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The rise and spread of Dengue and its vectors in India: A Review

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ABSTRACT

The dengue as an illness has been recognized for more than 200 years and the role of *Aedes aegypti* as the vector of this arbovirus has been known for the last 90 years. About half of the world's population is now infected with an estimated 100–400 million new infections occurring each year. Dengue is found in tropical and sub-tropical climates worldwide, mostly in urban, semi-urban and rural regions. The first reference of dengue was mentioned in Mumbai, Pune and Kolkata in 1871 and after that reported from Ganges valley as far as Ludhiana , Kerala coast and from Calicut to Quilon. The dengue vector *Aedes aegypti* was also distributed all over India in 1934s in a faunistic survey done by Barraud. . The vector species was even reported from all over India and even from Lahaul and Spiti in Himachal Pradesh. The species was also confirmed by the following surveys. In India dengue was first reported and documented in 1956 from Vellore. Thereafter, there was an outbreak in Kolkata during 1960s. During this period, reports of Chikungunya spread was also seen in different parts of the country, potentially because both viruses were circulating in the same place at the same time. Following that, an epidemic of haemorrhagic fever was reported in Kolkata in 1963 and febrile illness in Nagpur city in Maharashtra during 1965. 50% of the infected population were affected by severe joint and body pain. Now dengue is endemic in the country and reported in 36 states/UTs . The cases of dengue increased from 101,192 in 2018 to ,233,251 in 2022. Similarly dengue deaths also increased from 172 (2018) to 303 (2022).

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INTRODUCTION

Dengue is the most prevalent viral infection transmitted by *Aedes* mosquitoes. More than 3.9 billion people in over 129 countries are at risk of contracting dengue, with an estimated 96 million symptomatic cases and an estimated 40,000 deaths every year. Through the ages, dengue fever (DF) has been a cause of public health concern in the WHO regions of Africa, Americas, Eastern Mediterranean, South-East Asia and the Western African Region. After World War II, there was a dramatic increase in the frequency and number of epidemics in South- East Asia, with the emergence of the severe forms , dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Globally, 2.5 to 3 billion people are estimated to be at risk of infection with dengue viruses. Affecting mostly children, the case fatality rates range from less than 1% to 10% (average 5%).

Dengue is caused by a virus spread by *Aedes* (*Stegomyia*) mosquitoes. Over the past two decades there has been a dramatic global increase in the frequency of dengue fever (DF) dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS) and their epidemics, with a concomitant increase in disease incidence

The World Health Report 1996 stated, that the "re-emergence of infectious diseases is a warning that progress achieved so far towards global security in health and prosperity may be wasted[1.] The report further indicated that "infectious diseases range from those occurring in tropical areas (such as malaria and DHF which are most common in developing countries) to diseases found worldwide (such as hepatitis and sexually transmitted diseases, including HIV/AIDS) and food-borne illnesses that affect large numbers of people in both the richer and poorer nations.[1]In May 1993, the 46th World Health Assembly (WHA) adopted a resolution on dengue prevention and control. It involved strengthening national and local programmes of DF, DHF and DSS control. It was recommended that these be prioritized by WHO Member States where the disease is endemic[2]. The resolution also provided insight about strategies to mobilize external resources such as adequate water supply, trained manpower for control operations waste disposal and engineering to remove stagnation in water canals drains etc. In response to the WHO resolution on dengue prevention and control, a global strategy for operationalization of vector control was developed based on five major components. One of the major pillars of the global strategy is to increase laboratory-based surveillance for DF/ DHF and its vectors. Effective surveillance requires that DHF be made a reportable (notifiable) disease by all DF/DHF endemic countries. These WHO guidelines are based on the regional strategy developed in 1995, which emphasizes disease surveillance, case management, integrated vector control and epidemic preparedness. containing the spread and increasing incidence of dengue in a manner sustainable by countries, community health education be improved, health promotion be encouraged, research be strengthened, dengue surveillance be expanded and guidance be given in vector control as there is no treatment nor vaccine is available. The cases of dengue increased from 101,192 in 2018 to ,233,251 in 2022. Similarly dengue deaths also increased from 172 (2018) to 303 (2022) Table 1.

