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Review Article

Dengue - The Breakbone Fever: A Crisis within a Crisis

Wahied Khawar Balwan[1*], Arashdeep Singh[2], Sachdeep Kour[3]

[1]Assistant Professor and Head, Department of Zoology, Govt. Degree College Kilhotran, Doda, Jammu & Kashmir, India
[2]DFO Rajouri, Forest Department, Jammu & Kashmir, India
[3]Educator at Cypress Fairbanks Independent School District, Houston, Texas, USA

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Abstract: Dengue is one of the most critical and rapidly spreading vector borne disease in the world. It is caused by an RNA virus that belongs to the Flaviviridae family. The dengue virus is transmitted by mosquitoes (arthropods) and thus is an arbovirus. Dengue spreads through the bite of female *Aedes* mosquitoes. *Aedes* mosquitoes also serve as vectors of chikungunya, yellow fever and Zika viruses. The symptoms may range from asymptomatic fever to dreaded complications such as hemorrhagic fever and shock. Dengue is an endemic disease, which means that it occurs regularly, in tropical regions of the world. According to World Health Organization (WHO), almost half of the world's population lives in areas with a risk of contracting dengue virus [1]. The risk of contracting dengue infection has increased dramatically since the 1940s. This upward trend is due to increases in long-distance travel, population growth and urbanization, lack of sanitation, ineffective mosquito control, and increases in the surveillance and official reporting of dengue cases.

Keywords: Dengue, Arbovirus, Diagnosis, Epidemiology, Viremic, Serotype, DENV.

INTRODUCTION

Dengue is an acute viral infection with potential fatal complications. Dengue fever was first referred as 'water poison' associated with flying insects in a Chinese medical encyclopedia in 992 from the Jin Dynasty (265-420 AD). The word 'dengue' is derived from the Swahili phrase Ka-dinga pepo, meaning 'cramp-like seizure'. The first clinically recognized dengue epidemics occurred almost simultaneously in Asia, Africa, and North America in the 1780s. The first clinical case report dates from 1789 of 1780 epidemic in Philadelphia is by Benjamin Rush, who coined the term 'break bone fever' because of the symptoms of myalgia and arthralgia. The term dengue fever came into general use only after 1828. Dengue is a mosquito borne viral disease that occurs in tropical and subtropical areas of the world. Dengue Fever (DF) is commonly known as *breakbone fever*. It is caused by the dengue virus (DENV), which is transmitted by female *Aedes* mosquitoes of species *Aedes aegypti* and *Aedes albopictus.* The mosquito becomes infected when it bites a person with DENVs in their blood. DENVs are maintained in cycles that involve blood-sucking vectors and vertebrate hosts.

EPIDEMIOLOGY

Dengue is a mosquito borne viral disease that has rapidly spread in all regions of the world in recent years. Due to urbanization, population growth, frequent international travelling, and global warming, the incidence of dengue has increased almost 30-fold in the last five decades. An estimated 400 million dengue infections occur worldwide each year, with about 96 million resulting in illness [6]. Dengue disease is endemic in more than one hundred countries including Southeast Asia, the western Pacific islands, Latin America and Africa. However, the disease has been spreading to new areas, including local outbreaks in Europe and southern parts of the United States [2]. Most people with dengue recover without any problems. The fatality rate is 1–5%, and less than 1% with adequate treatment. Severe dengue is a leading cause of serious illness and death in some Asian and Latin American countries. Dengue inflicts a serious health, social and economic burden on the people of endemic areas.

PROGNOSIS

Most people with dengue recover without any ongoing problems. The risk of death among those with severe dengue is 0.8% to 2.5%, and with adequate

***Corresponding Author:** Dr. Wahied Khawar Balwan
Assistant Professor and Head, Department of Zoology, Govt. Degree College Kilhotran, Doda, Jammu & Kashmir, India

treatment this is less than 1%. However, those who develop significantly low blood pressure may have a fatality rate of up to 26% [1]. The risk of death among children less than five years old is four times greater than among those over the age of 10. The elderly people are also at higher risk of a poor outcome.

