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Monograph
Dengue

Editors
Jyotirmoy Pal
Nandini Chatterjee
Sekhar Chakraborty

3rd Edition

Foreword
Alaka Deshpande

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Chapter 4

Changing Epidemiology of Dengue in Southeast Asia

Pradip Kumar Chowdhury, Nandini Chatterjee, Shilpa Tomar, Tanuka Mandal

INTRODUCTION

The epidemiology of dengue fever (DF) and dengue hemorrhagic fever (DHF) is complex and it involves many factors i.e. host, viral and vector status which are further influenced by demographic, economic, behavioral and various societal factors. It is thus crucial to properly understand the evolving pattern and trend of DF/DHF epidemiology for the success of prevention and control programs of dengue.

In South east Asia (SEA) countries, DF is typically a disease of early childhood, whereas clinical DF in adults is uncommon. In these areas, the DHF and dengue shock syndrome (DSS) occurs mostly in children aged between 2–15 years. Older and most of the younger are usually immune and escape DHF, due to their acquired immunity against primary infection. Although, there is an increase incidence in older age groups (15–45 years) reported in Thailand, Nepal, Singapore, Indonesia, Bangladesh, Sri Lanka, Cuba and India in the last major outbreaks. It has been hypothesized that the time interval between two sequential infections are the determinant factor for this phenomenon. Many studies from SEA region suggest that males are more affected than females in DF/DHF hospitalized cases (reported from Singapore, Malaysia, India and Bangladesh) which can be linked to the health seeking behavior of the people and only few studies suggest no sex difference in incidence. Studies in India by Shekhar et al. and in Malaysia by Kabra et al. reported that a higher rate of mortalities noticed among females than males, suggesting different pathogenesis processes or immune response in females.

Sequential infections or secondary infections are the important determinants for the severity of the disease. The risk of DHF with different sequences of dengue viruses infections are shown in **Table 1** which are revealed from studies in Thailand.

Small genotypic changes and virulence of the dengue viruses are also the important determinant of DHF revealed from a Sri Lankan study.

TABLE 1: The risk of dengue hemorrhagic fever in relation to sequence of infection.

Sequence of infection	*Risk of dengue hemorrhagic fever*
1. DENV-1 2 DENV-2	500-fold
2. DENV-3 2 DENV-2	150-fold
3. DENV-4 2 DENV-2	50-fold

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The age is an important modulator of clinical dengue. There is no time limit for sensitization after a primary dengue infection. If after a long-interval secondary infection occurs, it results decreased neutralizing antibody from the primary infection and thus accounting for more DHF/DSS in adults. In SEA, dengue virus (DENV) infection in the higher age groups is linked to higher risk of clinical attack.

Dengue fever/DHF is believed to be a primarily urban disease as the vectors are well adapted to human habitation. However, dengue has been spread into rural areas from where it had not been reported earlier due to modernization and consequence from all development of rural areas. In some countries the incidence of dengue is higher in rural than in urban areas.

Dengue incidence, particularly dengue epidemics, is currently associated with the rainy season when temperature falls down and humidity increases as *Aedes aegypti* is a hygrophilic (humidity-loving) species, but relative importance of these factors varied with geographical areas. More evidences and studies are required to investigate vector behavior.

Climate change (such as increased temperature and rainfall and extreme weather events) may facilitate dengue expansion. In East Asia, climate change has raised concerns that dengue fever has become endemic, particularly in cities or countries neighboring the Tropic of Cancer.

Socioeconomic, cultural factors and individual susceptibility plays an important role in the variable incidence of dengue infection. In dry and hot climatic region of India, desert cooler, water stored in baked-soils containers are the major source of *Aedes* mosquito species breeding in lower socioeconomic group. Sometimes transmission occurs from "work sites" rather than from the residential houses due to unsuccessful vector control programs in work site.

Epidemics occur every 3–5 year cycles with increasing number and severity throughout SEA. A total of 187,333 dengue cases were reported to WHO in 2010 from these regions. Eight SEA countries are now considered as hyper endemic with all four serotypes. Severe dengue is endemic and 18 times higher in most SEA countries compared to Americas.

CHANGING EPIDEMIOLOGY OF DENGUE IN INDIA

The epidemiology of DF in the Indian subcontinent has been steadily changed over past 6 decades in terms of prevalent strains, severity of infection and affected geographical areas. The DF first reported in India in the year 1946. Thereafter, there was no significant dengue incidence for the next 18 years in the country. An initial epidemic of DF reported on the Eastern coast of India in 1963–1964. It then spread toward the North and reached to Delhi in 1967 and to Kanpur in 1968.

