable for the transmission of dengue and other vector borne diseases like malaria and chikungunya. From 1 January to 7 August 2023, the Ministry of Health and Family Welfare of Bangladesh reported a total of 69,483 laboratory-confirmed dengue cases and 327 related deaths, with a case fatality rate (CFR) of 0.47%. Of these, 63% of cases and 62% of the deaths were reported in the month of July 2023 (https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON481).

Dengue virus belongs to the family Flaviviridae and genus Flavivirus. Dengue virus (DENV) has four serotypes: DEN-1, DEN-2, DEN-3 and DEN-4. It has been observed that infection with one serotype does provide a long-term immunity to homologous serotype but not to the other serotypes and subsequent infection with a different serotype is responsible for increase in a disease severity [1]. While about 80% of DENV infections are asymptomatic, others exhibit only mild flu like symptoms including high fever, headache, body aches, nausea and rash. Most cases get recovered within 1–2 weeks, while some patients develop severe symptoms like dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS) and may need hospitalization. Various studies have shown a possible correlation between DEN-2 and DEN-4 with severe dengue cases [2].

Dengue is vector borne viral disease transmitted to humans through the bite of infected mosquitoes and is prevalent in tropical and subtropical regions of the world. The primary vector responsible for transmitting the disease to humans is *Aedes aegypti* mosquitoes and to a lesser extent *Aedes albopictus*. After feeding the DENV infected person, the virus replicates in the midgut of the mosquito and then disseminates to secondary tissues, including the salivary glands. The time taken from ingesting the virus to its actual transmission to a new human host is termed as the extrinsic incubation period (EIP). This EIP is about 8–12 days under an ambient temperature of 25–28 °C and is influenced by temperature fluctuations, virus genotypes and initial viral load. Studies have reported that mosquitoes can get infected by a human if they bite them 2 days before they show the symptoms and up to 2 days after the fever is resolved. There is evidence of a possibility of maternal transmission, but the rate of vertical transmission is low and is linked with the trimester of pregnancy (https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue). Babies from a pregnant women infected with DENV may suffer from pre-term birth, low birth weight and fetal distress. Transovarial transmissions of the virus within the mosquitoes have been reported and this has helped the virus overcome the winter season. Rare cases of transmission via blood products, organ transplantation and transfusions have also been reported (https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue).

Dengue is diagnosed by non-structural protein-1 (NS-1) antigen capture assays, which is detectable up to 9 days after the onset of symptoms in primary infection. In the case of secondary infections, NS-1 is detectable for a much shorter period due to an anamnestic response. Although serological assays by IgG or IgM antibody capture are available, they suffer from cross-reactivity with other flavivirus infections [3]. Various nucleic acid amplification tests (NAATs) with varying degrees of sensitivity are available to detect viral RNA. Such NAATs, which could be employed to detect DENV RNA in serum, plasma or whole blood include reverse transcription polymerase chain reaction (RT-PCR), real-time RT-PCR and reverse transcription loop mediated isothermal amplification (RT-LAMP) [4]. These molecular methods can provide a same day diagnosis for DENV during the acute phase of the disease and can also detect virus serotype. Apart from this, plaque reduction neutralization tests (PRNT) quantifying virus specific neutralizing antibody titers can distinguish DENV from other flaviviruses [5].

Being a vector borne disease, an effective vector control method is critical in achieving a sustained reduction of dengue disease. Common dengue vector control measures include use of insecticide treated materials, cleaning of water storage tanks and elimination of mosquito breeding sites or use of larvicides. WHO promotes Integrated vector management (IVM) to control *Aedes* species. The major aim of IVM is to remove potential breeding sites, reduce vector populations and minimize individual exposure (https://www.who.int/westernpacific/activities/integrating-vector-management). Since *Aedes* mosquitoes are active at dawn and dusk, personal protective measures like topical application of skin repellents to exposed skin or treatment of clothing and use of long sleeves shirts and pants are recommended. Apart from these traditional vector control methods, novel vector control methods include deployment of genetically modified mosquito and use of *Wolbachia pipientis* bacterium [6]. The need of the hour is regular monitoring of breeding sites in endemic areas and revamping of the nation's capacity to diagnose and manage clinical Dengue cases.

