# Dengue Fever Epidemic in Pakistan and Its Control Measures: Where Are We Moving?


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**Abstract** Dengue fever is one of the significant health issues throughout the world, especially in tropical and subtropical territories. The cause of dengue fever is the dengue virus, which is a single-stranded RNA virus that is part of Flaviviridaeviruses family and has four distinct serotypes: DENV-1, DENV-2, DENV-3, and DENV-4. Dengue virus is spread to humans by the bite of the mosquitoes *Aedes aegypti* and *Aedes albopictus*. Clinically dengue fever symptoms range from mild (headache, nausea, vomited, pain in muscles and bones) to severe form such as dengue haemorrhagic fever and dengue shock syndrome. Since 1994 Pakistan has suffered from dengue endemic. Nevertheless, since 2006, the world has faced the worst dengue attack situation in which the disease has infected thousands of people and hundreds of people have been killed. DENV-2, DENV-3 and DENV-1 are most predominant serotypes in Pakistan.Popular diagnostic techniques being used in Pakistan are Enzyme-Linked Immunosorbent Assay (ELISA), polymerase chain reaction and rapid diagnostic tests, during differential diagnosis. Critical issues with dengue diagnosis include shortcomings in screening tests and a weak health-care system. The major factors responsible for dengue epidemics in Pakistan are favourable climatic conditions, unplanned urbanisation, population growth, commuting and many socioeconomic factors etc. This chapter offers updates on Pakistan's dengue epidemic and explains how to strengthen the region against dengue virus.

**Keywords** DENV-1 · DENV-2 · DENV-3 · DENV-4 · Emergence · Immunity · Serotypes · Endemic · Aedes aegypti · Ae. Albopictus · N, N-diethyl-m-toluamide · *Bacillus thuringiensis*

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S. I. Ahmad (ed.), *Human Viruses: Diseases, Treatments and Vaccines*, https://doi.org/10.1007/978-3-030-71165-8_3

## 1 Introduction

Mosquito-born disease caused by the dengue virus is dengue fever. Symptoms of dengue fever are associated with flu-like symptoms which develop after three to fourteen days of viral infection (Kularatne 2015). Other symptoms may include high fever, nausea, vomiting, skin rashes, muscles and joints pain. Recovery generally takes place within 7 to 10 days.

In some cases dengue fever becomes severe, such as the occurrence of low platelets, bleeding and blood plasma leakage; while in dengue shock syndrome, blood pressure of patient becomes dangerously low, hepatomegaly and shock (Heydari et al. 2018). Dengue, which is an enveloped single-stranded RNA virus, belongs to the genus Flavivirus and family Flaviviridae (Ahmad and Poh 2019). The virus is transmitted to humans via the bite of an infected female mosquito of the genus Aedes, usually *Aedes aegypti* (Ae Aegypti) and rarely *Ae. Albopictus*. The Ae Aegypti grow in stagnant water collected at different areas in tropical and sub-tropical regions, and it is a day-biting mosquito. These mosquitos carrying the virus, their biting to the person can transmit the virus to a non-infected person. Dengue can also be transmitted by infected blood products and organ donations (Dean et al. 2018). Vertical transmission from mother to foetus during pregnancy has also been reported (Wiwanitkit 2010). According to World Health Organization (WHO), dengue fever is the fastest spreading dengue-endemic disease affecting the health of peoples of tropical and sub-tropical countries of the world. Dengue is the primary cause of hospitalisation, and it is estimated that annually 500,000 people infected with severe dengue required hospitalization in which children are dominant. In contrast, about 2.5% of the affected people die annually (Yousaf et al. 2018).

## 2 Dengue Serotypes

There are four serotypes of dengue viruses: DEN-1, DEN-2, DEN-3, and DEN-4. They are antigenically different but closely related serotypes of dengue show 65–70% sequence homology (Ali et al. 2016). Each serotype has different genotype with extensive genetic variability, which causes vaccine development difficulties against all four dengue serotypes. If a person has been diagnosed with dengue from one serotype and is later recovered from dengue it will keep him immune from this serotype throughout life. While cross-immunity to the different dengue, serotype is short-lived (Ali et al. 2016). Re-infection of dengue with new serotype can present a high risk of creating dengue hemorrhagic fever due to antibody-dependent change, a miracle where specific antibodies to infection strengthen infectious disease, and sometimes infection replication within monocytes/macrophages and granulocytic cells can aid (Wahala and De Silva 2011). Infection caused by all four dengue

serotypes is analogous, but several studies have shown that DEN-2 and DEN-3 are related to severe dengue infection, whereas DEN-1 is causing mild disease (Passos et al. 2001).