Table 1: Dengue Cases and Deaths in the Country since 2018

NO.	Affected States/UTs	2018		2019		2020		2021		2022		2023*	
		C	D	C	D	C	D	C	D	C	D	C	D
1	Andhra Pradesh	4011	0	5286	0	925	0	760	0	5391	0	926	0
2	Arunachal Pradesh	1	0	123	0	1	0	7	0	114	0	17	0
3	Assam	166	0	196	0	33	0	103	0	826	2	604	6
4	Bihar	2142	0	6712	0	493	2	533	2	3972	32	515	7
5	Chhattisgarh	2674	10	722	0	57	0	086	0	679	10	733	0
6	Goa	335	1	992	0	376	0	549	0	443	1	264	0
7	Gujarat	7579	5	18219	17	1564	2	0983	4	5682	7	3334	1

8	Haryana	1898	0	1207	0	1377	0	1835	3	3996	18	.892	4
9	Himachal Pradesh	4672	7	344	2	21	0	349	0	3326	1	596	0
.0	J & K	214	0	439	0	53	0	709	4	3269	18	.192	0
.1	Jharkhand	463	1	825	0	79	0	120	1	290	0	958	2
.2	Karnataka	4427	4	.6986	13	3823	0	393	7	1889	9	3185	0
.3	Kerala	4083	32	4652	16	4399	5	251	27	4432	29	3770	37
.4	akshadweep	0	0	0	0	0	0	1	0	67	0	286	0
.5	dhya Pradesh	4506	5	4189	2	806	0	3592	1	3318	2	.544	0
.6	Meghalaya	44	0	82	0	4	0	129	0	26	0	59	0
17	Maharashtra	11011	55	14907	29	3356	10	2720	12	3578	27	3496	2
.8	Manipur	14	0	359	0	37	0	203	0	503	4	521	0
.9	Mizoram	68	0	42	0	67	0	83	0	.868	5	821	1
20	Nagaland	369	0	8	0	1	0	24	0	154	0	400	0
21	Odisha	5198	5	3758	4	496	0	548	0	7063	0	5563	0
22	Punjab	14980	9	.0289	14	3435	22	3389	35	1030	41	.246	0
23	Rajasthan	9587	10	13706	17	2023	7	0749	36	3491	10	3094	6
24	Sikkim	320	0	444	0	11	0	243	1	264	0	163	0
25	Tamil Nadu	4486	13	8527	5	2410	0	039	8	5430	8	1148	3
26	Tripura	100	0	114	0	24	0	349	0	56	0	744	0
27	Telangana	4592	2	13331	7	2173	0	135	0	3972	0	5138	0
28	ttar Pradesh	3829	4	10557	26	3715	6	9750	29	9821	33	5742	5
29	Uttrakhand	689	3	.0622	8	76	1	738	2	2337	0	.588	14
30	West Bengal			NR	NR	5166	0	264	7	7271	30	NR	NR
31	A& N Island	49	0	168	0	98	0	175	0	.014	3	540	0
32	Chandigarh	301	0	286	0	265	0	596	3	910	1	93	0
33	Delhi	7136	4	5077	0	1269	0	3089	13	0183	9	5221	1
34	D&N Haveli	493	0	1491	2	248	0	547	0	685	0	478	0
35	aman & Diu	163	0	625	2	71	0	279	0	228	0	94	0
36	Puducherry	592	2	2030	2	633	1	625	1	1673	3	1233	2
	Total	01192	172	57315	166	4585	56	3245	46	33251	03	4198	91

Provisional till 17th Sept. 2023, c =cases , d = deaths
Source -https://nvbdcp.gov.in/index4.php?lang=1&level=0&linkid=431&lid=3715

Historical Overview

The dengue as an illness has been recognized for more than 200 years, the role of mosquito *Aedes aegypti and Aedes albopictus* has been known for more than 70 years. Dengue has been the cause of massive epidemics of disease in Asia, the Americas and Mediterranean region; during World War II it was common enough in Pacific area to impede military operations. Carey et.al (1971) [3] and Kemp et.al (1978)[4] believe that the chikungunya virus was responsible for the 1824-1825 outbreak involving Kolkata, Chennai and Gujarat. During 1828 to 1824 dengue epidemics were reported in Pondicherry north to Kolkata, and the Ganges valley up to Varanasi (then Banaras). Disease incidences were also reported in 1848 from Kolkata and Kanpur; and again in 1872 from Mumbai, Pune and Kolkata. In 1873 disease occurred in Ludhiana (Punjab state), in Kerala coast from Calicut to Quilon and Chennai. Dengue again appeared in 1901 in Kolkata. In 1913 dengue was reported from Meerut (Uttar Pradesh). Dengue has been known to exist in the country and two strains of dengue virus were first isolated by Sabin in 1945 from human sera in Kolkata[5]. National institute of Virology in 1952, only two arboviruses were recognized. These were dengue and sand fly fever, and only DEN-I had been isolated[6].

