

# Frequent Dengue Outbreaks in South Asian Countries: Analysis of Associated Risk Factors and Possible Preventive Measures

By

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A project submitted to the School of Pharmacy in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy (B. Pharm)

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## **Declaration**

It is hereby declared that

1. The project submitted is my own original work while completing a degree at BRAC University.
2. The project does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The project does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

**Student's Full Name & Signature:**

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## Approval

The project titled “Frequent Dengue Outbreaks in South Asian Countries: Analysis of Associated Risk Factors and Possible Preventive Measures” submitted by Mohibul Islam (19346077) of Summer, 2019 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy on March 2024. .

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## **Ethics Statement**

This study doesn't involve any human or animal trial.

## **Executive summary**

Dengue, a mosquito borne viral disease has now become one of the most alarming threats of the world. Each year approximately 400 million people are affected by dengue globally. Among them 100 million people get sick by the dengue virus along with 40,000 deaths. Asia pacific region is the most favorable place for dengue borne mosquitoes to raise their descendants due to the hot and humid environment and heavy rainfall. The objective of my project is to find out the reasons of high dengue viral fever spreading in south Asian regions, the associated risk factor that is cause by dengue and the possible preventive method to stay safe from dengue. The data and information of the project were taken, reviewed and analyzed from different verified data source which includes Scopus, PubMed, Sciencedirect and Google Scholar. Throughout my project I find out few points that trigger the high dengue cases in south east Asia. The large population, unplanned urbanization, low per capita income, low quality of life, poor economic structure makes it more difficult to control the outbreak of dengue in the Asia pacific region. Dengue severity mainly lasts for two to three months. So, if this time frame can be monitored effectively, the severity should be lessened to a greater extent. Severe dengue requires immediate supportive care to save the affected patient's life. Doctor counseling is mandatory for them to get rid of fetal severity. Few vaccines showing promising result in market along with few upcoming vaccines that are in clinical trial phase.

**Keywords:** Dengvaxia, Qdenga, Severe dengue, Organ damage, Hemorrhagic fever, Dengue Shock Syndrome (DSS).

## **Dedication**

Except for the help of Almighty Allah, I wouldn't be able to complete the writing. I would also like to thank my project supervisor Dr. Md. Rabiul Islam sir, all the members of my defense committee board, all other faculties of the school of pharmacy, my parents, my other family members and all of my well-wishers.

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## **List of Acronyms**

CFR: Case Fatality Rate

CVPA: Control of Vectors and Pesticides Act

CYV: Chimeric Yellow Fever Virus

DEET's: N, N-diethyl-meta-toluamide

DENV1: Dengue Virus 1

DGHS: Directorate General of Health Services

DSS: Dengue Shock Syndrome

EMA: European Medical Agency

EU: European Union

NIH: The National Institute of Health

SEA: Southeast Asia

USD: United States Dollar

USFDA: United States Food and Drug Administration

WHO: World Health Organization

# Chapter 1

## Introduction

### 1.1 Dengue Outbreak

Dengue is a mosquito borne and pandemic prone viral infection which is prevalent in many parts of the world. It spreads to human species by mosquito bites. Dengue is caused by a virus belonging to the Flaviviridae family. It is a RNA virus and it has four distinct serotypes. Dengue virus is spread via the bite of mosquito mostly *Aedes Aegypti* (*Ae. aegypti*) and also *Aedes Albopictus* (*Ae. Albopictus*) mosquitoes cause dengue fever to a lesser extent (WHO, 2009). The mosquitos become infectious when it bites an infected individual. It then carries the dengue virus and is injected into other individuals. These mosquitoes lay eggs in water and intrigues the spreading of the infected mosquitos. Dengue virus incubation period is normally 4 to 10 days. Dengue has four serotypes which are DENV1, DENV2, DENV3 and DENV4 (Huang et al., 2004). Dengue virus 1 (DENV1) was reported primarily in 1943 in French Polynesia and Japan. After the first report it was again detected in Hawaii in 1944 and 1945. Dengue virus 2 (DENV2) was primarily detected in the Philippines in 1944 (Messina et al., 2014). The report of affecting DENV2 also found in Indonesia and Papua New Guinea in 1954-1956. In 1953, DENV3 and DENV4 were first reported in the Philippines and Thailand. Furthermore, in 2007 a new serotype of dengue virus, DENV5 was introduced in Malaysia. *Aedes* mosquitos are usually found in urban and suburban areas as they like to breed in stagnant water. Mosquitos thrive in stagnant water and also spread viruses like zika and chikungunya. The WHO warned that the cases of mosquito borne disease are bound to rise due to climate change in coming years. Experts say south Asian countries reported dengue outbreaks due to a combination of climate change and south Asian warm and humid weather patterns. In recent days African countries have also been found to be badly affected by

dengue fever. Because of the absence of effective vaccines and drugs that are specifically able to treat the disease, it has become an alarming issue in recent years. The prevention and control of dengue mainly depends on control of the vector, detection of the disease early and proper medical care. WHO reports claims that, about 3.5 billion people around the world live in countries which are marked as dengue endemic regions and among them around 1.3 billion people living in dengue endemic areas are from 10 countries of Southeast Asia. Additionally, experts from the Republic of Korea claims, Southeast Asian region contains half of the world's global burdens of dengue. Among 30 highly endemic countries of the world, 5 Southeast Asian countries (Myanmar, Thailand, Sri Lanka, India, and Indonesia) are present. From 2015 to 2019 Southeast Asian dengue cases have increased by 46% (WHO, 2023). Factors that intrigue the dengue outbreak in SEA (Southeast Asia) include rapid population growth, poor sewer management system, development of hyper endemicity in urban areas, changes in public health policy, rise in global commerce and tourism, poor waste management system and global warming. Due to the absence of effective treatment and lack of comprehensive vector control, dengue outbreak has become a very heavy burden for Southeast Asian regional countries.

## **1.2 Objective**

Dengue outbreaks can indeed be catastrophic in endemic regions, causing significant public health challenges. Prevention efforts, including vector control measures and community awareness, are crucial in managing and mitigating the impact of dengue fever. The main objective of my review article is to uphold the severity report of dengue in south Asian regions (Also some other regions), the reasons of the high spreading of the disease in southeast Asian region and the preventive measures that can be taken to control the highly spreading endemic disease. Dengue is a heavy burden for a country and it is becoming more severe day by day.

Most of the south Asian countries has poor economic status and it is cause destructive effect on the people of this region. Research affiliated with dengue in the South Asian region is crucial because the area experiences a high burden of the disease due to factors like climate, population density, and urbanization. Understanding local epidemiology, transmission dynamics, and developing region-specific prevention and control strategies are essential to mitigate the impact of dengue outbreaks in this region. Controlling the dengue viral vector, primarily the *Aedes* mosquito, is crucial for preventing the spread of dengue fever. By targeting and reducing mosquito populations, we can significantly decrease the transmission of the virus, thereby reducing the incidence of dengue fever outbreaks and the associated health burden on communities. Effective vector control measures include eliminating breeding sites, using insecticides, and implementing community education and participation programs. The objective of dengue vaccine research is to develop safe and effective vaccines to prevent dengue virus infection, thereby reducing the burden of dengue fever and its associated complications. Over all this review article is conclude a short summery about the dengue mitigation and prevention procedure to prevent the rapidly endemic disease dengue.

### **1.3 Methodology**

The review work is summarized from various relevant literatures. The information and data for this review came from various articles and academic journals which were found on the digital libraries. I searched information from Scopus, PubMed, Google Scholar, Sciencedirect. I searched information by using specific words (Dengue, Dengue fever, Dengue hemorrhage fever, Dengue outbreak). The relevant topics from the articles were found and the further important topics were looked into. After analyzing the data outline was created with all necessary information. PubMed is a free online research tool that works like a digital library from which helps me to get valuable information like the history of different types of vaccine, their process of working, their production procedure, relevant data of



clinical trial, post marketed surveillance and region of use of these approved vaccines. All the clinical study data that is present in my writing is collected from PubMed. All the statistics that were given about dengue in this article were collected from the health ministry of those respected countries and from the published journal from WHO reports and health bulletins. WHO monthly health bulletin helped me to find month to month dengue update in different region of the world. Google Scholar is a very necessary tool to find a large database of scholarly articles which helps to find relevant information on the topic. The Science Direct provides me with the latest information about the topic which helps to enhance my knowledge in the virology field. The websites of different countries health ministry helped me a lot to find out monthly update of the countries along with their regional dengue outbreak reports. Manually APA in-text citations were performed on the essay.

#### **1.4 Common Symptoms of Dengue Viral Fever**

Common dengue symptoms include:

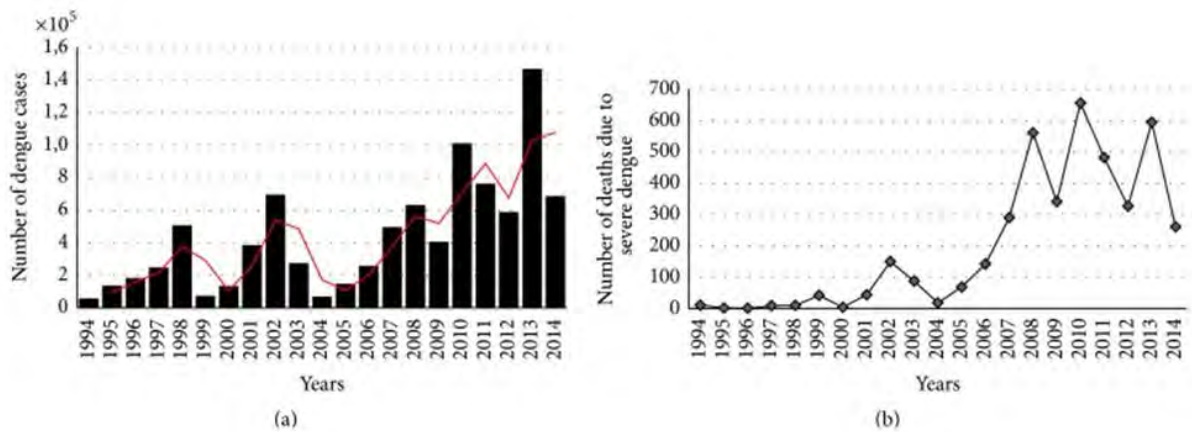
- a)** High fever (104 F or 40 C)
- b)** Nausea
- c)** Vomiting
- d)** Loss of appetite
- e)** Muscle pain
- f)** Anorexia
- g)** Joint pain
- h)** Redness of eye and throats