## 3 Prevalence of Dengue Serotypes in Pakistan

Dengue was first discovered in Karachi, a congested city of Pakistan with a seaport causing the importation of eggs of infected mosquitoes usually with tyres from foreign countries (Yousaf et al. 2018). This virus is endemic in Pakistan mostly in the post-monsoon period and can stay dormant for several years, and several outbreaks have been reported in different regions of this country at a different time (Table 1).

Why dengue endemic in Pakistan?

Pakistan is suffering from dengue endemic since 1994, and now this virus has become a significant public health concern. Although started in 1994 but from 2006 it has taken status of the epidemic in which the disease has infected thousands of people and hundreds of people lost their lives. From 1995 to 2019, there have been around 1,47,200 instances of dengue infection and over 800 deaths. Dengue serotype 2 is the most usual circulating serotype in Pakistan, with few reported cases of serotype 3 (Fatima 2019).

**Table 1** Distribution of dengue serotypes in various geographical areas of Pakistan

| Year | Serotype | Region | References |
|---|---|---|---|
| 1985 | DEN-2 | Karachi | (Cobelens et al. 2002) |
| 1994 | DEN-2 | Karachi | (Chan et al. 1994) |
| 1995 | DEN-2 | Baluchistan | (Paul et al. 1998) |
| 1997 | DEN-2 | Karachi | (Qureshi et al. 1997) |
| 1998 | DEN-1, DEN-2 | Karachi | (Akram et al. 1998) |
| 2003 | DEN-2 | Nowshehra, Haripur, Khushab | (Khanani et al. 2011) |
| 2005 | DEN-3 | Karachi | (Jamil et al. 2007) |
| 2006 | DEN-2, DEN-3 | Karachi | (Khan et al. 2008) |
| 2007 | DEN-2, DEN-3 | Lahore | (Fatima et al. 2011) |
| 2008 | DEN-2, DEN-3 | Lahore | (Fatima et al. 2011) |
| 2009 | DEN-2, DEN-3 | Lahore | (Fatima et al. 2011) |
| 2010 | DEN-1, DEN-2 | Gujranwala, Lahore, Sheikhupura | (Mahmood et al. 2012) |
| 2011 | DEN-2 | Punjab | (Fatima et al. 2012) |
| 2013 | DEN-2, DEN-3 | Swat | (Khan 2013) |

There are several factors involved in spreading of this virus; the most important is the favorable climate. As the climate in this country is most beneficial to the mosquito to grow and reproduce, especially in the post-monsoon period when there are hot and humid conditions. Another factor supporting the growth and reproduction of Ae Aegypti is the moderate temperature in which vector replication and maturation are enhanced (Ahmed et al. 2017; Rasheed et al. 2013). Another factor favoring mosquito growth is the unregulated and unplanned urbanization which provide favorable breeding ground to Ae Aegypti. Other reason includes the inability of environmental sanitation to clean up the plethora of waste containers (Pulford et al. 2012). Overpopulation, lack of fresh consuming water, inadequate mosquito control, air travel, poor socio-economic conditions, lack of public health and lack of awareness are other vital reasons for the dengue epidemic (Ahmed et al. 2017; Tahir et al. 2015).

## 4 Seasonal Effects of Dengue Outbreak

Cases of dengue infection increased during and after rainy seasons as compared to winter and summer seasons. high humidity, optimum temperature and rainfalls remain significant predictors of dengue incidence in Pakistan. The surge of cases occurs between July and October as shown in Fig. 1 (Shaikh et al. 2014).

