International Journal of Research in Engineering, Science and Management
Volume 4, Issue 7, July 2021
https://www.ijresm.com | ISSN (Online): 2581-5792

A Literature Review on Dengue

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***Abstract*: Dengue fever is a viral infection spread through mosquitoes. Every year, roughly 20 million people in tropical and subtropical regions are infected with the dengue virus. The Aedes aegypti mosquito transmits the disease, which is caused by either of the four dengue viruses (DENV 1-4). They are closely related serotypes. Dengue fever symptoms include a high fever, a severe headache, and significant pain behind the eyes that is noticeable when moving the eyes three to 15 days after being bitten by a mosquito. Other symptoms include joint discomfort, muscle and bone pain, a rash, and minor bleeding. Low back discomfort is a common complaint among those who have been afflicted. There is no specific medication or treatment for dengue fever. If a patient suspects they have dengue fever, headache, or joint pain, then over-the-counter pain medicines should be taken.**

***Keywords*: Dengue, Dengue fever, Virus, Aedes Aegypti, Disease spread, Treatment of dengue.**

1. Introduction

Dengue fever is a mosquito-borne viral infection that can be found in tropical and subtropical climates all over the world, primarily in urban and semi-urban regions. The global burden of dengue is large; an estimated 50 million infections per year occur across approximately 100 countries, with potential for further spread. The spread of efficient mosquito vectors across most of the tropical and subtropical world has been the cause of the establishment of dengue as a public health issue. The mosquito vector, the urban-adapted Aedes aegypti, has spread rapidly across tropical and subtropical latitudes.

It originated in Africa during the slave trade from the 15th to the 19th centuries, expanded to Asia through commercial exchanges in the 18th and 19th centuries, and has now spread globally with greater travel and trade in the last 50 years. The spread of eggs and juvenile forms of these arboviral vectors into new territories is assumed to be aided by globalisation of trade, namely the exchange of tires from used vehicles.

Dengue fever is caused by a virus from the Flaviviridae family. There are four different serotypes of the virus that cause dengue fever (DENV-1, DENV-2, DENV-3 and DENV-4).

Dengue fever symptoms often occur four to seven days after the initial infection. In many cases, the symptoms will be minor. It's possible that they'll be mistaken for the flu or other contagious disorders. Young children and people who have never been sick may have a milder infection than older children and adults. Symptoms can occur up to seven days after being bitten by the virus-carrying mosquito. They are as follows: high temperature extreme, headache, discomfort behind the eyes, vomiting and feeling sick, hurting muscles and joints, recurring body rash. Dengue fever can lead to a more deadly form of the disease known as dengue haemorrhagic fever in a small percentage of people.

There is no specific treatment for dengue fever other than supportive measures and cautious hydration therapy. Clinical trials have investigated a range of therapy methods with various degrees of success during the previous 50 years.

2. Disease Spread

A. Overview

In the tropics and subtropics, dengue fever (DF) and dengue haemorrhagic fever (DHF) are becoming more common public health issues. Dengue fever has been identified in over 100 nations, with a population of 2.5 billion people living in places where the disease is endemic. The disease is endemic in the Americas, Southeast Asia (SEAR), the Western Pacific (WPR), Africa, and the Eastern Mediterranean, with the three first regions bearing the greatest disease burden.

Depending on epidemic activity, an estimated 50–100 million cases of DF and several hundred thousand cases of DHF occur each year. Annually, between 250 000–500 000 cases of DHF are officially reported; however, the exact incidence is unknown. Dengue and DHF cases totalled 12 million in 1998, with 3442 deaths reported to the World Health Organization. In Asian countries, case fatality rates range from 0.5% to 3.5%. Dengue fever has become more common in endemic locations in recent years, particularly in the American region (AMR); nevertheless, in the last three years, the case fatality rate has been higher in Southeast Asia and the western Pacific regions.