## Chapter 2

### Global Prevalence of Dengue Fever

#### 2.1 Dengue Outbreak in Brazil

Brazil is one of the tropical countries in the world and for this reason the dengue outbreak in Brazil is high. Due to the hot and humid environment the prevalence of the disease is also high. Tropical weather is favorable for rapid growth of *Aedes aegypti*. The reports state that Dengue emerged in Brazil in the 1980s and soon it spread to both the rural and urban areas. Average mortality rate of people who are affected by Dengue in Brazil is 3.05 among 100,000 inhabitants (Barcellos et al., 2014). From 2003 to 2019 total 11,137,664 people were affected by dengue. Since the introduction of the disease and till now in total five epidemic years have passed and among them the highest 1,544,987 people were reported in 2019 (Araujo et al., 2020). Contributing factors for rapid dengue transmission in Brazil are Environmental heterogeneity, demographic, socioeconomic, climatic factors. In between December to April, on average 1000-1800 mm rainfall triggered the growth of mosquitos (Asgarian et al., 2021). Additionally, heavy rainfall in amazon forest boosts the growth of the mosquito. The rain water accumulated and mosquitoes lay eggs there and increased their population. Low relative humidity increases the longevity of the mosquito and their vector's living capacity and low temperature inhibits the longevity and lessens the vector's living capacity. The low humidity and high temperature of Brazil act as blessings to long living of mosquitos and increase the living capacity of Dengue viral vectors (Barrera et al., 2011).



**Figure 1:** Epidemiological Scenario of Dengue in Brazil (Raffaele et. al, 2015)

Here figure (a) and (b) represent the total cases and number of patients who died in Brazil from dengue in between 1994 to 2014.

There is a confirmed death rate in Brazil and these people are affected by dengue. The graph which has shown here is taken from the Brazilian Health Ministry website, accessed at <http://portalsaude.saude.gov.br/>. The patient was affected by dengue or not was confirmed by laboratory tests. In this graph the red line represents the rapid moving rate of Dengue.

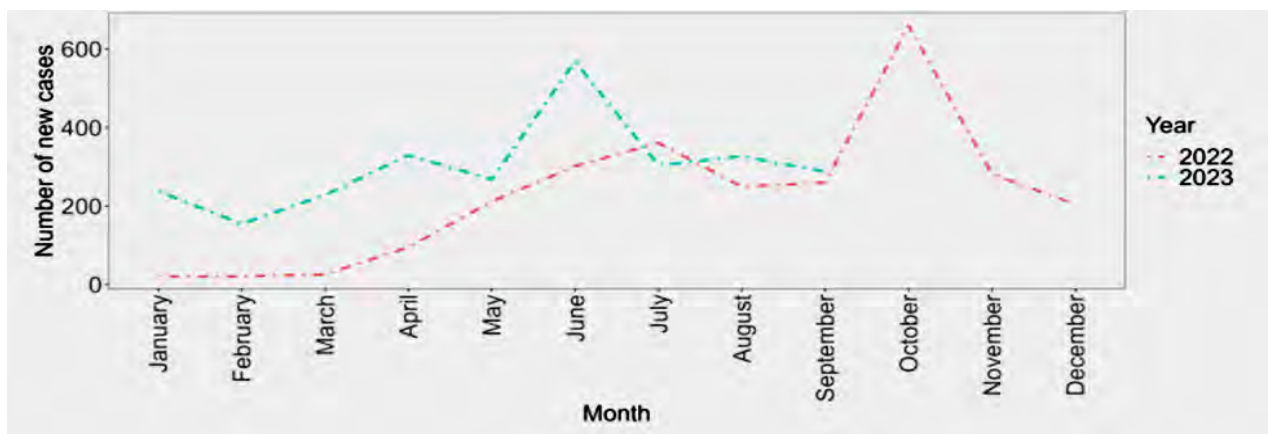
## 2.2 Dengue in South Asian Countries

The world health organization estimates about 2.5 billion people are at risk of dengue globally and among them 70% are in the Asia pacific region. According to DR Duane Gubler, (director of Asia pacific institute of tropical medicine and infectious disease) the reasons for high dengue rate in the south Asia region are Poor vector control capacity (not have good mosquito control method), not have vaccine yet, no good clinical diagnosis management, Poor management etc. (Gubler, 2020).

He also states the ignorance rates of physicians and nurses about dengue. If they were concerned the fatality rate of dengue should not be more than 0.5%.

South Asian countries including Maldives, Afghanistan, Pakistan, India, Bhutan, Nepal, Bangladesh, Sri Lanka etc. are heavily affected by dengue.

**Maldives:** Current study suggests the number of total dengue affected people in Maldives is increasing year after year. A total 2707 cases of dengue have been reported in Maldives in between January and September 2023 which was much higher compared to the previous year. In 2022 in between January to September 1548 cases were reported. Within a year total number of dengue affected people increased by 75% (WHO, 2023a)

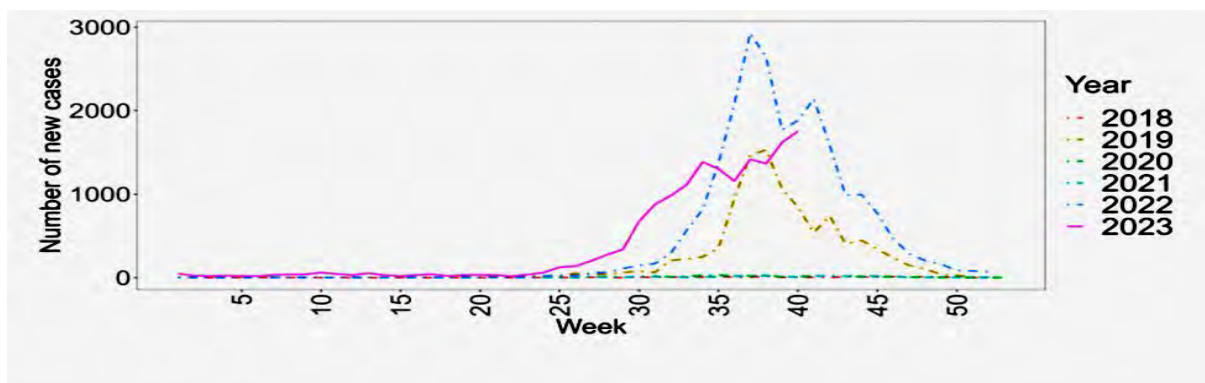


**Figure 2:** Ministry of Health, Republic of Maldives: <https://health.gov.mv/en/publications?search=Monthly&category=&department=>

WHO South-East Asia Region Epidemiological Bulletin, (13th edition, 18 October 2023).

The figure 2 describes the number of new cases of dengue by month in Maldives from January 2022 to September 2023

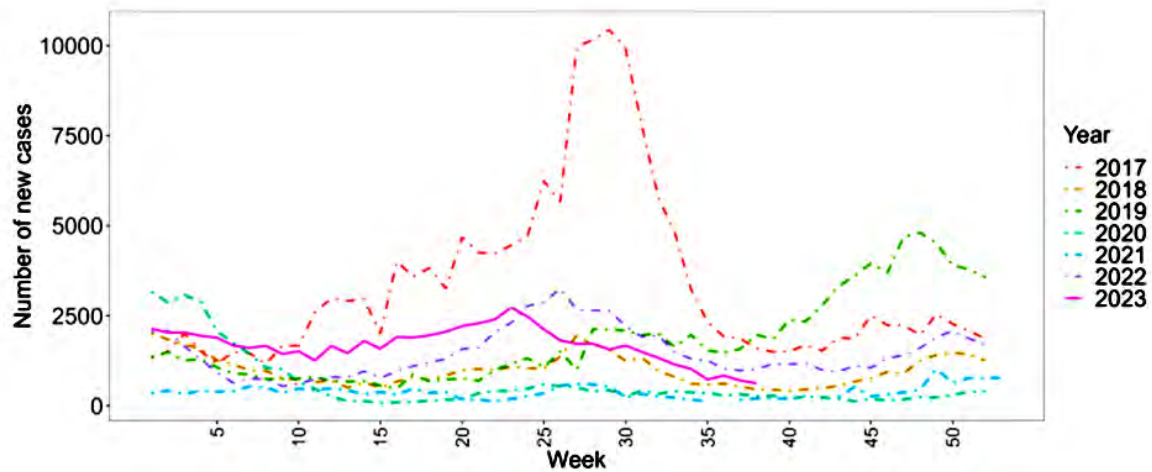
**Nepal:** In Nepal, 39,360 cases of dengue have been reported in between 1 January to 13 October including 20 deaths. Among these cases, more than 50% cases were from two districts. From Sunsari district almost 41% cases were reported which is 18,111 and from Tanahun district 1472 cases were reported which is around 13%. The total number of patients that were affected by dengue in week 39 (From September 24 to September 30, 2023) increased by 8.4% in week 40 (October 1 to October 7, 2023). A total 1755 cases were reported in Nepal in week 40 (WHO, 2023b).



Source: Government of Nepal, Ministry of Health and Population, Department of Health Services, Epidemiology and Disease Control Division. EWARS Weekly Bulletin. <https://edcd.gov.np/resources/newsletter>

**Figure 3:** Number of new cases of dengue by week reported by the Early Warning Reporting System (EWARS) in Nepal from January 2018 to 7 October 2023

**Sri Lanka:** In September 2022 around 57,454 dengue cases were reported. However, the number of cases has been increased 1.1 times in 2023. As of 23 September 2023, around 64,109 dengue cases were reported throughout Sri Lanka (WHO, 2023c).



Sources: Epidemiology Unit and National Dengue Control Unit, Ministry of Health.