The first case was reported from Philadelphia by Benjiman Rusof in 1789. When dengue virus was first isolated, the disease was termed "break bone

fever" because of the symptom of myalgia [3]. The term dengue fever came into general use only after 1828. Dengue virus was isolated in Japan in 1943 by inoculation of serum of patients into suckling mice[3] and at Calcutta (now Kolkata) in 1944 [7]. The first epidemic of clinical dengue-like illness was recorded in Madras (now Chennai) in 1780 and the first virologically proven epidemic of DF in India occurred in Calcutta and Eastern Coast of India in 1963-1964 [3,5,7]. The first major epidemic of the DHF occurred in 1953-1954 in the Philippines followed by a quick global spread of epidemics of DF/DHF[8]. DHF was occurring in the adjoining countries but it was absent in India for unknown reasons as all the risk factors were present. The DHF had been simmering in various parts of India since 1988[9–11]. The first major wide spread epidemics of DHF/DSS occurred in India in 1996 involving areas around Delhi[12] and Lucknow[13] and then it spread to all over the country[14]. Dengue is a mosquito-borne viral infection and a major public health concern throughout the tropical and subtropical regions of the world. Dengue has been identified as one of the 17 neglected tropical diseases by the World Health Organization Dengue occurrence is very common after the rainy season. It causes a severe flu-like illness and can be lethal. The incidence of dengue has increased 30-fold over the last 50 years. Up to 50-100 million infections are now estimated to occur annually in over 100 endemic countries, putting almost half of the world's population at risk. Dengue Fever (DF), also known as breakbone fever, is a viral infection caused by the dengue virus that is transmitted through the bite of the infected Aedes mosquito. Dengue fever signs and symptoms comprise the abrupt onset of high fever; severe frontal headache; pain behind the eyes (retro-orbital pain), which worsens with eye movement; muscle and joint pains; measles-like rashes over the chest and upper limbs; nausea, and vomiting[15]. Dengue virus infection is usually self-limiting and mild, but can also result in severe complications such as dengue hemorrhagic fever/dengue shock syndrome or severe dengue as described in World Health Organization guidelines[16,17].

Dengue burden

In recent decades the incidence of dengue has grown dramatically worldwide. It is estimated that, about 390 million dengue virus infections occur per year (95% credible interval 284–528 million), of which 96 million (67-136 million) manifest clinically (with any severity of disease). Another study on the prevalence of dengue estimated that 3.9 billion people are at risk of infection with dengue viruses[18]. Despite a risk of infection existing in 129 countries, 70% of the actual burden is in Asia. The number of dengue cases reported to WHO increased over 8-fold over the last two decades, from 505,430 cases in 2000 to over 2.4 million in 2010, and 4.2 million in 2019. Reported deaths between the years 2000 and 2015 increased from 960 to 4032, affecting mostly younger age groups. The total number of cases decreased during the years 2020 and 2021, as did reported deaths. However, the data is not yet complete and the COVID-19 pandemic might have hampered case reporting in several countries. The largest number of dengue cases ever reported globally was in 2019[19].

All regions were affected, and dengue transmission was recorded in Afghanistan for the first time[20]. In 2020, dengue affected several countries, with increases in case numbers reported in Bangladesh, Brazil, Cook Islands, Ecuador, India, Indonesia, Maldives, Mauritania, Mayotte (Fr), Nepal, Singapore, Sri Lanka, Sudan, Thailand, Timor-Leste and Yemen. Dengue continues to affect Brazil, India, Vietnam, the Philippines, the Cook Islands, Colombia, Fiji, Kenya, Paraguay, Peru and the Reunion islands, in 2021[20]. The burden of dengue in India is very complex and has changed considerably in terms of prevalent strains, affected geographical locations and severity of disease over the past six decades. The first evidence of the occurrence of dengue fever in the country was reported in 1956 from the Vellore district in Tamil Nadu. The first Dengue Hemorrhagic Fever (DHF) outbreak occurred in Kolkata, West Bengal in 1963 [21, 22]. All States/UTs reported dengue cases except Lakshadweep and Ladakh during the last two decades. Recurring outbreaks of dengue have been reported from various states/UTs e.g., Andhra Pradesh, Chandigarh, Delhi, Goa, Haryana, Gujarat, Karnataka, Kerala, Maharashtra, Rajasthan, Uttar Pradesh, Puducherry, Punjab, Tamil Nadu, Telangana and West Bengal. In 1996, one of the most severe outbreaks occurred in Delhi with 10,252 cases and 423 deaths. Most of the Indian states have been classified as having frequent or continuous risk of dengue transmission (Fig-1,2,)