SIGNS AND SYMPTOMS

Dengue is a flu-like illness that affects infants, young children and adults, but seldom causes death. Symptoms range from mild to severe and usually last for 2–7 days, after an incubation period of 4–10 days followed by the bite from an infected mosquito [3]. Severe symptoms include dengue shock syndrome (DSS) and dengue hemorrhagic fever (DHF). These usually require hospitalization.

The World Health Organization (WHO) classifies dengue into 2 major categories: dengue (with / without warning signs) and severe dengue [1, 4]. The sub-classification of dengue with or without warning signs is designed to help health practitioners triage patients for hospital admission, ensuring close observation, and to minimize the risk of developing the more severe dengue.

Dengue

Dengue should be suspected when a high fever (40°C/104°F) is accompanied by 2 of the following symptoms during the febrile phase:

- Severe headache
- Pain behind the eyes
- Muscle and joint pains
- Nausea
- Vomiting
- Swollen glands
- Rash

Severe Dengue

A patient enters what is called the critical phase normally about 3-7 days after illness onset. It is at this time, when the fever is dropping (below 38°C/100°F) in the patient, that warning signs associated with severe dengue can manifest. Severe dengue is a potentially fatal complication, due to plasma leaking, fluid accumulation, respiratory distress, severe bleeding, or organ impairment [4].

Warning signs during severe dengue phase include:

- Severe abdominal pain
- Persistent vomiting
- Rapid breathing
- Bleeding gums
- Fatigue
- Restlessness
- Blood in vomit.

If patients manifest these symptoms during the critical phase, close observation for the next 24–48 hours is essential so that proper medical care can be provided, to avoid complications and risk of death.

DENGUE VIRUS (DENV)

Dengue fever is caused by dengue virus (DENV). DENV is a single positive-stranded RNA virus of the family *Flaviviridae*; genus *Flavivirus* [5]. There are four distinct, but closely related, serotypes of the virus named DENV-1, DENV-2, DENV-3, and DENV-4. These four viruses are called serotypes because each has different interactions with the antibodies in human blood serum. The four dengue viruses are similar and share approximately 65% of their genomes but even within a single serotype, there is some genetic variation. Despite these variations, infection with each of the dengue serotypes results in the same disease and range of clinical symptoms. Recovery from infection is believed to provide lifelong immunity against that serotype. However, cross-immunity to the other serotypes after recovery is only partial, and temporary. Subsequent infections (secondary infection) by other serotypes increase the risk of developing severe dengue.

VECTOR

A vector is a vehicle that carries and transmits a disease to its host organism. Vectors include animals and microorganisms that transmit different diseases. The most common vectors are arthropods, which are invertebrate animals with an external skeleton called an exoskeleton. Arthropods include mosquitoes, ticks, lice, flies, and fleas. For instance, ticks can carry Lyme disease, and some mosquitoes can carry yellow fever, malaria, and dengue fever.

The dengue virus is carried and spread by female mosquitoes in the genus *Aedes*, which includes several mosquito species. Of these species, the primary vector of the dengue is *Aedes aegypti* [1]. It is the principal dengue vector responsible for dengue transmission and dengue epidemics. Other mosquito species in the genus *Aedes*, including *Aedes albopictus*, *Aedes polynesiensis* and *Aedes scutellaris* have a limited ability to serve as dengue vectors. [1] [5] *Aedes* mosquitoes also serve as vectors of chikungunya, yellow fever and Zika viruses.

Both male and female mosquitoes feed on plant nectars, fruit juices, and other plants sugars as their main energy source. However, female mosquitoes require blood to produce eggs, so they bite humans. Each female mosquito can lay multiple batches of eggs during its lifetime, and often *Aedes aegypti* take several blood meals before laying a batch of eggs. When a female mosquito is infected with the dengue virus, the virus is present in its salivary glands. When 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. This injection of saliva infects the host with the dengue virus.