Since 2000, epidemic dengue fever has spread to new locations and intensified in already impacted areas. Dengue fever was reported in eight countries in 2003: Bangladesh, India, Indonesia, Maldives, Myanmar, Sri Lanka, Thailand, and Timor-Leste. Bhutan's first dengue outbreak was recorded in 2004. In 2005, the World Health Organization's Global Outbreak Alert and Response Network (GOARN) responded to an outbreak in Timor-Leste that had a high case-fatality rate (3.55 percent). For the first time in November 2006, Nepal reported indigenous dengue fever cases. The Democratic People's Republic of Korea is the only country in the South-East Asia region where indigenous dengue fever has not been reported.

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More than 30 countries in the Americas reported a total of 4 332 731 dengue cases between 2001 and 2007. 106 037 cases of dengue haemorrhagic fever (DHF) were reported within the same time period. Between 2001 and 2007, 1299 people died from dengue fever, with a DHF case fatality rate of 1.2 percent. Dengue virus serotypes DEN-1, DEN-2, DEN-3, and DEN-4 are all present in the area. During this time, all four serotypes were found concurrently in Barbados, Colombia, Dominican Republic, El Salvador, Guatemala, French Guyana, Mexico, Peru, Puerto Rico, and Venezuela.

Dengue fever does not naturally occur in continental Europe, although the conditions are favourable for transmission, and the danger of transmission is increasing (e.g., establishment of Ae. albopictus mosquito and viraemic travellers). Due to a lack of surveillance data and cases and outbreaks not reported to WHO12, the incidence of dengue fever in Africa is mainly unknown. Since 1980, however, epidemic dengue fever caused by all four serotypes has been confirmed throughout Africa, with occasional instances reported in 22 countries. In limited serologic investigations, a high prevalence of dengue virus antibodies suggests endemic dengue virus infection in many places of Africa.

3. Transmission of Dengue

A. Overview

Dengue viruses are transmitted to humans by mosquito bites from infected Aedes species (Ae. aegypti or Ae. albopictus). The mosquitoes that spread the Zika and Chikungunya viruses are the same ones. Mosquitoes lay their eggs in containers that store water, such as buckets, bowls, animal dishes, flower pots, and vases, near standing water. These mosquitoes prefer to bite people and can be found both indoors and outdoors in close proximity to humans.

B. Vector ecology

The various serotypes of the dengue virus is spread to via bites from infected Aedes mosquitos, primarily Aedes aegypti. Although Aedes aegypti is now found in metropolitan areas across Africa, Asia, Australia, the South Pacific, the Americas, and portions of the Middle East, the species is thought to have originated in Africa. It is not an exaggeration to suggest that the life cycle of Aedes aegypti is entirely reliant on human-created surroundings. Around human habitations, larvae breed in a variety of artificial containers such as jars, abandoned cans, flower vases, cement tanks, ant traps, old tyres, and plastic buckets.

Furthermore, the species likes dark, wet areas for blood feeding and resting. The indoors and urban locations appear to be preferred by the Aedes aegypti rather than the outdoors and suburban/rural areas. As a result, the species is common in the indoors and urban areas in tropical nations, and its close connection with humans plays a significant role in the effective transmission of dengue viruses. Furthermore, because it is highly anthropophilic, bites multiple times before completing oogenesis, Aedes aegypti is one of the most efficient vectors for arboviruses.

Aedes albopictus, commonly known as the Asian tiger mosquito, can also spread dengue fever viruses. Aedes albopictus is found in and around forested areas near residences. Like Ae. Aegypti, the immature forms of the Asian tiger mosquito can be found in artificial containers that hold stagnant water, such as Tires, flower pots, , buckets, tin cans, clogged rain gutters, etc. Because these mosquitoes can breed in almost any water-filled container, they can become highly widespread and unpleasant, even in areas where mosquitoes are generally scarce.