Fig 1 The distribution of *Aedes aegypti* in India before partition

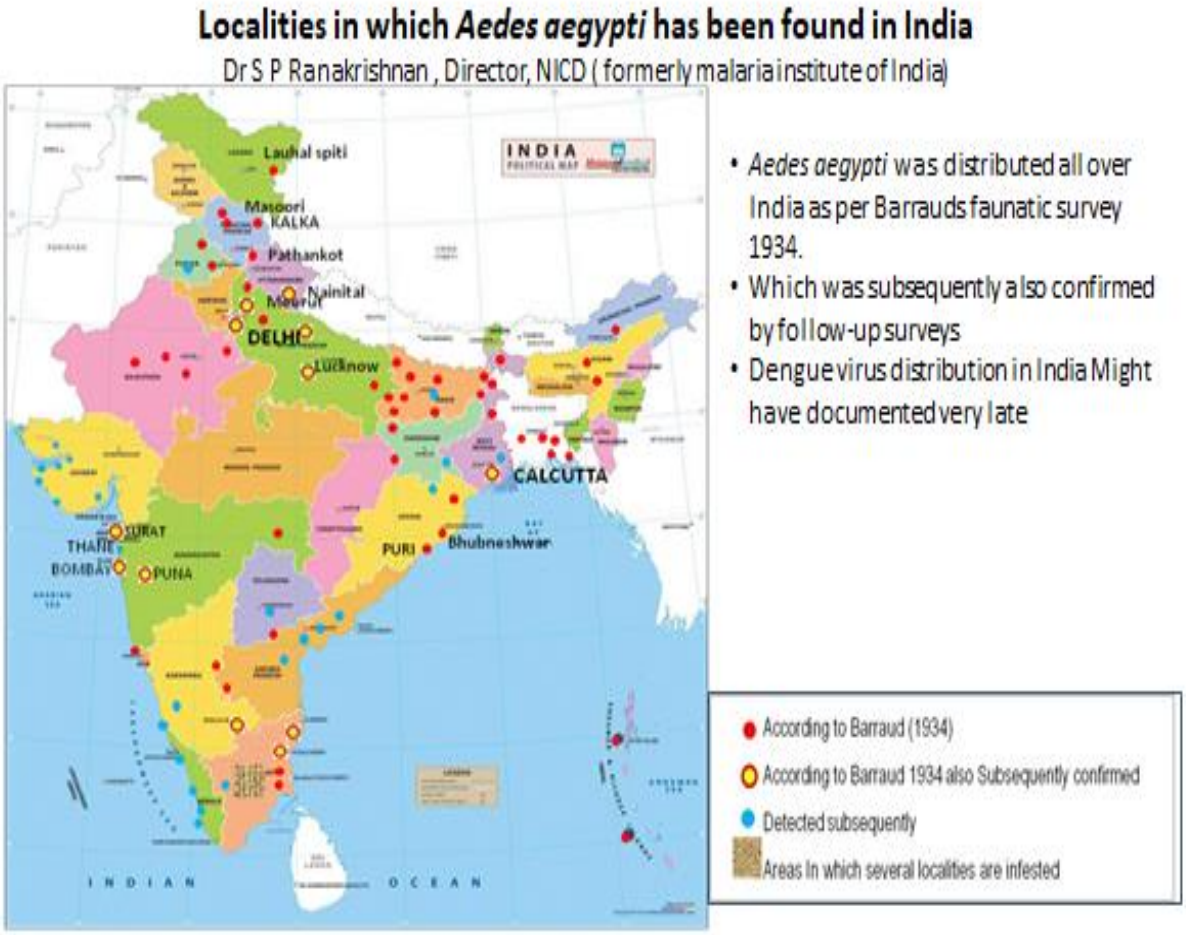
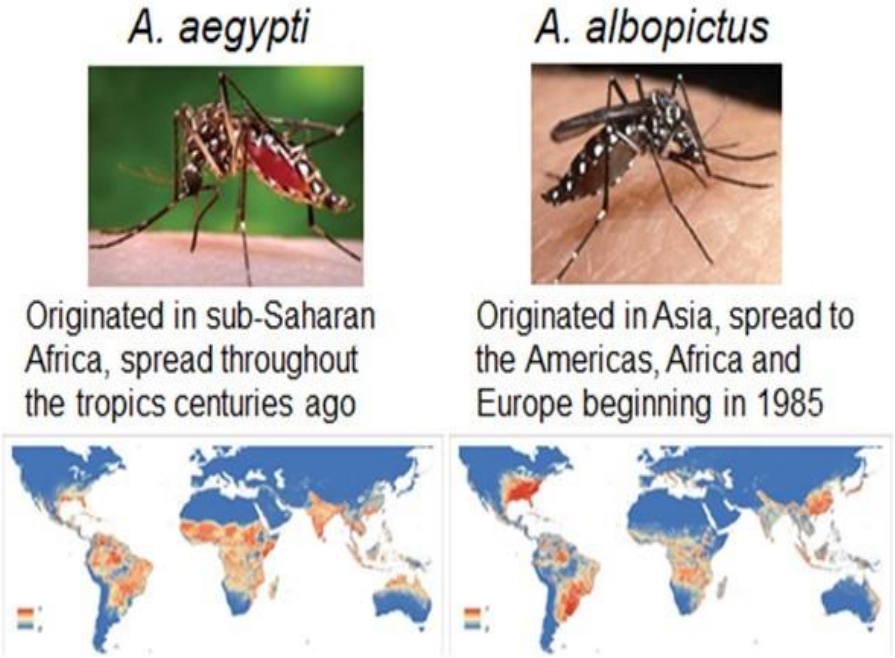