VECTOR ECOLOGY

Aedes aegypti mosquito is considered the primary vector of DENV. It is a small, dark mosquito that can be identified by the white bands on its legs and a silver-white pattern of scales on its body that looks like an ancient Greek musical instrument called a lyre. It lives in urban habitats and breeds mostly in man-made containers. *Aedes aegypti* is a day-time feeder; its peak biting periods are early in the morning and in the evening before sunset. Female *Aedes aegypti* frequently feed multiple times between each egg-laying period. Once a female has laid her eggs, these eggs can remain viable for several months, and will hatch when they come in contact with water.

Aedes aegypti dwell in tropical and subtropical regions all over the world, mainly between the latitudes of 35°N and 35°S where the winter temperature is no colder than 10°C. Although some mosquitoes may travel farther north or south of these latitudes, they are unable to survive cold winters. Because *Aedes aegypti* require a warm climate, they typically do not live at altitudes above 1000 m, where the temperature is colder [6].

Aedes albopictus, a secondary dengue vector in Asia, has spread to more than 32 states in the USA, and more than 25 countries in the European Region, largely due to the international trade in used rubber tyres (a breeding habitat) and other goods (e.g. lucky bamboo). *Aedes albopictus* is highly adaptive. Its geographical spread is largely due to its tolerance of colder conditions, as an egg and adult. *Aedes albopictus* has been implicated as the primary vector of DENV in a limited number of outbreaks, where *Aedes aegypt*i is either not present, or present in low numbers [7].

Fig 1: *Aedes aegypti* mosquito bites a person

LIFE CYCLE

Aedes aegypti have a complex life cycle that includes aquatic and terrestrial stages. These mosquitoes lay their eggs inside containers, and new *Aedes aegypti* hatch when the containers are filled with water. Dengue poses the greatest risk in highly populated regions with rainy seasons where there are large populations of *Aedes aegypti* with a high degree of contact between the mosquitoes and humans. The life cycle of *Aedes* mosquito comprises of four life stages: egg, larva, pupa, and adult. It takes about 8-10 days for an egg to develop into an adult mosquito [9].

Eggs

- Adult, female mosquitoes lay eggs on the inner walls of containers with water, above the waterline.[10]
- Eggs stick to container walls like glue. They can survive drying out for up to 8 months.
- Mosquitoes only need a small amount of water to lay eggs. Bowls, cups, fountains, tires, barrels, vases, and any other container storing water make a great breeding ground.

Larvae

- Larvae live in the water. They hatch from mosquito eggs. This happens when water (from rain or a sprinkler) covers the eggs [9, 10].
- Larvae can be seen in the water. They are very active and are often called “wigglers.”

Pupae

- Pupae live in the water. An adult mosquito emerges from the pupa and flies away [10].

Adult

- Adult female mosquitoes bite people and animals. Mosquitoes need blood to produce eggs.
- After feeding, female mosquitoes look for water sources to lay eggs.
- *Aedes aegypti* and *Aedes albopictus* don’t fly long distances. In its lifetime, these mosquitoes will only fly within a few blocks [11].
- *Aedes aegypti* mosquitoes prefer to live near and bite people.
- Because *Aedes albopictus* mosquitoes bite people and animals, they can live in or near homes or in neighboring woods.
- *Aedes aegypti* mosquitoes live indoors and outdoors, while *Aedes albopictus* live outdoors.