[https://www.epid.gov.lk/epid/public/index.php/weekly-epidemiological-report/weekly-](https://www.epid.gov.lk/epid/public/index.php/weekly-epidemiological-report/weekly-epidemiological-report)

[epidemiological-report](https://www.epid.gov.lk/epid/public/index.php/weekly-epidemiological-report/weekly-epidemiological-report)

(2017

to

2023)

[https://www.dengue.health.gov.lk/web/index.php/en/publication-and-](https://www.dengue.health.gov.lk/web/index.php/en/publication-and-resources/publications/category/20-weekly-dengue-update)

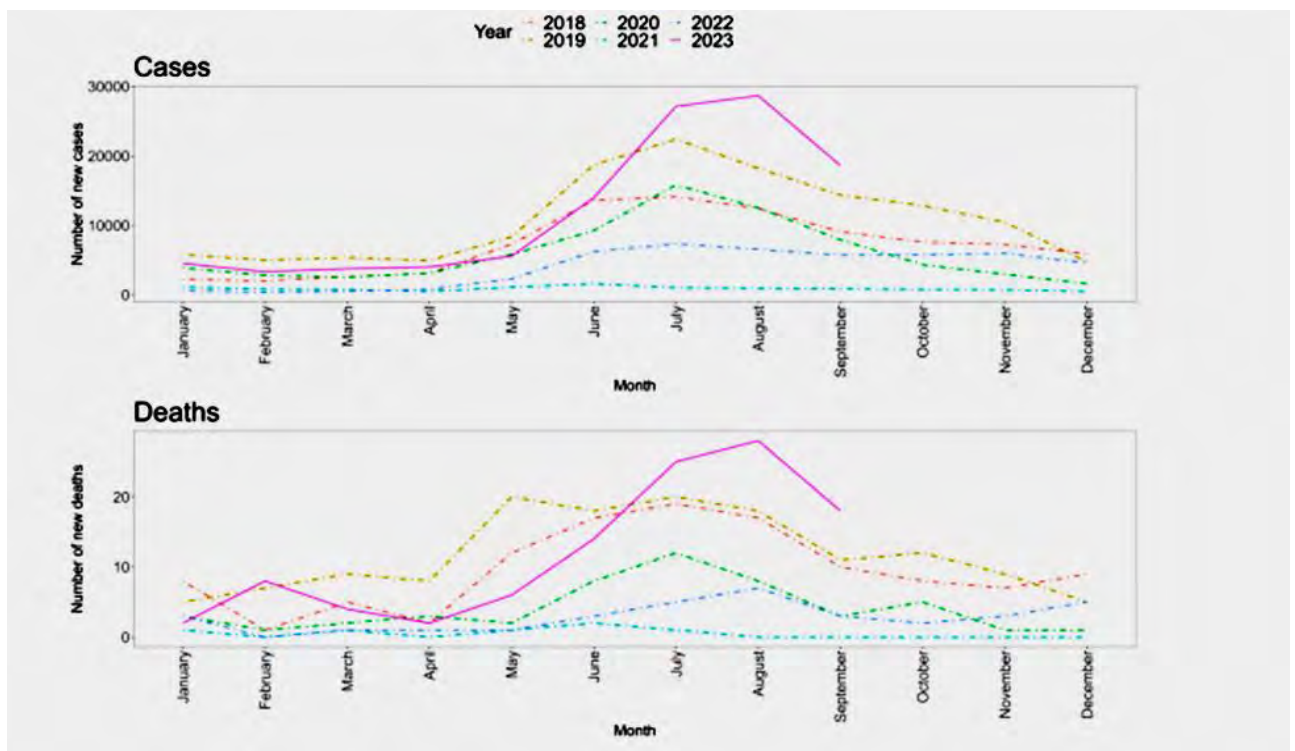
[resources/publications/category/20-weekly-dengue-update](https://www.dengue.health.gov.lk/web/index.php/en/publication-and-resources/publications/category/20-weekly-dengue-update) (2022 and 2023)

**Figure 4:** Number of new cases of dengue by week in Sri Lanka from January 2018 to 22 September 2023 (week 36)

**Thailand:** in Thailand in 2023, A total 110,809 dengue cases were reported and among them 107 death cases were reported. Among affected people 84,392 people (approximately 76.2%) were affected by dengue fever and 23% of them were affected by dengue hemorrhagic fever. Also, 898 patients suffer from dengue hemorrhagic fever shock syndrome (WHO, 2023d).

In Between September 2018 to September 2022, approximately 18,604 dengue affected people were reported (Faisal, 2022).

In previous years the death rate of dengue affected people was also very less. Only 18 deaths were recorded inside this timeline. The cases that were reported in 2023, 50.8% of patients were male, 35.1% were aged between 5 to 14 years and 22.6% reported patients were aged between 15 to 24 years. Its alarming report that most of the affected patients are younger patients and aged in between 25 (Wahab et al., 2023).



Sources: Bureau of Epidemiology, DDC, MPH.

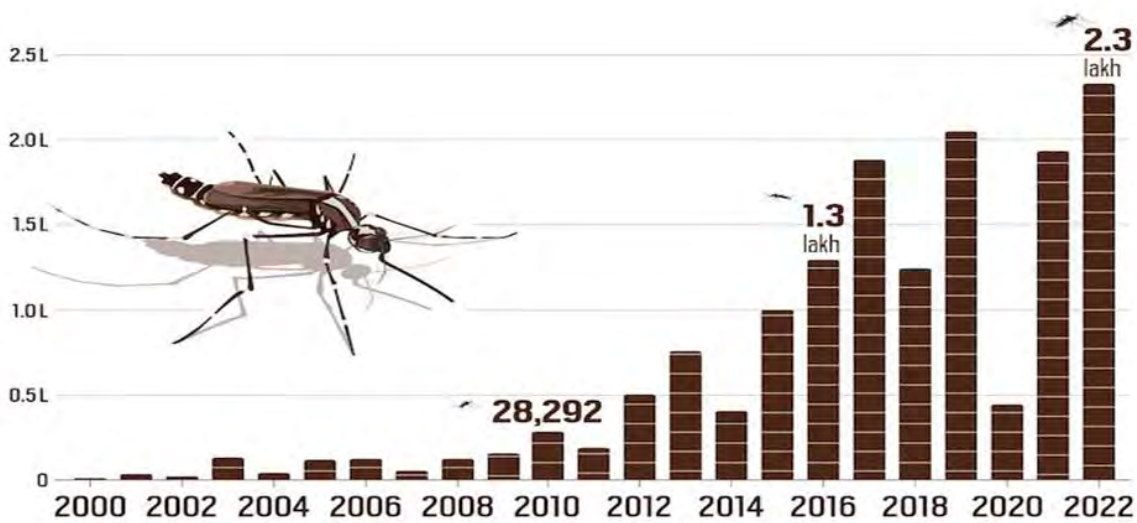
<http://doe.moph.go.th/surdata/disease.php?ds=66>,

<http://doe.moph.go.th/surdata/disease.php?ds=26> and

<http://doe.moph.go.th/surdata/disease.php?ds=27>

**Figure 5:** Number of new dengue cases and deaths by month in Thailand from January 2018 to September 2023

**India:** According to the report that is published in Times of India, In July 2022 daily around 600 people all over the country are affected by dengue. Another report published in Hindustan times claims in 2022, 76000 people were affected by dengue in only West Bengal and the rate is 10000 higher than the previous year (Sony, 2023). In 2023, approximately 2.3 lacks people affected by dengue overall in India which is the sum of all cases that are reported in between 2002 to 2012. In 2020 total people all over India affected by Dengue are 44,585 and the number will increase by 1.88 lacks in 2022 and total number of dengue affected people's 233251 in 2022. This statistics signifies the severe effect of dengue in India by 2022 (Sharma, 2023).



Source: India Today. Dengue cases in India by year from 2000 to 2024. (<https://www.indiatoday.in/diu/story/dengue-fear-grips-india-as-receding-flood-water-may-act-as-a-catalyst-2414897-2023-08-01> Accessed on August, 2023)

**Figure 6:** Dengue cases in India by year (2000-2022)



Dengue cases reported in 2022 were higher than sum of all cases reported in the previous decade 2002-2012

**Pakistan:** Dengue outbreaks in Pakistan in 2019. In this year 2019, around 52485 cases were reported and among the 91 deaths had been reported. According to the report that is published by National Institute of Health Islamabad states that from 1 January to 27 September (2022), total 25932 people reported as dengue affected and among them 62 people died. Around 74% cases were reported in September among them 32%, 29%, 25% and 14 cases were reported from Sindh, Punjab, Capital Islamabad, Khyber and Baluchistan respectively. From July to November 2019, 47120 dengue cases were confirmed and among them 75 people died (Tabassum et al., 2023).

**Bangladesh:** Bangladesh is heavily affected by dengue in recent days. According to WHO, the recent dengue outbreak is Bangladesh's most severe outbreak in recent years. WHO claims this mosquito borne disease has caused 600 lives since the outbreak began out of the 300 that were recorded last month August 2023. In 2023, over 135000 cases had been reported (WHO, 2023e). Common symptoms of dengue include fever, nausea, vomiting, muscle aches, joint aches and bone aches and even convulsion. Between January 1 to October 15 (2023), a total 239,614 dengue cases have been identified. Among them the number of patients died is 1169 and case fatality rate (CFR) is 0.49%. The number alarmingly increases during September 2023. 396 deaths have been recorded in this single month. Total 79,598 cases were reported in September 2023 (DGHS, 2023). In the 40th week (During October 2 to October 8) the total number of dengue case reports was increasing and during the 41th week of Dengue outbreak report in Bangladesh (During 9 to 15 October, 2023), a total 16,050 cases of dengue have been reported. In the 41th week the death rate increased by 3.8% (UNICEF, 2023).