Fig- 2 Distribution of *Aedes aegypti* and *Aedes albopictus*



Causative agent

The causative agent of dengue i. e. Dengue virus (DENV) belongs to the genus Flavivirus, family flaviviridae. The virus contains single-stranded RNA and is small in size (50 nm). There are four different serotypes of the dengue virus: DENV-1, DENV-2, DENV-3 and DENV-4. Infection with any one serotype confers lifelong immunity to that virus serotype, which means that in humans, one serotype produces lifelong immunity against re-infection but only temporary and partial immunity against the other serotypes. Subsequent infections (secondary infection) by other serotypes increase the risk of developing severe dengue[20]. All the four serotypes have been isolated in India and outbreaks recorded in different state**s (Table-2)**

Table 2. Virus detection in dengue cases encountered in India

Year	Place of occurrence	Isolations
1956-60	Vellore	DEN 1,2
1963	Kolkata	DEN 2
1964	Vellore	CHIK
1964	Visakhapatnam	DEN-2
1965	Nagpur	DEN - 4
1965	Chennai	DEN-1,3
1966	Jabalpur	DEN- 3
1966	Vellore	DEN-3
1967	Asansol	DEN-2, 4
1967	Delhi	DEN-2
1968	Vellore	DEN-1,2,3,4
1968	Kanpur	DEN-4
1969	Kanpur	DEN-4,2
1969	Ajmer	DEN –1,3
1970	Gwalior	DEN-3
1970-71	Bangalore	DEN-1,2
1970	Delhi	DEN-2
1970	Hardoi	DEN-2
1971	Jaipur	DEN –1,2
1974	Jammu	DEN-2
1974	Trichur	DEN-2
1982	Delhi	DEN-1, 2
1986	Miraj	DEN-2,3
1988	Delhi	DEN-2
1990	Kolkata	DEN-2
1993	Mangalore	DEN-2
1996	Ludhiana	DEN-1,2,3,4
1996	Lucknow	DEN-2
1996- 97	Delhi	DEN-1,2
1996	Haryana	DEN-2
2001	Dharampuri, TN	DEN-2
2001	Gwalior	DEN-2
2001	Chennai	DEN-3
2003	Dehi & Gwalior	DEN-3
2005	Kolkata	DEN-3
2006	Delhi	DEN-3
2008	Ernakulam	DEN-2,3