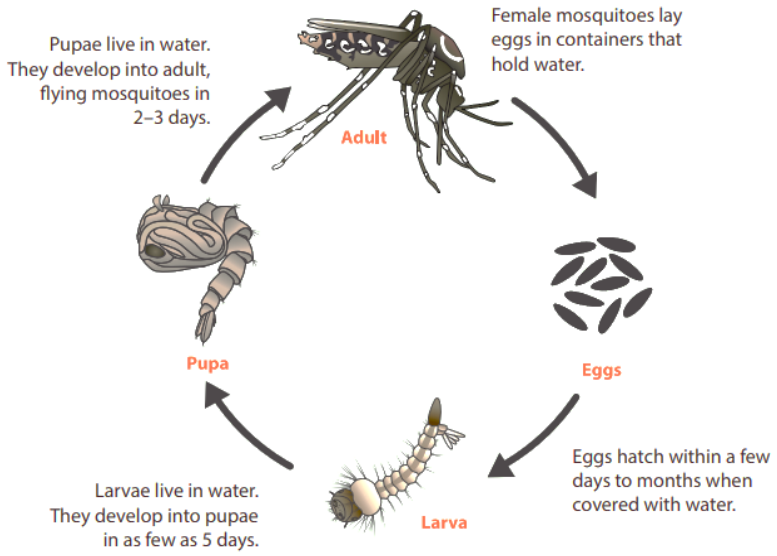

Fig 2: Life cycle of *Aedes aegypti* mosquito

TRANSMISSION OF DENGUE

Dengue cannot spread directly from one person to another, and mosquitoes are necessary for transmission of the dengue virus (DENV). The dengue virus is spread through a human-to-mosquito-to-human cycle of transmission. Dengue is transmitted to humans by the bite of an *Aedes* mosquito infected with a dengue virus (DENV). The female *Aedes* mosquito becomes infected when it bites a person who has dengue virus (DENV) in his or her blood [5]. An infected mosquito can then spread the dengue virus to healthy people by biting them.

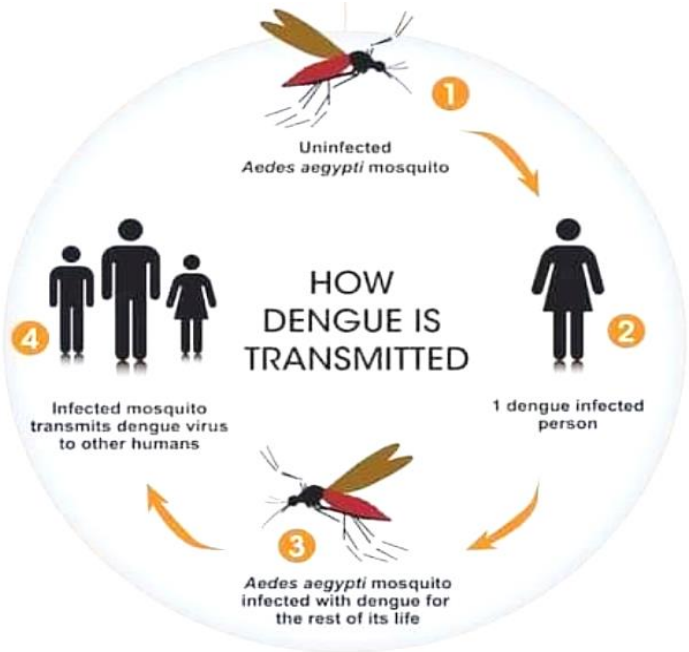

Fig 3: Dengue transmission

Mosquito-to-Human Transmission

Dengue virus is transmitted to humans through the bites of infected female mosquitoes, primarily *Aedes aegypti* and, to a lesser extent, *Aedes albopictus*. These mosquitoes bite during the day, usually just after sunrise and around sunset. Typically, four days after being bit by an infected *Aedes aegypti* mosquito, a person will develop viremia, a condition in which there

is a high level of the dengue virus in the blood. Viremia usually lasts for five days but can even last up to twelve days [12]. On the first day of viremia, the person generally shows no symptoms of dengue. Five days after being bit by the infected mosquito, the person develops symptoms of dengue fever, which can last for a week or longer.

