

INTRODUCTION

Dengue, an arboviral infection transmitted by *Aedes aegypti* and *Aedes albopictus* mosquitoes, has emerged as one of the most important mosquito-borne viral disease. It is a global public health problem causing 50 to 390 million annual infections ranging from dengue fever, dengue hemorrhagic fever (DHF), to dengue shock syndrome (DSS). Climatic change, spread of dengue vectors to new geographic locales, increasing international travel, global trade, and rural to urban migration have collectively brought about far reaching changes in the patterns and trends of dengue.

Dengue in India has dramatically expanded over the last few decades. Although a notifiable disease in India since 1996, the impact of dengue has been underestimated because of insufficient information from the national reporting systems. Between 2006 and 2012 the National Vector Borne Diseases Control Program (NVDCP) reported an annual average (\pm SD) of 20,474 (\pm 13,760) dengue cases and 132 (\pm 57) deaths caused by dengue, a

number which is still thought to be underestimating the full impact of the disease

BRIEF HISTORY OF DENGUE IN INDIA

The epidemiology of dengue in India has seen major evolution and changes. The first reported occurrence of dengue fever in India documents back to 1946. Since then there were no major outbreaks in the country for almost two decades. Calcutta faced a major epidemic in 1963–1964. It gradually spread to involve parts of northern and southern India in 1967–1968 with cases being reported of all four serotypes (DENV 1-4) of dengue virus. This was followed by a relative period of quiescence of almost three decades. The next major outbreak of DF/DHF was reported from Delhi in 1996 where 10,252 cases and 423 deaths occurred. This outbreak was caused by DENV-2, genotype IV strain of the virus. Similar strains of the DENV-2 were reported from central India and southern India, indicating that the predominant circulating strain in India that time was DENV-2.

Serotypes of the virus kept changing from year to year, and each time there was a change in serotype the areas reported a higher burden of dengue cases. In 2003, another major outbreak engulfed northern and central India (particularly in Delhi and Gwalior), and at this time, all four serotypes were seen for the first time in Delhi with the predominant serotype being DENV-3. The re-emergence of this epidemic strain of DENV-3 in Delhi in 2003 and its persistence in subsequent years marked a changing trend in DENV circulation, showing the shift in the epidemiology of dengue virus in India. Subsequently, all four serotypes were reported from various parts of the country. Distribution of various serotypes in some of the recent outbreaks in India is depicted in Table 1. Concurrent infection with multiple serotypes of dengue was also seen. Thus, it became more evident that India had gradually moved to being a hyperendemic area of dengue virus infection.

Evolution of dengue case definition

Earlier guidelines classified dengue into three categories:

- Dengue fever (DF): an acute febrile illness
- Dengue hemorrhagic fever (DHF grades 1 and 2): a syndrome characterized by increased vascular permeability
- Dengue Shock Syndrome (DSS): a state of altered homeostasis with progression to hypovolemic shock (grades 3 and 4).

Table 1: Recent outbreaks of dengue and involved serotypes

Year of study	Region	Predominant dengue virus serotype
2001	Gwalior, Madhya Pradesh	DENV-2
2003	Northern India (Delhi and Gwalior)	DENV-3
2003-05	Delhi	2003 DENV-1-4, 2005 DENV-3
2005	Kolkata	DENV-3
2006	Delhi	DENV-1 & 3
2008	Delhi	DENV-1,2,3
2008	Ernakulam, Kerala	DENV-2,3
2009	Delhi	DENV-1-4
2009-10	Pune, Maharashtra	DENV-4
2010-11	Delhi	DENV-1
2009-12	Uttar Pradesh	DENV-1,2,3
2013	Delhi	DENV-2
2015	Delhi	DENV-1-4, (DENV-2 predominant)

In 2009 the new revised clinical classification of dengue was proposed which now divides the clinical cases into two categories: dengue with or without warning signs, and severe dengue infection.

EVOLVING CHANGES IN DENGUE EPIDEMIOLOGY

The epidemiology dengue is complex and it involves host, viral and vector status that are further influenced by demographic, economic, behavioural societal factors. It is thus of utmost importance to understand the evolving pattern and trend of the epidemiology of dengue.

CHANGES IN AGE DISTRIBUTIONS

Dengue has traditionally been a disease of early childhood with most cases of DHF/DSS occurring in children aged 2-15 years, adults being usually immune and escaped DHF, as they have acquired immunity against primary infection. However, there has been a significant increase incidence in the older age group in recent outbreaks of dengue.

SEX PREDILECTION AND DENGUE

Males outnumber females in the majority of the reports of dengue outbreaks in India, and in a few studies the male to female ratio was as high as 3–5:1. An interesting finding however is an apparent difference between sexes in term of severity of illness and case fatality ratio. A previous study reported a higher rate of mortalities among females than males, suggesting different pathogenetic processes or immune response. Further research into determining the sex differences both in infection and severity of the disease is needed to assess the disease pattern in the community.

SEASONAL VARIATIONS IN DENGUE

The seasonal character of dengue epidemics in India has been documented by ecological studies. Outbreaks of DF and DHF most commonly occur during the warm and humid conditions of the rainy season which are favourable for abundant mosquito growth. In a study of the influence of climatic factors on the pattern of dengue infections, the interaction between rainfall, temperature and relative humidity were found to be associated with the distribution of serologically confirmed dengue cases with a peak occurrence rate at the end of the monsoon season during the months of October and November. In contrast, few studies have reported dengue outbreaks during the dry summer months from Rajasthan and Maharashtra indicating local variations in the pattern of outbreak.