Vector

Aedes aegypti is the primary vector and *Ae. albopictus* the secondary vector for dengue transmission. *Ae. aegypti,* is a "*nervous feeder*" (multiple host feeder for completing a single blood meal). It has been mainly associated with dengue outbreaks in India. It is a very efficient vector and can build up high transmission potential even at a low population level because of (i) restricted dispersal, and (ii) its day time biting habit where a female is obligated to take a single blood meal from one or more peeople. *Ae. albopictus* has also been identified as the disease vector in outbreaks of dengue fever and chikungunya virus in suburban and rural areas. It can be considered as a secondary vector in forest fringe (sylvatic) areas. Climate change is influencing the incidence of *Aedes aegypti* and *Aedes albopictus* mosquito-borne dengue illnesses. The *Aedes aegypti* mosquito vector was found to be prevalent in the western, northern, Indo-Gangetic and eastern plains as well as in Assam valley and the coastal areas of Orissa state in India (Fig. 1). Being hygroscopic, the species shows a phenomenon of 'annual pulsation'. It tends to move to 'mother foci' in the central parts of cities which are humid during the dry season and spreads out during the wet season. *Aedes albopictus* was encountered in the peripheral areas of towns where it replaced the *Ae. aegypti* populations. However, in the eastern plateau, the species penetrated up to the central parts, probably due to lack of intra-species competition from *Ae. aegypti* which is very scant in the region[23].

Dengue vectors and Climate change

India has witnessed a five-fold increase in dengue incidence in the past decade. However, the nation-wide distribution of dengue vectors, and the impacts of climate change are not known. Species distribution modeling was used to predict the baseline and future distribution of Aedine vectors in India on the basis of biologically relevant climatic indicators. Known occurrences of *Aedes aegypti* and *Aedes albopictus* were obtained from the Global Biodiversity Information Facility database and previous literature. Bio-climatic variables were used as the potential predictors of vector distribution. After eliminating collinear and low contributing predictors, the baseline and future prevalence of *Aedes aegypti* and *Aedes albopictus* was determined, under three Representative Concentration Pathway scenarios (RCP 2.6, RCP 4.5 and RCP 8.5), using the MaxEnt species distribution model. *Aedes aegypti* was found prevalent in most parts of the southern peninsula, the eastern coastline, north eastern states and the northern plains. In contrast, *Aedes albopictus* has localized distribution along the eastern and western coastlines, north eastern states and in the lower Himalayas. Under future scenarios of climate change, *Aedes aegypti* is projected to expand into unsuitable regions of the Thar desert, whereas *Aedes albopictus* is projected to expand to the upper and trans Himalaya regions of the north [25]. Overall, the results provide a reliable assessment of vector prevalence in most parts of the country. These can be used to guide surveillance efforts, despite minor disagreements with dengue incidence in Rajasthan and the north east, possibly due to behavioral practices and sampling efforts.

Transmission

Dengue viruses are transmitted to humans through the bite of an infected female Aedes mosquito. Most vector mosquitoes are an autogenous, which means that females require a vertebrate blood meal for egg production and development. Female Aedes mosquitoes bite humans and animals. After feeding on a DENV-infected person, the virus replicates in the mosquito midgut, before it disseminates to secondary tissues, including the salivary glands. The time it takes from ingesting the virus to actual transmission to a new host is termed the extrinsic incubation period (EIP). The EIP takes about 8-12 days when the ambient temperature is between 25-28°C. The length of time required for this extrinsic incubation depends in part on environmental conditions, especially ambient temperature. Several factors can influence the dynamics of virus transmission- including environmental and climate factors, host-pathogen interactions and population immunological factors. Once infected, the mosquito is capable of transmitting the virus for the rest of its life[20]. The mosquito, once infected, remains infected for life, transmitting the virus to susceptible individuals during probing and feeding. Infected female mosquitoes may also pass the virus to the next generation of mosquitoes by transovarial transmission, which is a mechanism by which infected female mosquitoes pass the virus to their offspring via their eggs. Each female *Ae. aegypti* mosquito can lay multiple batches of eggs during its lifetime and often takes several blood meals before laying a batch of eggs. While taking a blood meal, an infected female mosquito injects its saliva into the human host to prevent the host's blood from clotting and to ease feeding. As the virus remains in saliva, this injection of saliva infects the host with

the dengue virus. The symptom of high fever is related to high viremia in infected humans. This is the period when the infected person (patient) is most contagious, as another mosquito vector may pick up the virus via a blood meal during the viremic period which last 2-6 days. Thereafter the virus is neutralized by the host immune response in most cases, except severe dengue.