Cross-border collaboration with neighboring countries will also help in controlling vector borne diseases. Bangladesh shares 94% of its land border with India with frequent population movement across border. Dengue is already endemic in India, which includes the eastern Indian states where *Aedes* mosquitoes breed and circulate, which share land borders with Bangladesh. Due to social and economic reasons, many people from Bangladesh migrate to other countries thereby increasing the risk of international spread to dengue disease. Bangladesh does receive a huge volume of international tourists and thus the possibility of travelers acquiring the disease and contributing its spread outside the

https://doi.org/10.1016/j.nmni.2023.101183
Received 13 September 2023; Accepted 15 September 2023
Available online 20 September 2023

country cannot be ruled out. Climate change along with heavy rains in neighboring countries also increases the likelihood of vector-borne disease transmission. A tetravalent Dengue vaccine called Dengvaxia has been approved by USFDA since 2019 should be approved in Bangladesh. All four serotypes of the dengue virus have been reported in Bangladesh with the predominance of DENV-2 until 2018, when it was replaced by DENV-3 as the predominant serotype in 2019. In this outbreak DENV-2 was identified as the primary circulating serotype, this may result in severe dengue infections and hospitalizations due to second infection with a heterologous serotype.

The current Bangladesh healthcare infrastructure is in dilapidated state due to COVID-19 pandemic, this needs to be revamped. The existing hospitals assigned for the management of COVID-19 patients are required to be repurposed for management of dengue cases. Large scale capacity building for doctors and nurses on clinical management of dengue cases should be carried out across the country. Mass awareness campaigns via television and print media and community awareness by the local ward counsellors should be strengthened further. As there is no specific treatment for dengue infection, early detection and access of appropriate healthcare management can drastically reduce mortality. Addressing all these concerns will pave the way for controlling the vector borne disease outbreak in the Asian subcontinent.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Bhatt S, et al. The global distribution and burden of dengue. Nature 2013;496 (7446):504–7.
[2] Balmaseda A, Hammond SN, Perez L, et al. Serotype-specific differences in clinical manifestations of dengue. Am J Trop Med Hyg 2006;74:449–56.
[3] Cleton NB, Godeke GJ, Reimerink J, et al. Spot the difference-development of a syndrome-based protein microarray for specific serological detection of multiple flavivirus infections in travelers. PLoS Neglected Trop Dis 2015;9(3):e0003580.
[4] Nunes PCG, Lima MRQ, Dos Santos FB. Molecular diagnosis of dengue. Methods Mol Biol 2022;2409:157–71.
[5] Sirivichayakul C, Sabchareon A, Limkittikul K, et al. Plaque reduction neutralization antibody test does not accurately predict protection against dengue infection in Ratchaburi cohort, Thailand. Virol J 2014;11:48.
[6] Utarini A, Indriani C, Ahmad RA, et al. Efficacy of Wolbachia-infected mosquito deployments for the control of dengue. N Engl J Med 2021;384(23):2177–86.

Subrat Kumar*, Ritesh Pattnaik
School of Biotechnology, Campus-11, KIIT Deemed-to-be-University, Bhubaneswar, Odisha, 751024, India

Subhra Subhadra
Virology Lab (VRDL), ICMR-Regional Medical Research Centre, Bhubaneswar, Odisha, 751023, India
E-mail address: ssubhadra@yahoo.com.

Priyadarshi Soumyaranjan Sahu
Faculty of Pre-clinical Medicine, Medical University of the Americas, Nevis, St. Kitts & Nevis
E-mail address: priyadarshi_sahu@yahoo.com.

* Corresponding author.
E-mail addresses: Subrat_kumar@yahoo.com (S. Kumar), rpattnaik@kiitbiotech.ac.in (R. Pattnaik).
Handling Editor: Patricia Schlagenhauf