Human-to-Mosquito Transmission

Mosquitoes can become infected from people who are viremic with DENV. This can be someone who has a symptomatic dengue infection, someone who is yet to have a symptomatic infection (pre-symptomatic), but also people who show no signs of illness as well (asymptomatic). Human-to-mosquito transmission can occur up to 2 days before someone shows symptoms of the illness, up to 2 days after the fever has resolved. When a mosquito feeds on the blood of someone infected with the dengue virus, that mosquito becomes a dengue vector. The mosquito must take its blood meal during the period of viremia, when the infected person has high levels of the dengue virus in the blood [13]. After feeding on an 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. Variations in the extrinsic incubation period are not only influenced by ambient temperature; a number of factors such as the magnitude of daily temperature fluctuations, virus genotype, and initial viral concentration can also alter the time it takes for a mosquito to transmit virus. Once infectious, the mosquito is capable of transmitting virus for the rest of its life. Risk of mosquito infection is positively associated with high viremia and high fever in the patient; conversely, high levels of DENV-specific antibodies are associated with a decreased risk of mosquito infection.

OTHER MODES OF TRANSMISSION

The primary mode of transmission of DENV between humans involves mosquito vectors. In rare events, dengue can be transmitted during organ transplantations or blood transfusions from infected donors [14]. There is also evidence that an infected pregnant mother can transmit the dengue virus to her fetus. When a mother does have a DENV infection when she is pregnant, babies may suffer from pre-term birth, low birth weight, and fetal distress. Despite these rare events, most dengue infections are transmitted by mosquito bites.

DIAGNOSIS

Diagnosing dengue fever can be difficult because its signs and symptoms can be easily confused with those of other diseases such as chikungunya, Zika virus, malaria and typhoid fever. Several methods can be used for diagnosis of DENV infection. Depending on the time of patient presentation, the application of different diagnostic methods may be more or less appropriate. Patient samples collected during the first week of illness should be tested by both methods mentioned below:

Virus Isolation Methods

The virus may be isolated from the blood during the first few days of infection. Various reverse transcriptase–polymerase chain reaction (RT–PCR) methods are available and are considered the gold standard [15]. However, they require specialized equipment and training for staff to perform these tests. The virus may also be detected by testing for a virus-produced protein, called NS1. There are commercially produced rapid diagnostic tests available for this, and it takes only ~20 mins to determine the result and the test does not require specialized laboratory techniques or equipment.

Serological Methods

Serological methods, such as enzyme-linked immunosorbent assays (ELISA), may confirm the presence of a recent or past infection, with the detection of anti-dengue antibodies [15]. IgM antibodies are detectable ~1 week after infection and remain detectable for about 3 months. The presence of IgM is indicative of a recent DENV infection. IgG antibody levels take longer to develop and remains in the body for years. The presence of IgG is indicative of a past infection.

TREATMENT

There is no specific treatment for dengue fever. Patients should rest, stay hydrated and seek medical advice. Depending on the clinical manifestations and other circumstances, patients may be sent home, be referred for in-hospital management, or require emergency treatment and urgent referral. Supportive care such as fever reducers and pain killers can be taken to control the symptoms of muscle aches and pains, and fever [7, 26].

Fever reducers and pain killers can be taken to control the symptoms of muscle aches and pains, and fever. The best options to treat these symptoms are acetaminophen or paracetamol. NSAIDs (non-steroidal anti-inflammatory drugs), such as ibuprofen and aspirin should be avoided. These anti-inflammatory drugs act by thinning the blood, and in a disease with risk of hemorrhage, blood thinners may exacerbate the prognosis [15].

For severe dengue, medical care by physicians and nurses experienced with the effects and progression of the disease can save lives – decreasing mortality rates from more than 20% to less than 1%. Maintenance of the patient's body fluid volume is critical to severe dengue care. Patients with dengue should seek medical

advice upon the appearance of warning signs. Current efforts are to develop antiviral drugs that would be used for the treatment of dengue and prevention of severe complications. There are several plausible therapeutic approaches such as the inhibition of the viral RNA-dependent RNA polymerase inhibitor, viral protease inhibitors, entry inhibitors that stop the virus entering cells or inhibitors of the 5′ capping process, which is required for viral replication [16].