Dengue fever isn't transmitted directly from one person to another like the flu. In rare cases, dengue can be transmitted during organ transplantations or blood transfusions from infected donors. There is also evidence that an infected pregnant mother can transmit the dengue virus to her fetus. Despite these rare events, the majority of dengue infections are transmitted by mosquito bites. Dengue virus transmission likely originated from sylvatic cycles maintained between susceptible non-human primates and *Aedes* mosquitoes in the forests of Asia. Spillover of sylvatic dengue virus can occur in both rural and urban areas as zones of emergence. Given the adaptability of the sylvatic virus for the human host and documented past infections that resulted in severe clinical manifestations, this can potentially sustain the natural horizontal human-to-human transmission via *Aedes aegypti* and *Aedes albopictus* mosquitoes. Humans are known to be the main reservoir host in maintaining urban epidemic cycles of dengue. Local transmission may be established if DENV-infected travelers bring the virus to new locations and there is a presence of susceptible vectors[26].

Detection of dengue virus from *Aedes* mosquitoes

The virus detection was done in *Aedes aegypti* mosquitoes in Delhi and out of 2408 Aedes mosquitoes 14 tested positive with a minimum infection rate (MIR) of 5.8% [27]. A similar study in different cities of north India found MIR to be lower (1.6%) than Delhi [28]. The detection of the pathogen in a mosquito is an important indicator of risk of dengue transmission.

Epidemiology

In recent decades, the incidence of dengue has risen significantly around the world. Dengue epidemiology is a dynamic phenomenon that relies on a complex relationship between epidemiological factors, i.e., host (man and mosquito), virus and environmental (abiotic and biotic factors). The nature of the relationship between these factors ultimately determines the rate of transmission within an area. During inter-epidemic times, dengue transmission remains low due to extrem temperatures with low relative humidity. However, when environmental conditions become ideal for vectors during monsoons, transmission reaches its peak. Dengue transmission is usually associated with periods of higher rainfall in most endemic countries like India as it provides an environment conducive to mosquito longevity. In addition, more breeding grounds appear due to rainwater accumulating in discarded containers pots tyres etc. However, other factors such as higher humidity and moderate ambient temperatures associated with the rainy season increase survival of infected mosquitoes, thus increasing the chances of secondary transmission to other persons. In 1963-1964, an initial epidemic of dengue fever was reported on the Eastern Coast of India[7,29–32], which spread northwards and reached Delhi in 1967 [33] and Kanpur in 1968[34]. Simultaneously it also involved the southern part of the country[24,25] and gradually the whole country was involved with widespread epidemics followed by endemic/hyperendemic prevalence of all the four serotypes of DV. The epidemiology of dengue virus and its prevalent serotypes has been ever changing. The epidemic at Kanpur during 1968 was caused by serotype DV-4[34] and during 1969 epidemic; both DV-2 and DV-4 were isolated[35]. It was completely replaced by DV-2 during the 1970 epidemic in the adjoining city of Hardoi[36]. Myers *et al*[37-39] had reported the presence of DV-3 in patients and *Ae. aegypti* at Vellore during the epidemic of 1966 while during the epidemic of 1968, all the four types of DV were isolated from patients and mosquitoes[29]. In another study Myers & Varkey[39] reported an instance of a third attack of DV in one individual. DV-2 was isolated during the epidemics of dengue in urban and rural areas of Gujarat State during 1988 and 1989[40]. Outbreaks of dengue occurred in Rajasthan, which were caused by DV- 1 and DV-3[41],Madhya Pradesh by DV-3[43], Gujarat by DV-2[40] and in Haryana by DV-2[44]. DV-2 was the predominant serotype circulating in northern India, including Delhi, Lucknow and Gwalior[45] while DV-1 was isolated during the 1997 epidemic at Delhi[46]. The phylogenetic analysis by the Molecular Evolutionary Genetics Analysis programme suggests that the 1996 Delhi isolates of DV-2 were genotype IV. The 1967 isolate was similar to a 1957 isolate of DV-2, from India, and was classified as genotype V. This study indicates that earlier DV-2 strains of genotype V have been replaced by genotype IV[47]. The Gwalior DV-2 viruses were classified into genotype-IV, and were most closely related to Delhi 1996 DV-2 viruses and FJ 10/11 strains prevalent in the Fujian State of China. However, two earlier Indian isolates of DV-2 were