Year	Cases	Deaths	Case fatality rate (CFR)
2018	10,148	26	0.26%
2019	101,354	164	0.16%
2020	26,459	105	0.37%
2022	62,382	281	0.45%
2023 (till 19 <sup>th</sup> August)	97,476	466	0.47%

Data source: Directorate General of Health Services, (DGHS report, 2023) (\*data for 2020 is limited due to COVID-19)

**Table 1:** Dengue cases, Deaths and Case fatality rate in Bangladesh for 2018 – august 2023

After analyzing this figure, it is clear that the number of dengue cases has been increasing rapidly. As we can see in 2018 among 10,148 cases 26 people died. The death rate and total number of reported cases increase alarmingly in 2019. In total 101,354 cases were reported among them 164 were dead. During 2020 to 2022 data were limited because of COVID-19. However, dengue affects alarmingly in 2023 and breaks the record of death of people in a single year (466, as of august 19, 2023).

## **Chapter 3**

### **Reasons of High Dengue Prevalence Rate**

#### **3.1 Climate**

Climate change can heavily affect the growth of mosquitoes which includes the dengue viral vector containing mosquito species as well. Tropical and subtropical environments intrigue the growth of mosquitoes. Nowadays, deterioration in the ozone layer is causing increasing global temperature which is also known as Greenhouse effect. In tropical countries due to direct solar energy water is evaporated in higher latitudes (Lindsey, 2016). It influences condensation of air into clouds and causes heavy rainfalls. The rain water accumulated here and there. This stagnant water is the favorite place for mosquitoes to lay eggs and enrich their population. Due to heavy rainfall, dengue mosquito growth rate in tropical and subtropical regions is the highest among all other types of environment. We can see the total number of dengue patients is found in tropical and subtropical regions (Chandrashekhar, 2023).

#### **3.2 Environment**

Environment plays a key role in spreading the dengue virus containing mosquitos. Normally water and nutrition are the main factors for mosquitos to grow and trigger their population. Water is the place where they lay eggs and after laying eggs the mosquitos need proper nutrition to enlarge their population. In An environment where rain water is stagnant and kept unused for a longer period of time, the mosquitos lay eggs over there and spread their population (Faruk et al., 2022).

### **3.3 Population**

Populations might be a blessing for some of the countries but too high a population can bring grief for many of them. High population management is not easy and they require a high degree of maintenance which is not possible for all countries. High population needs lots of water, and they possess a lot of wastage which can cause blockage in drainage management. Mosquitoes use the stagnant water to lay eggs in those dirty places and grow their populations (Hossain et al., 2020)

### **3.4 Lack of Awareness**

Most of the people because of their ignorance provoke the mosquito growth. They don't have any knowledge about the spreading of dengue virus. They keep water uncovered and not manage the stagnant water. During the rainy season water accumulates here and there and they don't manage the water properly. Mosquitos lay eggs on it and enlarge their population.

### **3.5 Unplanned Urbanization**

Unplanned urbanization is one of the main contributing factors of dengue in the south Asian region. Most of the south Asian countries are overly populated and their modern lifestyle is mainly city based and for this reason most of the area of the town is overly populated. High population demands more buildings, cars and many more facilities. During the rainy season rain water is stagnant here and there and causes mosquitoes to lay eggs. In garbage beans, under constructed buildings, plastic drums, unused tires, barrels, metal cans, rooftop and drains, water is stagnant and creates a favorable environment for mosquitoes to lay eggs. Additionally, most of the people lead a very busy lifestyle and they don't get enough time to thinks about the control of dengue (Kolimenakish et al., 2023).

### **3.6 Human Mobility**

In cities people become very busy with their day to day life and don't get enough time to think about other social issues. For this reason, they don't give any concern about their stored water and this stagnant water is stored there for a longer period of time and mosquitos find a favorable place to lay eggs and spread their populations (Aguirre et al., 2023).

### **3.7 Access to Reliable Water Source**

In Dhaka city, because of the densely packed population direct source of water is not that much present and most of the people store water for their future use. That water plays a significant role in growing the population of mosquitos. Mosquitoes lay eggs and spread their population. In the water bucket, water barrel and water tank people store water for their use and in those water mosquitos lay eggs (Schmidt et al., 2011).

### **3.8 Unplanned Sewage and Garbage Management**

Garbage management system is a disaster in most of the highly dense south Asian countries like Bangladesh and India (Gupta, 2015a). Higher population produces higher amounts of garbage which pass through drains and fall into rivers. In drains stagnant water mosquitoes are heavily attracted and grow their population at higher rates. In fresh water mosquitos don't lay eggs. However, when water is motionless and polluted these water mosquitos find a favorable environment to grow their population (Gupta, 2015b).

### **3.9 Genetic Mutation of Dengue Virus**

Genetic mutation of dengue virus makes it one of the most rapidly extendable viruses of the world. Currently it has four serotypes DEN-1, DEN-2, DEN-3 and lastly DEN-4. Additionally, another new serotype named DEN-5 has been discovered (Mustafa et al., 2015). Though each serotype is 65 percent similar, they have variation in genes. Each serotype of the virus has a different interaction with human antibody that is present in blood serum. For this reason it is very difficult to diagnose and cure. No such medication has been discovered which can claim that it will completely cure dengue. Study that is performed on the genetic evolution of these different serotypes states that the mutation rates of these serotypes are approximately  $7.5 \times 10^{-4}$  mutations/position/year (Dang et al., 2020). If we compare the mutation ratio with other RNA viruses we can clearly see the high mutation rate of DENV is higher than others. It shows only a slower mutation ratio than HIV virus and Influenza virus. These data describe the severity of mutation of Dengue virus.

### **3.10 Poor Vector Control Monitoring System and Inadequate Health Infrastructure**

Vector control monitoring system includes different chemicals like insecticides, molluscicides and larvicides etc. These vector control methods need to be maintained on a regular routine basis to stop and control the growth of mosquitos. However, most of the South Asian countries are underdeveloped and do not have a strong enough economy to invest enough money to prevent spreading the vector control method. Additionally, the poor economic condition hampers the adequate supply of health infrastructure. These two problems synergistically increase the prevalence of spreading the dengue virus vector containing mosquitos. Inadequate health infrastructure can indeed contribute to the spread and severity of diseases like dengue (Buhler et al., 2023).

Insufficient healthcare facilities, lack of access to proper diagnosis and treatment, and limited resources for disease prevention and control can all exacerbate the impact of dengue outbreaks. In regions with inadequate health infrastructure, such as limited access to healthcare facilities, diagnostic tools, and treatment options, the impact of diseases like dengue can be significantly magnified. Without proper resources for disease surveillance and control, outbreaks may go undetected or escalate rapidly, placing additional strain on already burdened healthcare systems (Asian Development Bank and World Health Organization, 2013). Furthermore, the lack of preventive measures, such as vector control programs and public health campaigns, can allow the dengue virus to proliferate unchecked, increasing the risk of transmission. In such environments, addressing the root causes of inadequate health infrastructure becomes crucial for effectively combating diseases like dengue and safeguarding public health. Funding gaps can severely hinder efforts to control outbreaks like dengue. Adequate resources are crucial for implementing prevention measures, conducting research, and providing healthcare services. Without sufficient funding, it's challenging to effectively combat the spread of diseases like dengue (Bowman et al., 2016).

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<b>Sector</b>	<b>Funding Requirement (USD)</b>	<b>Funding available/received (USD)</b>	<b>Funding Gap</b>
<b>Health</b>	\$422,000	\$285,000 (USAID, Global Thematic fund, Reprogrammed)	\$137,000
<b>Wash</b>	\$2,907, 500	\$450,000 (USAID, Global Thematic fund, Reprogrammed))	\$2457,500
<b>Education</b>	\$1650,558	0	\$1650,558
<b>SBC</b>	\$265,500	\$246,000 (USAID, Global Thematic fund, Reprogrammed)	\$19,500
<b>Operational cost</b>	\$367,189	0	\$367,189
<b>Total</b>	\$5,612747	\$981,000	\$4,631,747

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**Table 2:** UNICEF BANGLADESH, Dengue Outbreak Situation Report #1, pg.5, <https://reliefweb.int/report/bangladesh/unicef-bangladesh-humanitarian-situation-report-no-1-dengue-outbreak-21-august-2023> Accessed on 21st August, 2023.

Here the table shows the funding gaps of Bangladesh to control and manage dengue. Not only in Bangladesh but in most of the south Asian countries because of their poor economic conditions, poor health infrastructure is monitored. Due to the poor economic condition, these countries face very difficulties to control the outbreak of dengue,



## **Chapter 4**

### **Impacts of Dengue**

#### **4.1 Health Impacts**

Dengue is the most severe disease that is caused by any arthropods all over the world. This mosquito borne disease is causing severe health damage including death. If a person is severely affected by dengue, he/ she has a higher chance of internal bleeding. During internal bleeding bloods came out of the vessels and extreme pain and swelling might be monitored depending on the keenness of the disease. Blood vessels that are present in the patient's body become leaky and they are damaged severely. Additionally, during that period platelets count in patients' body drops and clot forming factors can't be present in the site of damaged vessels in sufficient manners. For this reason internal bleeding can't be stopped easily. This internal bleeding is fatal and causes shock, damage of important organs and even death. Organ Damage is one of the most fatal physical damage which may lead to death. This situation of dengue is called dengue shock symptom, dengue hemorrhagic fever or severe dengue (Bhowmik et al., 2023).

#### **4.2 Impacts on Mental Health:**

Besides the serious health impacts dengue can also affect mental health heavily. People from all over the world are traumatized by this Dengue Fever from all over the place. Dengue affects personal well-being and affects the mental health of a person. People more often suffered from anxiety, depression, mental etc (Bhatia, 2017).

These contributing factors can provoke severe health related complications like hypertension, Stroke, diabetes. Furthermore, mental anxiety and depression might result from insomnia which is one of the main precursors that intrigue the high blood pressure. In addition to that, patients might also suffer from mood related disorders like personality change related disorder, anxiety related disorder, bipolar disorder, cognitive mode changing disorder etc.

#### **4.3 Impacts of Dengue in Pregnant Women and Infants:**

Dengue can cause serious physical complications for human beings specially, for pregnant women. If a pregnant mother is affected by dengue, she has a higher chance of spreading this dengue virus to her baby during her childbirth. The newborn baby will suffer from severe dengue related health complications afterwards. Moreover, the chance of mother death (Maternal mortality) and compromised baby (Still birth) is increased (Quang et al., 2018). Pregnant mothers while pregnant have a higher chance of giving birth before normal time (Preterm birth) or miscarriage. Furthermore, the newborn baby might have serious health related complexities like low body mass, Fetal distress (fetus not getting enough oxygen) etc. If the fetal distress is severe and the fetus didn't get sufficient oxygen as it required, the baby might die (Chong et al., 2023).