VACCINE

A partially effective vaccine for dengue fever has been approved and is commercially available in several countries. The vaccine is produced by Sanofi and goes by the brand name *Dengvaxia* [17, 18]. It is based on a weakened combination of the yellow fever virus and each of the four dengue serotypes. Studies of the vaccine found it was 66% effective and prevented more than 80 to 90% of severe cases [17]. As of 2022, the vaccine is only recommended in individuals who have been previously infected, or in populations with a high rate of prior infection by age nine. In those who have not had a prior infection there is evidence it may worsen subsequent infections [18]. For this reason, it is not suitable for wide scale immunization, even in areas where the disease is common. Given the limitations of the current vaccine, research on vaccines continues, and the fifth serotype may be factored in. One of the concerns is that a vaccine could increase the risk of severe disease through antibody-dependent enhancement (ADE). The ideal vaccine is safe, effective after one or two injections, covers all serotypes, does not contribute to ADE, is easily transported and stored, and is both affordable and cost effective.

PREVENTION AND CONTROL

For dengue prevention, traditional method is only restricted to vector control measures. The proximity of mosquito vector breeding sites to human habitation is a significant risk factor for dengue as well as for other diseases that *Aedes* mosquito transmit. As there is no effective vaccine against dengue, the prevention and control of dengue infections depends largely on preventing man-vector contact. At present, numerous strategies have been adopted to control the spread of dengue vector. These include environmental control, biological control, chemical control, and active case surveillance [19, 20, 25, 26].

Environmental Control Methods

The environmental control methods include:

- Prevention of mosquito breeding:
  - Preventing mosquitoes from accessing egg-laying habitats by environmental management and modification;
  - Disposing of solid waste properly and removing artificial man-made habitats that can hold water;
  - Covering, emptying and cleaning of domestic water storage containers on a weekly basis;
  - Applying appropriate insecticides to water storage outdoor containers;
- Personal protection from mosquito bites:
  - Using of personal household protection measures, such as window screens, repellents, insecticide treated materials, coils and vaporizers. These measures must be observed during the day both inside and outside of the home (e.g.: at work/school) because the primary mosquito vectors bites throughout the day;
  - Wearing clothing that minimizes skin exposure to mosquitoes is advised;
- Community engagement:
  - Educating the community on the risks of mosquito-borne diseases;
  - Engaging with the community to improve participation and mobilization for sustained vector control;

Biological Control of the Vector

- Biological control methods are targeted against the larval stages of the dengue vector. They include the use of larvivorous fish such as *Gambusia affinis* and *Poecilia reticulate*, endotoxin producing bacteria (*Bacillus thuringiensis* serotype H-14 and *Bacillus sphaericus* are currently used), and copepod crustaceans.[1] *Bacillus thuringiensis* serotype H-14 is more effective against *A aegypti* with very low levels of mammalian toxicity, and has therefore been accepted for use in household containers storing water.
- The use of mesocyclops (a copepod crustacean) in the Northern Province of Vietnam led to the eradication of the vector in many areas. They are most suitable for use in large containers (wells or concrete tanks) that are not cleaned regularly, as frequent cleaning leads to depletion of nutrients required by them. However, mainly due to their high cost, most of these methods have been restricted to small scale field operations.