classified into genotype-V. Genotype V of DV-2 has been replaced by genotype IV during the past decade, which continues to circulate silently in north India, and has the potential to re-emerge and cause major epidemics of DF and DHF[48]. DV-2 has also been reported from southern India, specifically in Kerala along with DV-3[49]. DV-3 has been isolated during the epidemics at Vellore in 1966[49], at Calcutta in 1983 and in 1990[50], at Jalore city, Rajasthan in 1985[41,42] at Gwalior in 2003 and 2004[51,52] and at Tirupur, Tamil Nadu in 2010[53]. Phylogenetic analysis showed that the Madurai isolates were closely related to Gwalior and Delhi isolates. The emergence of DV-4 has been reported in Andhra Pradesh[54] and Pune, Maharashtra[55], which was also implicated in increased severity of disease. At Delhi, till 2003, the predominant serotype was DV-2 (genotype IV) but in 2003 for the first time all four dengue virus subtypes were found to co-circulate in Delhi thus changing it to a hyperendemic state[56]. This was followed by a complete predominance of DV serotype 3 in 2005[57]. During the 2004 epidemic of DHF/DSS in northern India a sudden shift in serotype representation occurred; with DV serotype-3 (subtype III) replacing the earlier circulating serotype-2 (subtype IV)[58]. Co-circulation of DV serotypes in Delhi in 2003-2004 has also been reported[58], which may have implications for increased DHF/DSS. Co-circulation of several serotypes of dengue viruses has resulted in concurrent infection in some patients with multiple serotypes of DV[59]. Further, replacement of DV-2 and 3 with DV-1 as the predominant serotype in Delhi over a period of three years (2007-2009) has been reported[60]. Concurrent infection by Chikungunya and DV-2 was reported from Vellore[61] and Delhi[62] (Table 2).

RISK FACTORS AND CHALLENGES

Population Growth: The increasing population needs more and more of civic facilities such as regular water supply, intermittent supplies may lead water storing practice which in turn support breeding and increase vector population of *Aedes aegypti* .

Urbanization: Last few decades the urban population has increased manifold. This was triggered by rural "push" (for earning livelihood and "urban pull" (for availability of both medicare/ education opportunities) phenomenon.

Inclusion of other vector species: Due to population pressure all towns & mega cities are expanding and new settlements in peri-urban areas have come up. These peri-urban situations have low infrastructure which lead to inclusion of *Aedes aegypti* and *An. culicifacies (malaria vector in rural areas)* along with the vector of urban malaria *An. stephensi*.

Immigration: Particularly immigration of people from disease-endemic regions to urban cities/towns and creating favorable conditions for mosquito breeding.

Haphazard and unplanned growth of towns: poor housing and sanitary conditions promote vector mosquito breeding

Drinking water supply: Due to intermittent water supply communities developed water storage practices which increased breeding sites for Aedes vector mosquitoes.

Development project without Health Impact Assessment (HIA): resulted in VBD outbreaks

Inadequate health infrastructure: There are inadequate technical trained manpower for larval control activities.

CONCLUSION

To summarize, dengue fever has been long documented historically, and continues to cause a significant disease burden worldwide. Major health authorities like the WHO have noted that its prevalence has significantly increased in the past few years.

Intermediate disease hosts are *Aedes aegypti* (primary host) and *Ae. albopticus* (secondary host), They transmit the causative agent, the dengue virus (DENV, from the genus flaviviridae) of which there are 4 different serotypes. Dengue viruses are single stranded RNA viruses with an approximate diameter of 50nm.

This virus is primarily transmitted to humans via the bite of an infected female Aedes mosquito while taking a blood meal. Specifically, injection the female mosquito`s saliva is the point at which the human host becomes infected. It then causes viremia, or circulation within the blood. Despite there being very rare cases of dengue transmission via organ transplantation, blood transfusion, and from mother to foetus, mosquitos are the primary transmission route.

Factors posing challenges to dengue control include population growth, urbanization, contaminated water supplies, immigration, inclusion of other vector species, haphazard and unplanned town development, poor healthcare infrastructure, and

carrying out developments without health impact assessments.

Safe, cost effective and environmentally friendly treatment options, especially vaccines, will be crucial for dengue control into the future. Not only this, treatment should form part of a multifactorial approach to dengue control, which should also include larval source reduction, and cooperation between interdisciplinary departments ie. water supply department, non-governmental organizations, civic organizations and community groups

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