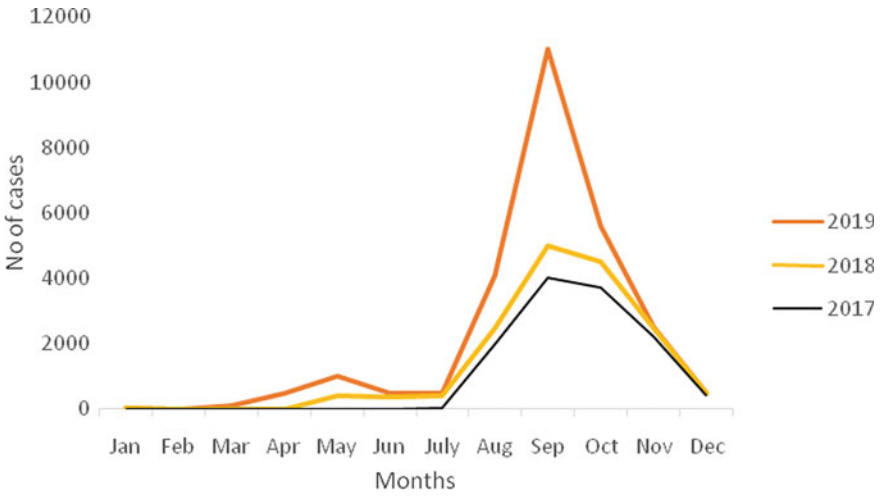


**Fig. 1** Dengue fever cases in Pakistan: monthly data collected from 2017 to September 2019 (n = 28,328) (Internal data source 2014)

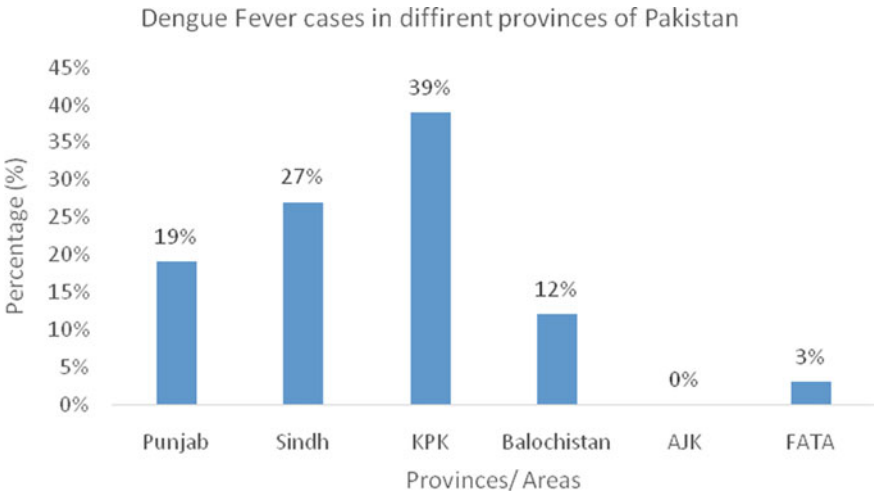


**Fig. 2** Represents the dengue fever cases in all provinces of Pakistan from 2017 to September 2019 (n = 28,328)

## 5 Climate Change Adds to Risk Factors

The key risk factors for dengue-endemic are urban population, indoor storage of water with neglected storage facilities, and poor sanitary conditions. But, an unmarked condition in this equation is climate change. The unplanned vector surveillance cannot be predicted for the post-monsoon, unexpected rain, where water drainage facilities are of poor quality, time after time. The open pockets of rainwater in the urban areas results in suitable nurseries for the dengue mosquito hence result in failures of most measures in controlling the vector population, by the end of the monsoon period.

## 6 Dengue Infection Statistics in 2019

According to the data of WHO, around the world, per 100 million people there are around 20,000 people die due to dengue virus infection (Guzman et al. 2016). According to weekly epidemiology report of National Institute of Health (NIH) Pakistan in November 2019: "there was a total of 24,336 cases including 2,686 cases in Baluchistan, 2847 cases in Islamabad and 5214 cases in Khyber Pakhtunkhwa (KPK). According to the report for Punjab and Sindh province, there were 8,770 and 2,937 cases respectively (Internal data 2014).