However, as per the data of National Vector Borne Disease Control Programme (NVBDCP) and earlier publications by National Institute of Virology (NIV) the dengue has been endemic in 16 states (Delhi, Puducherry, Punjab, Rajasthan, Andhra Pradesh, Goa, Gujarat, Haryana, Karnataka, Kerala, Madhya Pradesh, Maharashtra, Chandigarh, Tamil Nadu, Uttar Pradesh and West Bengal) since the beginning, but dengue has spread into the remaining states during 2010–2012 **(Fig. 1)**.

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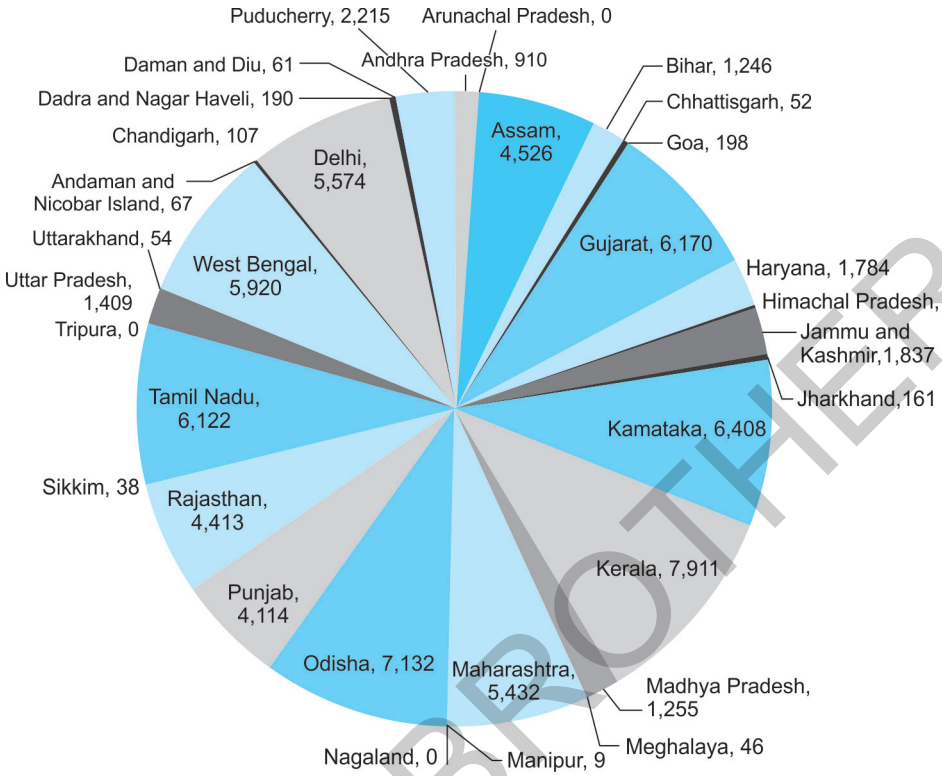

Fig. 1: Distribution of dengue cases in Indian states in 2013 (based on NVBDCP data).

Although the number of dengue cases has shown a steady rise with every passing year, the mortality has been decreased. The mortality rate was highest in 1996 outbreak which was above 3.0%. This was 1.2% in 2007, 0.25% in 2013 and dropped to 0.20% in 2015 **(Figs. 2 and 3)**. This reduction is probably the summative effects of increased diagnostic capabilities, earlier reporting of the cases and better patient management. The number of DSS cases in India is low compared to the rest of SEA.

The epidemiology of dengue and its prevalent serotypes are continuously changing. A study at the All India Institute of Medical Sciences (AIIMS), New Delhi, during 2003–2005 reported the maximum number of cases among 21–30 years age group and the peak was in October. In 2003, all the four serotypes was observed to cocirculate and DENV-3 was emerged as the dominant serotype in 2005. Another study in a tertiary care hospital of Delhi for 7 years (2002–2008), reported circulation of all four serotypes in 2003 and thereafter emergence of DENV-3 in 2004–2006, DENV-2 in 2007 and DENV-1 in 2008 as dominant strain. Another longitudinal study covering 6 years (2005–2010) in Pune city involving 24 private and government clinics cum hospitals revealed that most affected age group was 21–30 years throughout the 6 years and largest numbers in October with a positivity of 57.9%. The seropositive cases for DENV found in the urbanized villages were significantly higher (58.5%) compared to the rural villages (41.2%). All four serotypes were found