Chemical Control

- The chemical control methods include the application of larvicidal insecticides or space spraying. Space spraying is more widely used as larvicidal insecticides cost more. Insecticides used for treating containers that hold water includes Temephos 1% sand granules and insect growth regulators [20]. Regular monitoring of resistance patterns is essential as resistance to Temephos has been reported among some aedes mosquito species in the South East Asian Region. Insect growth regulators interfere with the development of the immature forms of the mosquito and have extremely low mammalian toxicity.
- Space spraying may be applied as thermal fogs or as ultra-low volume sprays. Although both methods are equally effective in killing adult mosquitoes, thermal fogging tends to be used more

widely. Although insecticides such as malathion 4%, fenitrothion 1%, or pirimiphos-methyl have proved to be very effective in many control programmes, mosquito vectors develop different patterns of resistance to them. Ultra-low volume applied bifenthrin, which has both adulticidal and larvicidal activities, was originally shown to be more effective than thermal fogging in the control of dengue vectors. Subsequent contradictory reports suggest ultra-low volume spraying have no effect on the oviposition of *Aedes aegypti* mosquitoes, possibly because very low amounts of the aerosol reach the primary resting sites of the vector.

WORLD DENGUE DAY

Growing population densities, unplanned urban development, poor water storage and unsatisfactory sanitary conditions are all common factors that contribute to the worsening burden of this mosquito-borne disease for many countries around the world. The *World Dengue Day* is observed every year on 15 June. The main goals of this anti-dengue campaign are to increase public awareness about dengue, mobilize resources for its prevention and control and, to demonstrate the Southeast Asian region's commitment in tackling the disease [21].

DENGUE IN INDIA

In India, the first epidemic of clinical dengue like illness was recorded in Madras (now Chennai) in 1780 and the first virologically proved epidemic of dengue fever (DF) occurred in Calcutta (now Kolkata) and Eastern Coast of India in 1963-1964. While dengue is not uncommon in India, this year, several states in northern and central India have seen a sharp rise in cases. Nowhere more than in Uttar Pradesh, where over 29,000 cases had been recorded by the state directorate of health services, as of December 2, two and a half times the number reported in 2019, the last year there was a spike in cases in the state. National data suggests that the total number of dengue cases is lower this year than in 2019. According to a response by the health minister to a question in Parliament, India has recorded 1.64 lakh dengue cases this year, compared to 2.05 lakh cases in 2019. Dengue is among the top ten diseases prioritized by the World Health Organization for the period 2019 to 2024. This is because incidence of this viral disease has increased over 30-fold in the last five decades. A third of the global burden of dengue is in India. Of the 96 million cases reported each year, 33 million of them are in India. However it's thought this is a huge underestimate of the number of cases worldwide. It's estimated the real figure could be as high as 400 million, since many are undiagnosed. A nationally representative, community based survey in India showed close to half of the population (48.7%) has been exposed to dengue infection in India at some point in their life. The highest numbers are in the southern states (76·9%), followed by the western (62·3%), and northern (60·3%) states. Given the makeup of these states, these statistics show urbanization is one of the main drivers for rising dengue incidence in India. No urban part of India is now untouched by the disease. This time, the challenge is compounded by patients with both COVID-19 and dengue. Since the initial presentation of dengue and COVID-19 infections are similar, they can be misdiagnosed, leading to catastrophic, including fatal, consequences. An outbreak of the viral disease Dengue is piling pressure on hospitals also treating COVID-19 infections. Hospitals are struggling to treat patients infected with both COVID-19 [22-24] and Dengue. Fifteen Indian states have been badly hit by a Dengue outbreak with the capital, Delhi reporting a five year high in the number of cases. Dengue and COVID-19 combined together has put the India's Health system under pressure [22-24, 26]. In India, as in many areas of the world, advancement in the field of dengue control, which comes under the purview of the NVBDCP, has been impeded by a lack of financial and human resources, poor availability of point-of-care diagnostics, and ineffective mosquito control methods. A concerted national effort to establish sustainable surveillance systems in India, improve dengue and flavivirus diagnostics, develop innovative vector control, and facilitate the development and testing of dengue vaccines, could bring about a paradigm shift in global dengue control. Researchers in India should come together to highlight ongoing work relating to the epidemiology of dengue disease in India, including the disease burden, circulating serotypes, vector epidemiology, and economic burden of dengue disease in India, as well as reviewing the state of vaccine development, with a note on novel approaches being developed in India.