#### **4.4 Impacts on Quality of Life and Family Income**

Dengue affects enormously in quality of life, especially in low income families. Most of the people living in South Asia lead very normal lives and most of the family depends on one single person for their living. The person who is the one and only earning member of a family, if the person is affected by dengue, the quality of the living of the family will be hampered. Most of the rickshaw pullers and day laborers are only earning members of their family and if they are affected by dengue their family suffer and the family. In addition to that, the cost of dengue can be twice or even trice of average monthly income of a family.

#### **4.5 Impact of Dengue on Blood Cells**

Dengue affects patient blood cells and can damage the person's platelet count. Normal platelet count of a healthy adult is between 150,000 to 450,000 mm<sup>3</sup> (In per microliter blood). However, dengue affected people affected by thrombocytopenia. In thrombocytopenia, blood cell counts lie below 150,000 (per microliter of blood). Total number of blood cell counts sometimes goes much lower than 100,000 mm<sup>3</sup> and sometimes lies in between 40,000 to 20,000 which is very alarming (Mulanovich et al., 2015). Dengue also damages bone marrow by producing its own antibody which destroys bone marrow.

#### **4.6 Economic Impacts**

The main problem related to any epidemic is, it never get rid of completely. Every year it affects the country and causes harm to the transportation sector, health sector, tourism sector and agricultural sector. Several studies have been performed and the study concludes the impacts of dengue on the economic sector of a country. The total annual cost of dengue is estimated in 2013. In which the annual cost for a total 50.40 million people is approximately 8.9 billion US Dollar (Lescano et al., 2015). It is estimated that, in every year, dengue costs 2.36 billion US dollars in Southeast Asia and 2.1 billion in the Americas. According to the study reports published in WHO of eight countries, the total cost of a fetal ambulatory care patient is 514 US dollar and non-petal hospitalized care patient 1394 US dollar. Another journal break dengue claims the global cost of dengue in most of the year is minimum 8 billion us dollar and among the cost 46% cases are hospitalized non fetal cases which cost 4,093 million US dollar, 33% are ambulatory non fetal case which costs 2987 million US dollar, 11% fetal cases which cost 1055 million US dollar and 8% non-medical case that includes 752 million dollar. The Southeast Asian countries' economy is not that good and strong enough to just ignore such an amount of cost very easily (Harving et al., 2016).

#### **4.7 Societal Impact**

Society people can't be able to escape from the black paw of dengue. During the rainy season, society people panic and do not get out of their homes during daylight in fear of dengue. As a result, social connections among society people collapse. People do not get out for a walk in the street and park; kids do not get out to play games on the playground. Normal lifestyles are hampered and people always live in fear of being bitten by mosquitos. Mental stress, anxiety, depression takes place and people suffer from different mental and physical disorders (Ladner et al., 2017).

#### **4.8 Impacts on Health Service**

Dengue causes serious problems in the health service system. During June to September, dengue affects very heavily and becomes endemic in most of the south Asian countries. As previously mentioned, most of the south Asian countries have poor health care service because of, their poor economic system. Furthermore, the population of these countries is high in comparison to the land ratio of the country. For these reasons, hospital bed capacity overflowed during the rainy season (July to September) and many hospitals were not able to provide enough facilities for all patients (Rehan et al., 2022). Additionally, patients who come to treat other physical complications don't get proper treatment because of the high number of dengue patients. Most of the hospital beds are occupied by dengue patients. The hospital committees do not even properly manage the patients, who are affected by dengue. They aren't able to provide enough beds to treat the patients that come to the hospital.

## **Chapter 5**

### **Possible Preventions**

#### **5.1 Short Term**

##### **5.1.1 Mosquito Net:**

Mosquito net is one of the best ways to prevent ourselves from getting bitten by mosquitos which contain dengue virus. Aedes mosquito bites during daylight, especially in the afternoon. Mosquito nets protect us from getting bitten by mosquitos during daylight. Furthermore, already dengue infected people must stay inside mosquito nets in order to further spread of the virus. Aedes mosquitoes can bite the infected person and can carry the virus. If the same mosquito bites another healthy person, the healthy individual will also get the virus. Ideal mosquito net should be compact and rectangular in shape with 156 holes per square inch, which will prevent the entry and exit of the mosquito from in and outside (Smith et al., 2010).

##### **5.1.2 Anti-Mosquito Spray**

Anti mosquito spray is poisonous for mosquitos and this spray effectively kill the mosquito population. The main ingredients of mosquitocidal spray are derived from the plant source. Permethrin kills mosquitoes very effectively and it is used to kill and control the amount of mosquitoes. For the resistant mosquito scientists developed more effective insecticidal spray which effectively killed the resistant mosquitoes. Malathion and naled are popular organophosphates that effectively kill mosquitoes. It affects the nervous system of mosquitoes and prevents their nervous system from acting properly and finally kills the mosquitos (Center for Disease Control and Prevention, 2020).

Anti-mosquito spray kills the mosquito and gives protection to the house for 3-4 hours.

### **5.1.3 Mosquito Trap**

Mosquito trap traps all the mosquitos inside it and is able to suppress the population of the mosquitos. Mainly carbon dioxide which emitted from humans attracts the mosquitoes. In this trap carbon dioxide is used to mimic the conditions like mammals and they attract the mosquitoes and entrap them via suction fans. In China, they make a park which is free from mosquitos. Mosquito-free Park attracts visitors in the Chinese city of Chengdu. In the Chinese park they installed over 50 mosquito trap machines. Mosquitoes track humans mainly by the amount of carbon dioxide exhaled. The trap sucks in carbon dioxide from air luring mosquitoes when carbon dioxide levels in the traps reach the same level as the human body. 12,000 mosquitoes caught by the device within three weeks (Chengdu, 2022). Mosquitos population also can be suppressed by mosquito traps in which polystyrene beads and oil are used.

### **5.1.4 Electric Mosquito killer Bat**

Electric mosquito bat is an effective and handy tool which can effectively kill the mosquitos and control the population of dengue born mosquitos. Portable plastic electric bat is very effective to kill the mosquitos that are present inside the household. Electric bats generate 1500-2000V (volt) which paralyze and finally kill the mosquito. Electric bat is rechargeable and portable and it can be carried from one place to another place. Mosquitoes when they encounter such high voltages of 1500-2000 volt, they can't survive and eventually get killed by bats (Barman, 2019).

### **5.1.5 Mosquitocidal Liquid Vaporizer Machine**

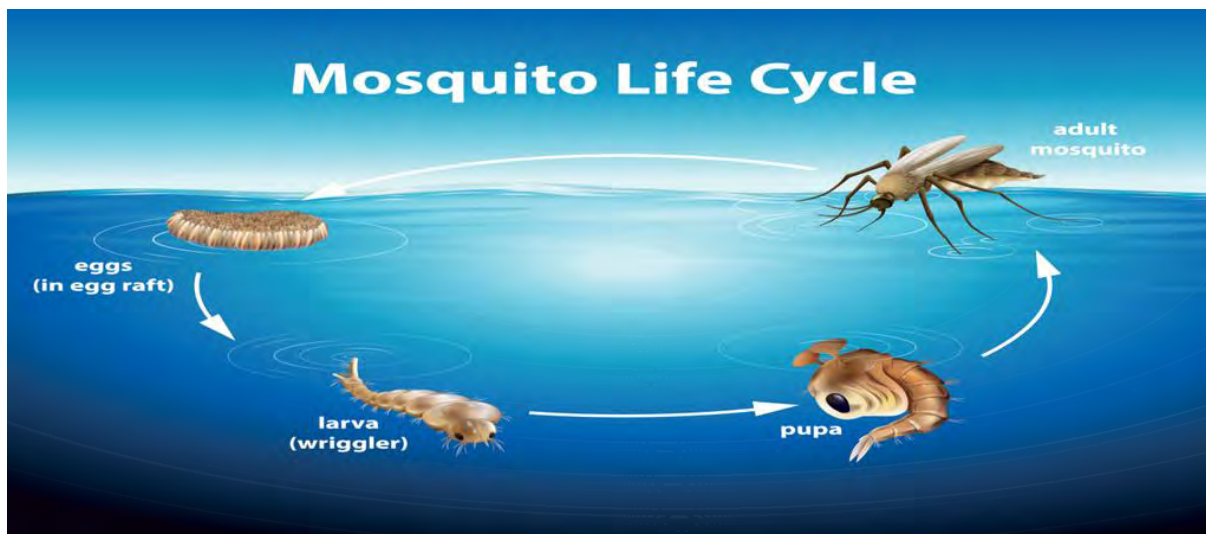
Liquid vaporizer machine evaporates the liquid poisonous substance which kills the mosquitos. The mosquitos that present inside the house are killed by these poisons. Liquid poisonous substances are very effective for mosquitos that are hiding inside the house.

### **5.1.6 Mosquito Repellent Cream**

The term repel means dislodge or impede. Mosquito repellent effectively prevents the mosquitoes from biting someone and infecting them by the dengue virus. The U.S. army first developed the repellents in 1946 and it was registered for application by people in 1957. One of the main ingredients that are used in mosquito repellents are DEET, Allethrin, N,N-diethyl benzamide and dimethyl phthalate. DEET's chemical name is N,N-diethyl-meta-toluamide (Das et al., 2011). It is widely used as the main ingredient of mosquito repellent and repels the mosquitoes to bite someone. Repellent has a unique smell, which prevents the mosquitoes from biting any person. It directly applied over the skin and after smelling the odor of the repellent the mosquitos flew away. Prallethrin (formulation 1.6% w/w vaporized liquid) is another chemical which is used as repellent and effectively prevents mosquito bites (Mittal et al., 2011). Recently Japan invented a very effective and cost friendly repellent which costs only 1.8 USD. Japanese mosquito repellent may curb dengue fever uptick in Southeast Asia: Japanese company kao invented Biore Guard mosquito repellent which potentially controls the spread of dengue fever. It makes a texture that mosquito finds intolerable. The bugs flew away upon landing. It reduces the chance of transmission. This is different from conventional repellents and blocks the insect sense of smell.