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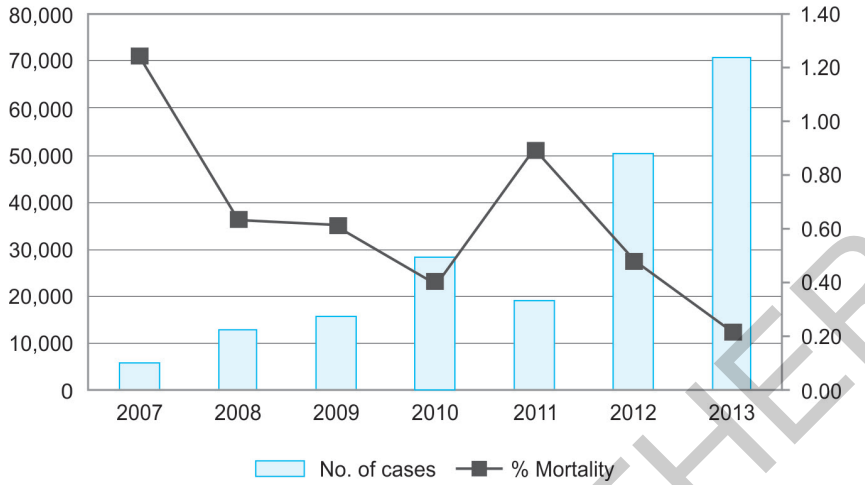

Fig. 2: Total dengue cases reported to NVBDCP (left axis) and percentage mortality (right axis) in India, 2007–2013.

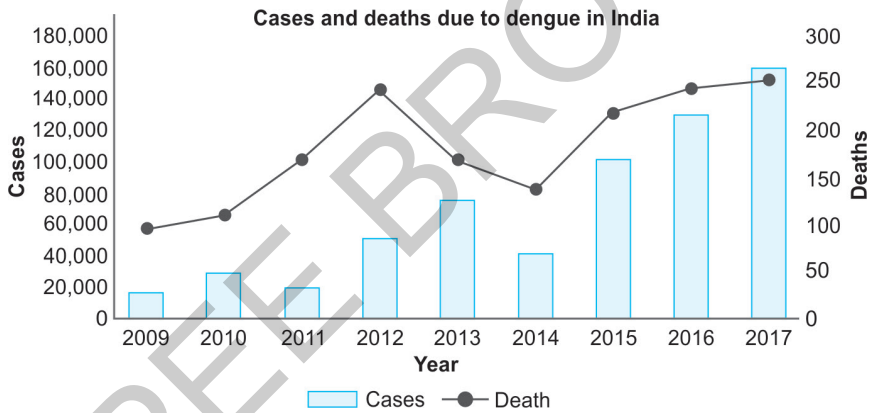

Fig. 3: Total dengue cases and dengue deaths in India reported up to 2017.

with predominance of one serotype. In 2005 and 2007 DENV-1 was dominant, DENV-2 in 2008 and DENV-3 was dominant in 2009. Both DENV-2 and DENV-3 were co-dominant in 2010. DENV-4 was rarely found with just one case for each year 2009 and 2010 and both the cases were DHF.

The number of dengue cases in India was 10,097, with 37 deaths in 2014. That have already been doubled with 19,704 cases with 41 death reported till 6th September 2015.

The number of dengue cases is continuously increasing and it was the highest in the last one decade, according to the data from NVBDCP and National Health Profile 2018. From < 60,000 cases in 2009, the cases increased to 188,401 in 2017—more than a 300% spike. When compared to 75,808 cases in 2013, it is more than a 250% spike. Maximum spike was observed in Southern and Northeastern states **(Fig. 4)**.

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However, a significant diminution I cases were noticed in 2021 and 2022 during the COVID Pandemic. In 2020, the number of cases were 44,585 and 56 patients died while that number decreased to193,245 cases in 2021 (346 deaths) and 10,172 cases (3 deaths) in 2022 (Upto May 31st). Probable causes were the lockdown and travel restrictions.

While Northeastern states such as Sikkim, Nagaland, Mizoram and Tripura have seen the highest leap in terms of percentage, the Southern states shared the maximum burden of numbers. For example, just four states had collectively recorded