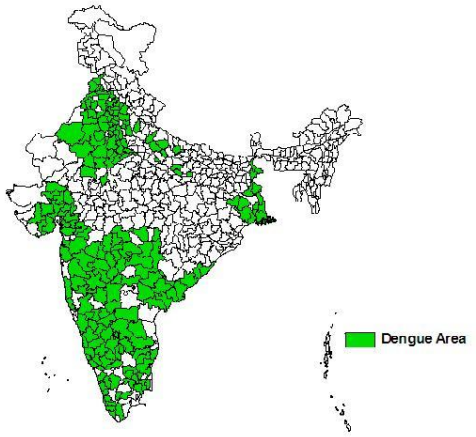

Fig 4: Distribution of Dengue in India (Source: National Center for Vector Borne Diseases Control (NCVBDC), Ministry of Health & Family Welfare, Govt. of India)

Table 1: Dengue situation in India: Dengue Cases and Deaths Since 2019 (Source: National Center for Vector Borne Diseases Control (NCVBDC), Ministry of Health & Family Welfare, Govt. of India)

S. No.	Affected States/UTs	2019		2020		2021 (Till Oct.)	
		Cases	Death	Cases	Death	Cases	Death
1	Andhra Pradesh	5286	0	925	0	3285	0
2	Arunachal Pradesh	123	0	1	0	0	0
3	Assam	196	0	33	0	55	0
4	Bihar	6712	0	493	2	396	2
5	Chattisgarh	722	0	57	0	854	0
6	Goa	992	0	376	0	1073	0
7	Gujarat	18219	17	1564	2	8013	2
8	Haryana	1207	0	1377	0	5671	0
9	Himachal Pradesh	344	2	21	0	195	0
10	Jammu & Kashmir	439	0	53	0	1051	4
11	Jharkhand	825	0	79	0	156	1
12	Karnataka	16986	13	3823	0	5062	5
13	Kerala	4652	16	4399	5	3794	1
14	Madhya Pradesh	4189	2	806	0	11354	0
15	Meghalaya	82	0	4	0	16	0
16	Maharashtra	14907	29	3356	10	10320	22
17	Manipur	359	0	37	0	44	0
18	Mizoram	42	0	67	0	34	0
19	Nagaland	8	0	1	0	0	0
20	Odisha	3758	4	496	0	6610	0
21	Punjab	10289	14	8435	22	16511	0
22	Rajasthan	13706	17	2023	7	10984	39
23	Sikkim	444	0	11	0	203	0
24	Tamil Nadu	8527	5	2410	0	3665	0
25	Tripura	114	0	24	0	31	0
26	Telangana	13331	7	2173	0	5983	0
27	Uttar Pradesh	10557	26	3715	6	21687	7
28	Uttrakhand	10622	8	76	1	641	1
29	West Bengal	NR	NR	5166	0	224	0
30	Andaman & Nicobar Island	168	0	98	0	157	0
31	Chandigarh	286	0	265	0	889	0
32	Delhi	5077	0	1269	0	2794	6
33	D&N Haveli	1491	2	248	0	383	0
34	Daman & Diu	625	2	71	0	219	0
35	Puduchery	2030	2	633	1	752	0
	Total	157315	166	44585	56	123106	90
NR=Not Reported							

CONCLUSION

Dengue has evolved as a global life-threatening public health concern, affecting around 2.5 billion individuals in more than 100 countries. The doctors should be aware about the varied clinical manifestations of this condition and ensure an early and adequate treatment plan. Future directions to combat this dreadful disease aim at methods of mosquito control, development of vaccine, and antiviral drug regimen.

Ethical Approval: Approval was not required.

Conflict of Interest: No conflict of interest to declare.

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