### 5.1.7 Larvivorous Fish

Larvivorous fish is a kind of fish that eat the larva of mosquitoes as their food. These fish can be an excellent way to control the mosquito population. Mosquitoes lay their eggs in water and the eggs convert and form larvae. Few fish like *Poecilia reticulata* or *Gambusia affinis* eat the larva of the mosquito as their food, which helps to control the mosquito population. Larva is eaten by the fish and mosquitos can't grow and mature (Tyagnes et al., 2021).



**Figure 7:** Mosquito life cycle, Mosquito.buzz.com, (2022)

Female mosquito lays eggs in water which flows in water. eggs hatch in water and form larvae. Larvae hatch in water, swim and survive in there and after a few days they take organic matter from water as food and reach mature steps pupa. pupa present in the deeper part of water. they don't take any food to survive. In this stage larvae grow and mature to form adult mosquitoes. Larvivorous fish eat eggs, larva and pupa as food. For this reason mosquito growth is controlled (Sayono et al., 2023).



### **5.1.8 Wear Protective Cloths**

Long cloths can provide good protection against mosquitos. Mosquitoes can bite through thin clothing and fabrics. Gauge, polyester, spandex these cloths should be avoided because these cloths are thin and mosquitos can easily bite people. Heavy fabric cloths can prevent mosquitoes from biting our skin. Clothes containing thick fabrics can easily prevent mosquito bites. Furthermore, tightly fitting clothes should be avoided because mosquitoes can bite through them very easily. To prevent mosquito bites, loose cloths and thick fabrics are the best option (Oleniacz, 2021).

### **5.1.9 Live in Well Air Conditions and a Well Screened House**

The more the temperature, the higher the chance of finding mosquitoes because they are cold blooded. Most of the mosquitoes exhibit their best function at 80 degree F and become tired and lethargic at 60 degree Fahrenheit (F) (Central Mass Mosquito Control Project, 2021). This data proves that if any person stays in a comparatively cooler temperature, the person might not be infected by dengue. Most of the air conditioned rooms are cooler during summer days which successfully suppress mosquito activity. In addition to that, air conditioned houses require closing all the doors and windows which prevent mosquitoes from flying into the house. The entrance way is blocked. Inside air does not directly pass inside and mosquitoes can't enter inside the home.

## **5.2 Long Term**

### **5.2.1 Policy Making**

Dengue has now become so serious which can't be eradicated overnight. Strict law and policy can be a huge precursor to make a strong shield to fight against dengue. Government can make policies which must be strictly followed by the people. Countries like Singapore have already made strict laws to fight against dengue. They made strict laws to control mosquitoes breeding which also include punishment protocol for those who don't follow the law under the act of Control of Vectors and Pesticides Act (CVPA, 2002). In Singapore, if any yard, premises and corridor are identified as such a place where mosquitoes can breed easily or mosquito larva is found the person will give a fine up to \$5000 or the person might be imprisoned for three months or both punishments might be applicable. Additionally, if any person's yard is found with the perfect place for mosquito breeding, the person will issue a fine and the court will send notice through email about which action they will take if the person does not take action against the mosquito breeding site. Other countries of south Asia should also follow the same procedure and make strict laws to control the mosquito vector breeding.

### **5.2.2 People Awareness:**

Public awareness is one of the main precursors which can successfully prevent dengue. As a sentient and aware person of the society we need to identify what is bad for us and need to gather knowledge about our threats accordingly. Dengue is one of the rapidly spreading endemic in south Asia. For this reason, people in every society must be aware about it and do the necessary precautions accordingly.

The necessary precautions might include using mosquito nets, mosquito spray which kill mosquitoes, electric mosquito bat, using anti-mosquito cream etc.

### **5.2.3 Long Term Health Hygiene**

Health hygiene is a huge precursor which can play a key role to prevent dengue in longer versions. Not being able to maintain health hygiene is being the main cause of dengue endemic in the Southeast Asian region. Health related knowledge is very important which can effectively control dengue. Health hygiene includes proper waste disposal, unused drums and container disposal, breeding ground of mosquito destruction, managing accumulated water on a regular basis, use of repellents and permethrin, wearing long sleeve clothing, staying in an air conditioned room etc (Wong et al., 2015).

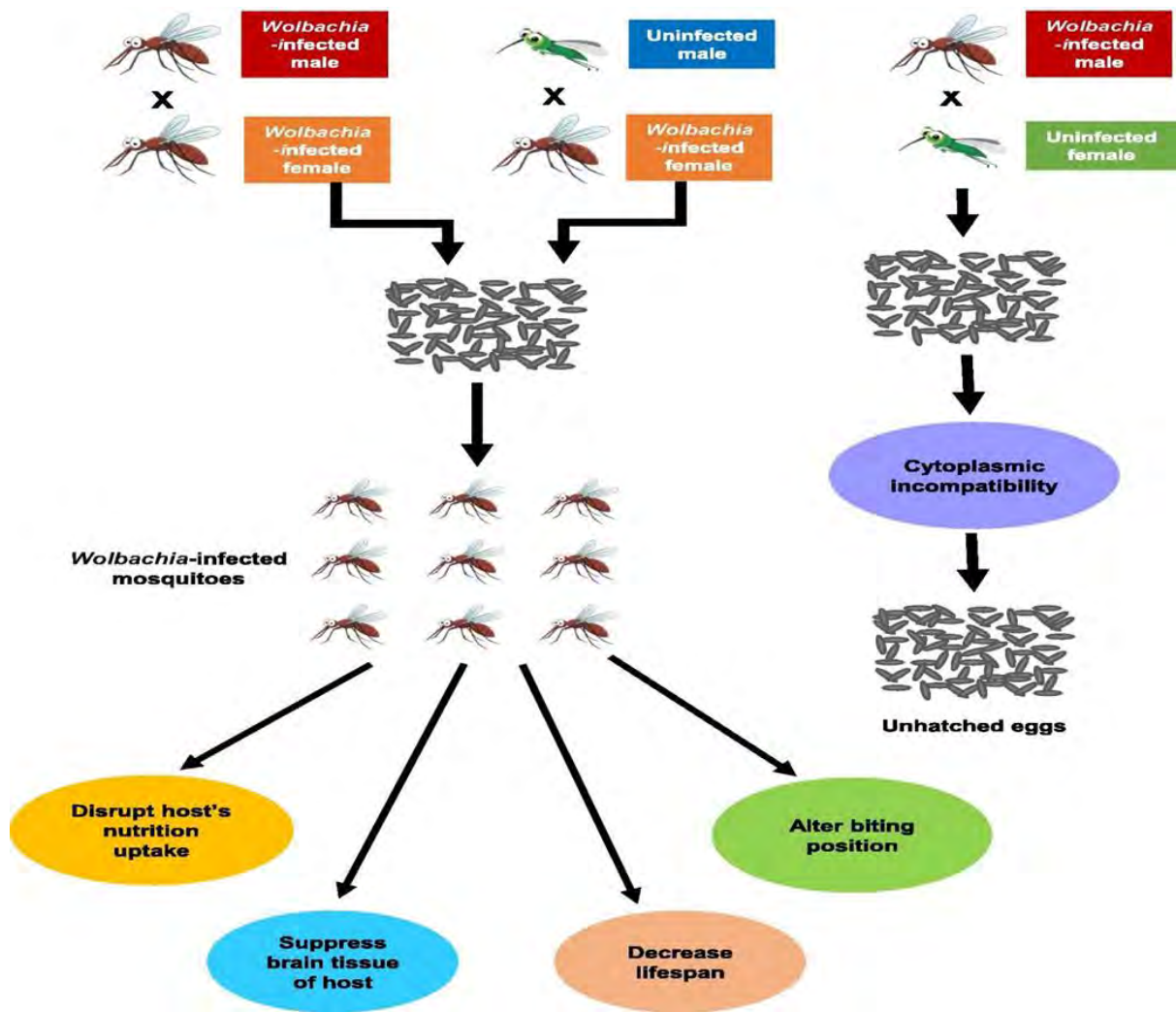
### **5.2.4 Non-Capricious Government:**

Eccentric government management system plays a huge role for the spreading of dengue. Especially in south Asia most of the people are not aware about political issues and political leaders can do whatever they want. For example in Bangladesh it is found that normal insecticides become resistant to *Aedes* mosquitos. After knowing that, the news wasn't published in the media because it was the election year (Das et al., 2023). South Asian countries became the perfect breeding ground for the mosquitos because of the irresponsible act of the government. Unregulated and unplanned high rise buildings, drums and tires that contain stagnant water, uncontrolled waste management that include polybags and others that block the water flow and make perfect environments for mosquito growth, all of these are main precursors for dengue mosquitoes to lay eggs and enlarge their population.

Government not takes proper action for unplanned urbanization, proper waste disposal system, or organized city planning committee. Furthermore, the government is not investing enough money to control the vector of dengue virus born mosquitos or invention of new insecticides. Capricious behavior often found among those people who are related to health services and government bodies. These factors triggered the suspicious breakthrough of dengue.

#### **5.2.5 Use Infectious Symbiotic Bacteria to Kill Mosquitoes**

*Aedes aegypti* is the mosquito, which transmit the dengue endemic in more than hundreds of countries. Using bacterial infection, such as Wolbachia, vector population can be controlled significantly. Wolbachia is a symbiotic bacterium which can reduce the transmission of dengue virus. Wolbachia bacteria can manipulate and alter the reproductive system of host mosquitos which are potential hosts of dengue virus. Male mosquitos are infected with Wolbachia bacteria and they are released to the environment. If these infected male come close to those female mates, the female mosquito can't lay eggs and no larvae will emerge (Guruprasad et al., 2014). Furthermore it is found that the dengue virus replication process is also inhibited by the Wolbachia bacteria and the mosquitos are no longer able to transmit dengue virus. Mosquitoes infect people with dengue virus via their saliva. Wolbachia delayed the production of the infectious saliva. For this reason infectious saliva production rates are tampered and mosquitos can't transmit the virus via their saliva effectively (Fox et al., 2023).