Dawn (*18 November 2019)* a Pakistan national media news channel claimed in 2019 reported a total 49,587 cases from the whole country. Thirteen thousand two hundred fifty-one cases from Sindh, 13,173 from Islamabad, 9,855 from Punjab,

7,776 cases from KPK, 3,217 cases from Baluchistan, and least number of cases 1,690 reported from Azad Jammu Kashmir (AJK). Other 625 cases were placed in 'other' categories such as the cases whose origin could not be determined. No deaths from KPK and Gilgit-Baltistan were recorded, while in the federal capital Islamabad, as many as 22 dengue patients died. Of the remaining 57 cases, 33 people died in the province of Sindh, 20 in Punjab, 3 in Baluchistan and 1 died in AJK (Countrywide 2019).

In Pakistan, several hospitals running the facilities to treat patients infected with dengue virus include Pakistan Institute of Medical Sciences (PIMS), Islamabad, Mayo, Jinnah and Ganga Ram Hospitals, Lahore, Civil, Jinnah and Agha Khan, Hospital, Karachi, and Allied Hospital, Faisalabad, Benazir Bhutto Hospital, Rawalpindi (Fig. 2).

## 7 Way Forward

In Pakistan control of dengue and other vector-borne diseases is extremely challenging due to insufficient expert entomologist, lack of quality assurance standards, adequate monitoring, assessment system and the lack of designated authority for dengue vector control interventions. Prevention of dengue in this country can be enhanced by adopting the following measures.

1. **Health care system up-gradation**

In Pakistan, weak health care systems may be responsible for the high mortality rate from dengue infection. Mortality rate can lessen by improving staff training and clinical management, early clinical and laboratory diagnosis, intravenous rehydration, and reorganizing hospital procedures. Pakistan's health ministry should organize health promotion programs to disseminate community information to eradicate mosquito breeding sites. Better hygiene procedures, personal safety measures, encouragement of the use of larvicidal agents, and treatment of unwanted stagnant water should be the objectives of the health care staff alongside the campaigns.

2. **Strengthening of surveillance system in Pakistan**

Surveillance is a critical step for any dengue prevention and control as it offers the required information for risk management and policy guidance, including disease response and policy evaluation. The weak dengue surveillance system in Pakistan is one of the main reasons of unsatisfactory dengue prevention. Application of functional and continuous dengue surveillance at every level is the primary requirement of dengue control in Pakistan, and it should be a part of the national health care program. Passive monitoring, active surveillance, and event-based data collection should be the valuable component of our monitoring program to assess dengue transmission, spread of serotypes, and investigate unexplained health incidents, including unknown etiology of fevers and case clustering.

3. **Personal protection**

Protective garb can reduce the risk of mosquito biting and hence it is recommended that socks, shirts and trousers be worn in full sleeves. Mosquito mats, coils, pressurized canned products and repellents are generally used for domestic safety. Plant extricates inclusive of Neem oil and chemical such as DEET (N, N-diethyl-m-toluamide) are repellents which offer protection against mosquitoes. Certain insecticides are available for those who use skin-tight clothing; their clothes can be treated with the chemical to avoid mosquito biting through skin-tight clothing. Their clothes ought to be treated with the recommended dose to prevent irritation on the skin. Precautions must be taken while the usage of repellents both natural and chemical and use of mats and coils (the locally produced insect repellent which when burnt slowly produce vapours acting as mosquito repellents) should be avoided to be used in tightly closed rooms.

4. **Environmental management**

Environmental management can also be effectively used to prevent mosquito growth and infection. Environmental management refers to the modifications in the environment to reduce man-vector contact and consequent transmission hazard. Quality waste management enhanced and effective water supply network, enough drainage system, maintenance of containers for domestic water storage, cleaning of flower vases and recycling of worn out tyres, are all part of environmental management. In Pakistan, government will enhance environmental protection to be helped by the society in controlling mosquito spread. Improper sanitation is the key problem in Pakistan, and the country should concentrate on street sweeping, improved drainage network and stagnant water removal.