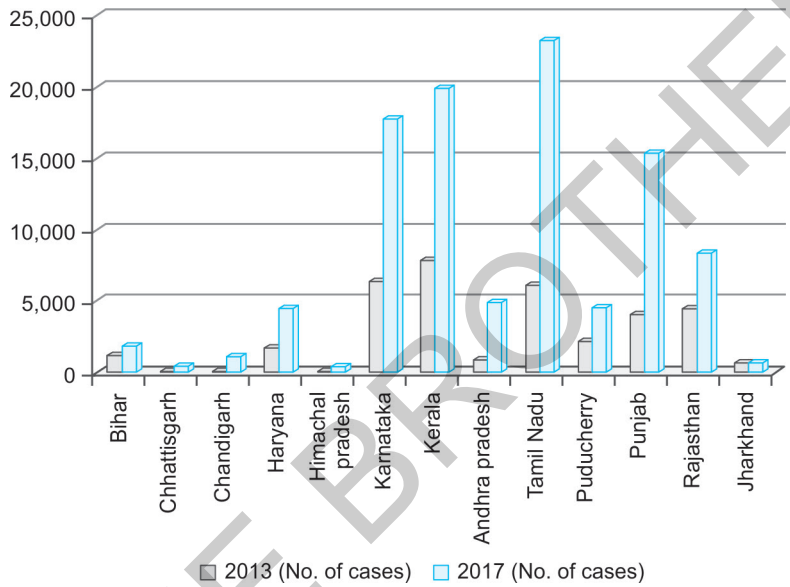

Fig. 4: Comparison of dengue cases of some districts in India between 2013 and 2017.

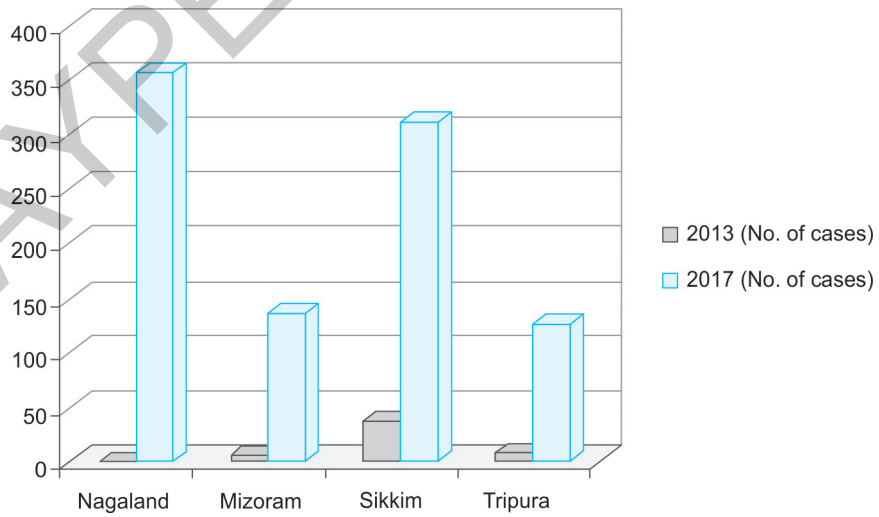

Fig. 5: Dramatic increase of dengue cases in Northeastern states in India.

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66,057 cases, which is close to 40% of the total cases recorded in the country. Northeastern states such as Mizoram, Sikkim and Tripura experienced between 1500% and 1700% rise in cases between 2013 and 2017 **(Fig. 5)**. The national capital Delhi has also seen its dengue cases almost double during this period. According to National Health Profile 2018, dengue outbreaks have continued since the 1950s but severity of disease has increased in the last two decades.

CONCLUSION

It is evident that almost 75% of the global population exposed to dengue lives in Asia-Pacific region. Almost 1.3 billion of these at-risk individuals live in 10 dengue endemic countries in SEA and dengue is a leading cause of hospitalization and the death in children from this region. The rates of disease reported in each of the SEA countries varies as they include either laboratory confirmed, probable, or suspected cases. As per WHO data, an overall expansion of dengue has occurred over the last decade in SEA. Not only the number of cases is increasing, the disease is spreading to new areas with explosive outbreak due to unplanned urbanization, increasing urban overpopulation with inadequate public health systems, global warming, poor control of stagnant water and vector, viral evolution and increased travel to endemic areas.

In the year 2020, the number of dengue cases reduced significantly. Li et al. showed that the impact of travel restriction is significant on dengue cases using a quasipoisson regression model taking account of weather predictors (i.e. temperature and rainfall).

The results confirmed that dengue incidence between 2013–2019 in Yunnan was closely linked with international importation of cases from neighboring countries and the reduction in 2020 was largely due to travel restrictions. These results along with phylogeographic analyses suggest that Yunnan is a regional sink for DENV lineage movement and that border restrictions may have substantially reduced the burden of dengue.

Preparing for and preventing a larger dengue outbreak after reopening international borders in these subtropical regions becomes urgently important. Improving dengue mosquito surveillance and testing and tracing policies for travelers arriving from endemic countries during large outbreaks or high risk dengue seasons may become critical steps to predict and control the global spread of dengue.

HIGH YIELD FACTS

- Major burden of dengue in Southeast Asian states
- 16 states of India declared as dengue endemic
- India experienced massive mortality due to dengue hemorrhagic fever in 1996 in Delhi
- All four serotype circulating in India since 2003
- Dengue infection in 2018 was caused by DENV 2 serotype.

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- Atypical presentations and complications
- Therapeutic and prognostic pointers
- New Suggested Reading

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