**Source:** Importance of Wolbachia-mediated biocontrol to reduce dengue in Bangladesh and other dengue-endemic developing countries (Debashish. et. al 2023)

**Figure 8:** Transmission of and mechanisms of Wolbachia viral control.

### 5.2.6 Community-Based Vector Control

Local community people participation is key precursor which can effectively control the dengue viral vector transmission. Local community people can identify the potential mosquito breeding site and they can eliminate these breeding sites. Elimination of the breeding site can eventually control the mosquito population in the community.

### **5.2.7 National Vector-Control Policy**

National vector control policy should be provided and strictly maintained for every Southeast Asian country. Main vector control strategies like environmental strategy, chemical strategy, biological strategy and mechanical strategy should be clearly defined under the act of the government and any deviation to fulfill the act should be penalized. How the combination of the main vector control policy will be functioned should also be stated clearly.

### **5.2.8 Coordinated Dengue Outbreak Mitigation Guidelines:**

Mitigation guideline is very important specially, during the outbreak of any endemic or pandemic (Kumar et al., 2023). Mitigation guidelines should be detailed and clearly instructed with the direction of the role of the society people. When an outbreak occurs everyone should stay home, wear protective clothes, close windows, use mosquito net daytime all these guidelines should be applied and generalized for the people so that they can handle the situation and don't panic during endemic weather.

### **5.2.9 Reduce Mosquito Habitat**

Mosquitos normally lay eggs in stagnant water. During the rainy season water accumulates here and there and people use water for other work which accumulates in many places. Mosquitos lay eggs in that stagnant water and their breeding takes place. If people are able to change the habitat of the mosquitos by eliminating excess water which accumulates, they can reduce the mosquito breeding site. By cleaning containers once a week, covering containers and water tanks, and applying insecticides on stagnant water, we can alter mosquito habitat and reduce their breeding habitat (Koishy, 2023).

## Chapter 6

### Therapeutics

#### 6.1. Prevention

##### 6.1.1 Vaccine

Dengue vaccine is a kind of vaccine that is able to effectively kill or inactivate the dengue virus. Scientists have been trying to develop an effective vaccine against dengue since 1920. Although it is very difficult to cure all different serotypes (DENV1, DENV2, DENV3, DENV4 and also 5) of dengue, as of 2023 two commercially available vaccines sold under brand name Dengvaxia and Qdenga (Scott et al.,2013).

Dengue vaccines can be made in two ways.

1. Replicated viral vaccine (Non-replicating virus)
2. Live attenuated viral vaccine

Replicated viral vaccines can be made of viruses attenuated by cell culture, viruses attenuated by mutagenesis and chimeric live viruses. Live attenuated viral vaccines are made of inactivated virus, Recombinant subunit protein, DNA vaccine, Vectored vaccine and virus like particles vaccine. Viruses are weakened by using enzyme or other toxoid component and they are converted into vaccine. The weakened virus pushes into patients body and produce strong immune response against the existed virus present in body. Dengvaxia and Qdenga have got market approved by FDA and MHRA and get approval for use in many countries. Other available vaccines are also showing satisfactory result in their Phase i, ii, iii trials.

### **6.1.2 Dengvaxia**

Dengvaxia is a live attenuated vaccine which is also known as CYD-TDV (chimeric yellow fever virus - DENV tetravalent dengue vaccine). Dengvaxia vaccine is prepared from yellow fever virus. Four subtype of CYD virus (CYD1, CYD2, CYD3 and CYD4) are taken and their pre membrane sequence and envelope protein sequence are replaced by Dengue virus serotypes (DENV1, DENV2, DENV3, DENV4) respectively. Supernatant Vero cells are cultured in African green monkey's kidneys and they are separated, purified, filtered and diluted to make stabilized vaccines. This vaccine does not contain any preservatives and in the final stage it is lyophilized. It is a recombinant vaccine and it has shown very satisfactory and effective efficacy against symptomatic dengue disease. Dengvaxia was first licensed in Mexico and other 11 countries in 2015. Following that incident, Dengvaxia was approved by the EU (European Union) in 2018 and in 2019, USFDA (United States Food and Drug Administration) approved the vaccine and it is certified that it will be medically used in the USA. Previously in 2016, 11 countries including Thailand, Philippines, Singapore, Indonesia, Brazil, Paraguay, Peru, Mexico, El Salvador, Costa Rica etc. commercially approved this vaccine. Study has been performed among the 9-16 years old dengue infected patients to show the efficacy of the vaccine (Smith et al., 2023). For hospitalized patients it shows 79% efficacy, the patients who have virologically confirmed dengue the vaccine show 82% efficacy and for severe dengue patients it shows 84% efficacy. Dengvaxia generally gives protection for the patient who has been affected by the dengue previously. This vaccine is only approved for seropositive patients, patients who have a documented history of being affected by dengue fever. It exhibits protection against dengue for 6 years or more after completing all three doses. Studies are still going on to improve the vaccine to provide more intense immunity for a longer period of time (Prompetchara et al., 2020).



### **6.1.3 Qdenga/ TAK-003**

This vaccine was originally developed by a University located in Bangkok named Mahidol University and TAK-003 and Inviragan (DENVax) funded them. Qdenga is a recombinant vaccine. It is a live attenuated chimeric vaccine. In 2022, Qdenga was first approved in Indonesia and the vaccine was intended to be used for 6 to 45 year old aged people (Torres et al., 2022). In 2021, EMA (European Medical Agency) approved marketing approval of TAK-003 (Qdenga) outside the European union. In 2022, the EU (European Union) approved the vaccine for people aged 4 years and above. In Thailand, Brazil, Argentina, UK (United Kingdom), Indonesia this vaccine also got their marketing approval. Takeda Pharmaceutical manufactured the vaccine and sold it under the brand name Qdenga. The backbone of this vaccine is serotype 2 of the dengue virus. It is a live attenuated vaccine. Dengue virus serotype II is collected and after that it is attenuated or weakened and pushed to the affected person's body. Patient immunity modifies this serotype and exhibits strong immunity against dengue. Qdenga is not administered for previously dengue affected patients, it is designed for patients with no previous history of dengue. This vaccine produced a sustained immune response by producing antibodies against all four serotypes of dengue virus strains. However, it exhibits the most efficacious immune response for DENV2 serotype. For DENV1, DENV3 and DENV4, it produces less number of antibodies and shows moderate efficacy. For symptomatic dengue fever it shows satisfactory success. It is a subcutaneous vaccine and it has two doses which are administered after 3 months prior to one another (Huang et al., 2021).

There are other vaccines that are showing promising results in their clinical trial. One of them is TV003.

### 6.1.4 TV003/TV005

NIAID (National institute of Allergy and infectious disease) developed this vaccine and the vaccines immunogenicity and safety were tested separately. Phase 1 and Phase 2 clinical trials are performed in many countries including Bangladesh, India, Thailand, Brazil and USA. The National Institute of Health (NIH) performed phase 1 and 2 clinical trials on over 1000 participants in the USA. Phase 3 trials have been performed in Brazil and India. Vabiotech, A Vietnam Company is planning to test safety and clinical trials in collaboration with three other companies from different countries. They named the vaccine TetraVax-DV vaccine and conducted their function in collaboration with NIH (Smith et al., 2023).

	<b>CYD-TDV (Dengvaxia) (Sanofi Pasteur)</b>	<b>TAK-003 (Tadeca Pharmaceutical)</b>	<b>TV003/TV005/NIH</b>
<b>License</b>	December 2015	2022	Not yet
<b>Phase 3</b>	Completed 5 years observation	Stage 1, 2 and 3 completed and published	Recruitment Closed, Phase 3 trial results not yet published
<b>Study region of phase 3 trial</b>	10 countries in Asia and Latin America	8 countries in Asia and Latin America	Brazil
<b>Age range of phase 3 study participants</b>	2-16	4-16	2-59
<b>Doses</b>	3 doses(6 months apart) but label change is imminent for doses only	2 doses (3 months apart)	1 dose
<b>Backbone</b>	Yellow fever	DENV2	Full genome of DENV 1, 3 and 4
<b>Dengue non-structural protein</b>	Not present in the vaccine construct	DENV2	DENV 1, DENV3 and DENV4

**Source:** Dengue vaccine development by the year 2020: challenges and prospects, (Smith et al., 2023)

**Table 3:** Comparison of the 3 leading tetravalent live-attenuated dengue vaccine candidate

(Note: Little information of this table was updated later on.)

## **6.2. Therapies**

### **6.2.1 Medications**

There is no such medication invented till now that can treat the dengue completely. However, take plenty of fluids, take bed rest and if body pain and fever is not in tolerable range take antipyretic and analgesic agents such as acetaminophen, also called paracetamol. Acetaminophen lowers the body temperature, which eventually lowers the fever. However, for pain relief, no pain killer such as Ibuprofen, Aspirin or any other class of NSAIDS drug must be avoided. These drugs have anticoagulant properties which can eventually increase the internal bleeding chance (Might also cause thrombocytopenia) for dengue patients. Supportive care is the key precursor to fight effectively against dengue (Das et al., 2022).

Other health complications of the dengue affected patients like depression, insomnia, mania can be effectively treated by antipsychotic and antidepressant drugs. Because of low family income, thought of threatening his life or many reasons, the dengue affected can suffer from these complexities. Prolong depression can be effectively treated by duloxetine 40 mg daily dose. Benzodiazepine, antipsychotic or combination of both can be used as mood stabilizer and successfully used to treat manic depression (Elavia et al., 2023).

Low dose antipsychotics are effective to treat problems related to psychosis. Lorazepam 4 mg per day, clozapine low dose used to treat patients with psychiatric comorbidity and psychiatric syndrome. Valproic acid or sodium valproate has been used effectively as an antimanic and mood stabilizer for the last 10 years. Patients suffering from both dengue and epilepsy can be treated by gabapentin, vigabatrin, and Tigabine. Lithium containing drugs control the energy production and effectively work as mood stabilizer (Dinakaran et al., 2022).