5. **Biological control**

Biological control agents can be used for the prevention of dengue. Larvivorous fish were commonly used for management of Ae. Aegypti in a large container of water and its output depends on the type of container or body of water being used similarly copepods have played a role in regulating Ae. Agypti (Guzmán and Kourı 2004). According to national dengue control guidelines in Pakistan, mosquito fish should only be used in limited, clean water bodies and should be released after comprehensive surveys of mosquito breeding sites. Fungi such as Beauveria bassiana and Metarhizium anisopliae have also been proposed as potential biological control agent of Ae. Aegypti. Also, bacterium *Bacillus thuringiensis* sub-sp. *israelensis* is useful to control mosquitoes. These bacteria should be applied only during first three instars of the larval stage. The use of endosymbionts such as *Wolbachia pipientis*, a gram-negative bacterium, has also been reported to control of mosquito-borne transmission of pathogens (Tahir et al. 2015).

6. **Chemical control**

Certain larvicides have also been found to be effective in controlling the dengue vectors by using larvicides. The agents are mostly used as a surface spray, limited to

domestic use and to be applied ona short term basis. Several different larvicides include pyriproxyfen, H-14 and temephos. Space spraying can also kill the mosquito by small droplets of insecticides in air, and it has been the primary method used in several countries to control dengue fever/DHF (Dengue Hemorrhagic Fever). Larvicides are occasionally applied at mosquito's breeding sites to control vector population, but precautions must be taken after proper and careful breeding sites assessment assays carried out.

7. **Research and development**

Research is Pakistan is also essential for dengue control. It should address the cost-effective enhancement of new control methods. Pakistan's research and development organizations such as Pakistan Science Foundation (PSF) and Pakistan Council of Scientific and Industrial Research (PCSIR) should focus on developing specific, sensitive and rapid test devices for dengue diagnosis, and development of effective vaccines against all serotypes and non-insecticidal methods to control Dengue virus.

8. **Dengue vaccines**

Sanofi Pasteur's first dengue vaccine, Dengvaxia (CYD-TDV), was reported late in 2015 and early in 2016. Generic name CYD-TDV and brand name Dengvaxia is a tetravalent chimeric, live attenuated vaccine. Other tetravalent live-attenuated vaccines such as TAK003, and Dengvaxia were developed by Takeda in Japan, have completed the phase II clinical trial in children of age 2-17 years in Asia and Latin America (Sáez-Llorens et al. 2017). Other vaccine candidates like V180, TDENV, and PIV developed by Merck from dengue virus envelope protein ((DEN-80E) effective against all serotypes of dengue have completed the first phase of clinical trials and shown promising results in some countries including Pakistan (Yousaf et al. 2018; Manoff et al. 2019). Vaccines remain the most effective method for combating infectious viral diseases. A secure, effective, and affordable dengue vaccine against all serotypes of dengue would result in considerable improvement in dengue management.

## 8 Treatment for Dengue Virus Infection

In terms of the medicines required for the treatment of dengue infection, intravenous fluids such as crystalloids or colloids may be given. Also, intravenous infusion employing antipyretics and oral rehydration salts are usually available at most hospitals. Other drugs to treat severe cases are injectable vitamin K1, calcium gluconate, sodium bicarbonate, glucose, furosemide, potassium chloride solution, vasopressors, and inotropes. But vasopressors, vasopressin and inotropes, Diltiazepam and Verapamil are not available in injectable form in Pakistan. These injectable drugs are highly essential to savethe lives of critically ill patients (Lo et al. 2017).

## 9 Conclusion

This chapter showed that dengue is widespread throughout Pakistan. Dengue growth in Pakistan is due to multiple factors that may consist of climate change alternatives, virus evolution, and social elements such as rapid urbanization, population boom, development, socioeconomic influences, and global tour and trade. For areas where humans interact with vector organisms, more efficient control steps for dengue mosquitoes are critical. Dengue is spreading to non-endemic regions globally. To minimize the spread and effect of this disease, the Worldwide Plan for the prevention and control of dengue as outlined by WHO must be enforced.

Recommended dengue management initiatives may include vector population abolition by using eco-friendly control methods, use of air conditioning, window/door screening in homes and workplaces, improved water garage practices, and waste cloth disposal, infrastructure that may minimize dengue vector breeding. There is dire need to revisit the policies regarding dengue control in Pakistan.

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