RURAL-URBAN DISTRIBUTION

Historically dengue was considered an urban disease. Rapid urbanization and unplanned constructions with deficient waste water management systems resulted in the ideal conditions for the proliferation and spread of the vector and the virus. While this is still the case, the disease has progressively made its presence felt in the rural settings. The first outbreak reported from a typically rural area occurred in northern India (Haryana) in 1996 and subsequent outbreaks in rural settings were reported from

Maharashtra and Tamil Nadu. The spread of dengue from urban to rural areas is related to both the phenomenon of peri-urbanization as well as improved reporting and surveillance systems. The gradual urbanization of the rural areas resulted in the proliferation of *Aedes aegypti* in such areas and has resulted in the transition of dengue from a primarily urban problem to a pan-India health concern.

SEROTYPE VARIATIONS IN DENGUE

The first serotype of dengue infection in India was DENV-1. DENV-2 emerged as the predominant serotype from the early 1970s to 2000, during which time it was responsible for the large epidemics of dengue. DENV-3 emerged as a predominant serotype in large outbreaks in 2003 and 2006. All four DENV serotypes were found to co-circulate in Delhi for the first time in 2003, which thus became a hyperendemic region for dengue. Co-circulation of multiple DENV serotypes has resulted in concurrent infection with more than one serotype, further leading to complexity in the serotypic distributions of dengue.

CLINICAL PRESENTATIONS AND SEVERITY OF DISEASE

A mild to moderate degree fever has been the most consistent finding in all the epidemics with an average duration of 5-7 days. Rashes, retro-orbital pain, myalgia, headache and vomiting have been the other traditional clinical presentations commonly documented in various studies. Thrombocytopenia has also been a classical laboratory abnormality frequently found in cases of dengue. Interestingly though not a criteria according to WHO, certain studies from Delhi have documented the presence of splenomegaly in a large number of cases.

Since the mid to late 1980s and early 1990s small numbers of severe dengue cases in the forms of DHF and DSS were reported gradually leading to the large epidemic in 1996. This pattern of a gradual increase from small numbers of sporadic severe dengue cases occurring for several years, leading to a major epidemic is typical of every region where epidemic DHF has become established. Following the epidemic of DHF in 1996, two other large epidemics with substantial numbers of deaths occurred in 2003 and 2006. However, the subsequent years noted a decline in the case fatality rates. This is a feature which is perhaps contributed by the increased awareness of the disease and consequent improved diagnosis and management.

CONCEPT OF “EXPANDED DENGUE”

Expanded dengue is a terminology developed in the WHO guidelines of year 2012 to describe cases which cannot be classified either as DHF or DSS and incorporates atypical findings and presentations of dengue. These comparatively unusual presentations may be on account of several factors including co-infections, co-morbidities or complications of prolonged and sustained shock. Table 2 shows certain atypical manifestations of dengue.

CONCLUSION

In recent years the epidemiology of dengue infection has evolved rapidly. Progressively larger outbreaks are being

Table 2: Atypical manifestations of dengue

Organ system involvement	Clinical spectrum
Renal	Acute Kidney Injury, IgA nephropathy
Cardiac	Conduction abnormalities, Atrio-ventricular dissociation
Neurological	Gullian Barre syndrome, acute encephalitis, encephalopathy, seizures
Hepatic	Hepatic encephalopathy, acute liver failure
Auto-immune	Dysregulated immune response leading to systemic lupus erythematosus
Kawasaki disease	Reported in a child with mucocutaneous involvement
Haemophagocytic syndrome	Evidence of pancytopenia with bone marrow haemophagocytosis

observed, accompanied by a shift in the paradigm of the disease from urban to rural settings. Disease patterns are also evolving rapidly with circulation of multiple DENV serotypes and expansion of the profile of clinical presentations.

REFERENCES

- Bethell DB, Gamble J, Pham PL, Nguyen MD, Tran TH, Ha TH et al. The non-invasive measurement of the microvascular leakage in patients with Dengue hemorrhagic fever. *Clin Infect Dis* 2001; 32:243-53.
- Chakravarti A, Arora R, Luxemburger C. Fifty years of dengue in India. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 2012; 106:273-82.
- Gupta E, Ballani N. Current perspectives on the spread of dengue in India. *Infection and Drug Resistance* 2014; 7:33-7.
- Gupta E, Dar L, Kapoor G, Broor S. The changing epidemiology of dengue in Delhi, India. *Viol J* 2006; 3:92-96.
- Halasa YA, Dogra V, Arora N, Tyagi BK, Nandand D, Shephard DS. Overcoming data limitations: design of a multi-component study for estimating the economic burden of dengue in India. *Dengue Bull* 2011; 35:1-4.
- Islam A, Abdullah M, Tazeen A, Afreen N, Deeba F, Naqvi IH, et al. Detection of All the Four Serotypes of Dengue Virus in New Delhi, India During Post Monsoon Season of 2015. *Indian Journal of Health Sciences and Care* 2016; 3:24-9.
- Murray NE, Quam MB, Wilder-Smith A. Epidemiology of dengue: past, present and future prospects. *Clinical Epidemiology* 2013; 299-309.
- Saxena P, Parida MM, Dash PK, et al. Co-circulation of dengue virus serotypes in Delhi, India, 2005: implication for increased DHF/DSS. *Dengue Bull* 2006; 30:283-7.
- Shepard DS, Halasa YA, Tyagi BK, Adhish SV, Nandan D, Karthiga KS, et al. INCLIN Study Group. Economic and disease burden of dengue illness in India. *The American Journal of Tropical Medicine and Hygiene* 2014; 91:1235-42.
- World Health organization Comprehensive guidelines for prevention and treatment of dengue and dengue hemorrhagic fever. New Delhi: WHO, SEARO; revised and expanded edition. SEARO Technical Publication Series No. 60, World Health Organization 2011.