Antibiotics can work only against bacterial infection, so during dengue antibiotic use is ineffective. However to prevent the secondary infection, sometimes doctors prescribe few antibiotics. Antibiotics are proven to reduce hospitalization time for patients. Points need to mention that antibiotics should only be prescribed by a doctor based on the patient's physical condition.

### **6.2.2 Supplements**

One of the most vital symptoms which increase the dengue viral fever mortality rate is Dengue Shock Syndrome (DSS). If the patient affected by DSS is not treated within 12 to 24 hours, the patient might die. All the patients who suffer from dengue shock syndrome and 30% patients who have dengue non-shock syndrome need to administer IV fluid therapy, which is basically a 0.9% saline solution (Hung et al., 2012). They hydrate the patient body and make the electrolytic imbalance of the patients back to normal, maintain isotonic intercellular and intracellular environment. Patients can also take electrolyte water and grapefruit, coconut water and orange juice. These fruit juices can also provide a good amount of vitamin C along with the minerals and micronutrients, which eventually increase the vessel wall strength and decrease bleeding chance in dengue. Vitamin C boosts immunity and helps to heal the wounds (Rajapakse, 2011).

During Dengue, platelet counts decrease drastically. To recover from the low platelet count situation, blood transfusion is one of the most effective methods. The blood injection is administered to the patients. That injection allows quick platelet recovery and increases platelet count. Most of the dengue cases are mild and can be gotten rid very easily after taking rest and plenty of fluids. However, many patients suffer from serious symptoms like sudden drop of platelet level because of deterioration in body platelet count and Hemorrhagic fever (Sudulagunta et al., 2016).

### **6.2.3 Foods**

Platelets or thrombocytes are sponge tissue like substances, which are produced from bone marrow, form clot and stop our bleeding caused by any internal or external wounds. For healthy adults, normal platelet level is 1.5 lakhs to 4 lakhs which can decrease drastically (Makroo et al., 2007). To avoid the decrease of the low platelet count, iron supplement and iron containing food is necessary along with vitaminB12, Vitamin C, omega-3 fatty acid. Furthermore, blood transfusion is effective to increase platelet level. Foods that contain high amounts of proteins like eggs, fish, poultry are essential for repairing damaged tissue of dengue affected people. Fried, Spicy, fatty and salty food along with caffeine and alcohol needs to be avoided.

For speedy recovery from dengue coconut water, pomegranate, turmeric, papaya leaves, and oranges can be taken to get fast recovery from dengue. Papaya leaves elevate the platelet level for dengue patients, which is very crucial in dengue. Turmeric boosts our body metabolism and it is also a potent antiseptic. Turmeric can be mixed with milk for more synergistic effect. Citrus fruits like lemon, orange etc. are filled with vitamin C and antioxidants which is essential for fast recovery.

#### **6.2.4 Effective Prevention Procedure**

**1. Taking Plenty of Fluids:** During fever, Dengue patients might suffer from vomiting, sweating and which might cause dehydration. Water consumption helps to eliminate toxic substances from the body, intrigue proper organ function and maintain body water balance. Water and coconut water both are essential to balance electrolyte level and heal dengue.

**2. Taking Food with Proper Nutrients:** A person who has strong immunity, will be able to strongly fight back and recover from dengue. Antioxidants, Vitamins (Vitamin A, B, C, K) and minerals is our body's building block and helps to boost immunity.

**3. Protein:** Protein repairs our damaged tissue, helps to heal them and repair them. Amino acid is essential for our body and exhibits many functions like immunity, cell repair, production of new blood cells etc.

**4. Omega-3-Fatty Acids:** Foods containing omega-3-fatty acids facilitate our body healing process by mitigating the inflammation. Sea fishes like sardines and salmon are good sources of omega-3-fatty acid along with cod liver oil.

**5. Iron:** Iron is an essential trace element for the body and an important element for the body to fight against disease. Iron binds with oxygen and forms oxy-hemoglobin, which is essential for sufficient oxygen supply throughout our body. Beans, meats, spinach, egg, and lentils are good sources of iron (Parthib, 2019).

**6. Avoid Junk Food:** Oily food, junk food and processed foods needs to be avoided. These foods are not able to give proper nutrients to our body to fight against dengue. Because of fever the amount of food consumption has already lessened. If the person starts taking junk food, the person's body won't get enough nutrients to heal from dengue. The food list should be prioritized to provide nutritional foods and avoid junk foods.

**7. Papaya:** It is rich with vitamin C, Potassium, Vitamin A, folic acid and antioxidants. It has wound healing capabilities. In addition to that, the fiber that is present in papaya helps in the digestive tract, control proper bowel movement and prevent constipation.

**8. Take Frequent Meals:** Taking meals 5-6 times a day can be very effective for dengue patients. Vomiting can be avoided by applying the strategy of taking small amounts of meals within short intervals (Narayana, 2023).

**9. Take Food that is Easy to Digest:** Dengue patients suffer from sweating and vomiting. For this reason the amount of fluid extraction from the body is high. Food that has a higher liquid portion is preferred to restore body fluid balance like soups, steam rice, soft vegetable, juice etc.

**10. Give Preference to Fruits:** Fruits are filled with vitamins and essential trace elements and minerals. Pomegranate, papaya, guava, dates, and apricots are good sources of iron and other nutrients which help to increase platelet level in blood. Pomegranate is a good source of Vitamin C and has an antimicrobial effect because of the presence of flavonoid polyphenols. Guava contains vitamin C. kiwi has potassium, folic acid, Vitamin C, E and K which helps to maintain electrolyte and platelet balance.

## **Chapter 7**

### **Situation Analysis and Recommendation**

#### **7.1. Outcome of the Analysis:**

The environment of south Asian countries is hot and humid. During summer the tropical area and forests are heavily flooded by a lot of rain water. The rain water and the humidity act as a blessing for mosquitoes to breed abnormally high rates in these subtropical regions. Water accumulated in those areas and mosquitoes lay eggs and enlarged their population. Additionally, South Asian countries are highly populated. The dense population causes the greater risk and they unconsciously make the perfect mosquito breeding site. Poor water management, improper knowledge about mosquito breeding habitat, lack of consciousness and education make things more complicated. Furthermore, due to the poor economic condition the government can't take proper initiative. Government inadvertence and negligence along with the poor economic structure makes things worse. Poor garbage management, improper waste disposal system, poor water distribution habits, unplanned construction and urbanization, no guidelines for waste disposal systems by industries are main barriers to not being able to control the outbreak properly. Poor health facilities in hospitals and lack of proper funding in the healthcare system, is a huge barrier to not being able to control the dengue pandemic. Inadequate vector control measures, lack of proper research from the health ministry is also responsible for increasing the mosquito population. The promising fact is, via little awareness, taking self-ministerial, maintaining proper diet is enough to prevent the viral fever. Furthermore, invention and utilization of new promising vaccines are linings for the people of this endemic region. Little more sensible behavior from the people and government parties is required to strongly inhibit the outbreak of dengue in southeast regions.



## **7.2. Possible Future Initiative:**

Dengue severity is not something that can be stopped overnight. The combined efforts of the government and the people living in the community, is the key precursor to stop the rapid spreading of dengue. Government should focus more on the upcoming technologies to control the vector and breeding site of mosquitos. Results have shown that few insecticides and pesticides show resistance and become ineffective to kill the mosquito larvae. Updated research and innovation needs to be started from the health ministry of the south Asian countries. Some south Asian countries introduce vaccines for effective prevention of dengue. Singapore has already introduced the dengue vaccine and introduced this programme as a part of effective dengue prevention procedure. Furthermore, symbiotic bacteria wolbachia have been introduced in Singapore, which effectively prevent the breeding capability of mosquitoes and reduce the lifespan of mosquitoes. WHO provides support to strengthen surveillance and boost the laboratory capacity in Bangladesh and other south Asian countries.

To sum up, I can conclude that, by following proper initiative, developing research and health facilities, developing updated insecticides and vaccine dengue severity can be lessened and nullified. Public awareness and safety is very essential to stop the rapid dengue growthy. Government should make strict laws to control the mosquito vector and if someone violates any law the person needs to be penalized. by maintaining all above initiatives dengue severity can be neutralized in a sensible amount.

## **Chapter 8**

### **Limitations of the Projects**

While undertaking my review article project, several limitations were aroused. First of all, the scope of available literature was limited. The limited knowledge potentially leads to gaps in the understanding of the topic. Additionally, the quality and reliability of the sources reviewed can vary, affecting the overall credibility of the review. Moreover, selection and interpretation of the collected information that were taken from the source can be biased and the conclusion of the review article might not be impressive for every readers. Furthermore, if further studies perform after completion my study, some of my information will be outdated. Lastly, the depth, breadth and quality of my articles completely influence by the expertise and perspective of the authors. For this reason, this lacks creative writing and only speaks about already existing things. Meta-analysis is not performed while doing review article, and this is the reason that lacks the quality of the writing.

## **Chapter 9**

### **Conclusion**

In South Asian countries frequent outbreaks of dengues are occurred due to lack of awareness of people, poor vector control, and inadequate health infrastructure. In this region the public are not aware of this risk which is associated with dengue. Besides, they do not take appropriate initiatives from dengue fever. Additionally, the government health infrastructure is inadequate in those areas. For example, the medical supply shortage and the personnel not properly trained. The poor vector control such as insufficient insecticide use that allows the mosquitos to grow faster and spread the virus which leads to frequent outbreaks of dengue (Urmi et al., 2023). Taking multiple initiatives can reduce the population of mosquitoes as well as the spread of dengue virus. For example, destroy the breeding sites of mosquitoes, improve the sanitation system, remove the stagnant water, dispose of the garbage properly, increase the use of mosquito nets, and anti mosquito cream. Besides the sufficient use of insecticides to control mosquitoes. But nowadays these techniques can not give the proper solution to kill mosquitos. Sometimes they become insecticides resistant. There are some solutions to overcome this problem such as improving the insecticides that can target the specific sites of the mosquitos that can destroy their birth disability, carbon dioxide based mosquito traps are used which attract the mosquitoes, and environmental friendly plant based insecticides are used to prevent the spread of mosquito.

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