Aedes albopictus is a very adaptable species. Its geographic distribution is partly owing to its ability to tolerate cooler temperatures as an egg and adult. In a small number of outbreaks, where Aedes aegypti is either absent or present in low numbers, Aedes albopictus has been identified as the predominant DENV vector.

C. Transmission of the virus

The virus's primary amplification host is humans. Female mosquitoes ingest the dengue virus that is circulating in the blood of viraemic people, during feeding. The virus replicates in the mosquito midgut after it feeds on a DENV-infected person. Subsequently, the virus spreads to secondary tissues, such as the salivary glands. The time between ingesting the virus and transmission to a new host is called the extrinsic incubation period (EIP), which lasts 8-12 days. The virus can be spread to other persons while probing or feeding after this extrinsic incubation period. Environmental factors, particularly ambient temperature, influence the extrinsic incubation period. The mosquito is then infectious for the rest of its life.

Virus transmission dynamics can be influenced by a variety of factors, including environmental and climate factors, host-pathogen interactions, and population immunological characteristics. Climate has a direct impact on the biology of vectors, as well as their number and dispersion, making it a key determinant of vector-borne disease outbreaks. Thus Dengue fever transmission is influenced by factors such as climate.

4. Dengue Viruses

A. Overview

Viruses are microscopic agents that can infect a wide range of living creatures, such as bacteria, plants, and animals. Dengue virus is a small structure that can only replicate inside a host organism, like other viruses. Dengue viruses (DENVs) comprise the dengue complex, In the genus Flavivirus, family Flaviviridae which consists of four antigenically related but distinct DENV serotypes (DENV-1, DENV-2, DENV-2, DENV-3, and DENV-4). DENV can produce a variety of symptoms, including asymptomatic dengue infection, dengue fever (DF), dengue haemorrhagic fever (DHF), and dengue shock syndrome (DSS).

B. Serotypes

Dengue fever is caused by a virus from the Flaviviridae family. There are four different serotypes of the virus that cause dengue fever (DENV-1, DENV-2, DENV-3 and DENV-4).

These four viruses are known as serotypes because they interact differently with antibodies found in human blood serum. Although the four dengue viruses are genetically similar (they share about 65 percent of their genomes), there is substantial genetic variation even within a single serotype.

Both DEN-1 and DEN-2 were discovered in Central America and Africa in the 1970s, and all four serotypes were found in Southeast Asia. However, by 2004, the four serotypes' geographical distribution had spread widely. Now, all four dengue serotypes are found in tropical and subtropical places around the world. The four dengue serotypes all exist in the same geographical and biological niche.

C. Dengue Virus Structure

The dengue virus has a roughly spherical shape with a diameter of 50 nm (1 nm equals one millionth of a millimetre). The nucleocapsid, a structure made up of the viral DNA and C (capsid) proteins, is the virus's core. The nucleocapsid is encased in a membrane known as the viral envelope, which is a lipid bilayer derived from the host. This lipid bilayer consists of 180 copies of the E (envelope) protein and M (membrane) protein.

5. Symptoms of Dengue

A. Overview

The primary symptoms of dengue fever develop three to 15 days after a mosquito bite and include a high fever and a strong headache, as well as significant pain behind the eyes that is noticeable when moving the eyes. Joint pain, muscle and bone pain, a rash, and slight bleeding are some of the other symptoms. Low back discomfort is a common complaint among those who have been afflicted.

In a symptomatic dengue infection, there is an incubation period of up to 2 weeks (commonly 5–7 days) after an infectious mosquito bite, after which the individual develops symptoms suddenly and the illness is divided into three phases: an initial febrile phase, a critical phase starting around 4–5 days after the onset of the fever when complications may develop, and a spontaneous recovery phase.

The febrile phase usually lasts 3–7 days during which the patient develops a high temperature (39°C–40°C) that is accompanied by nonspecific constitutional symptoms such as headache, nausea, vomiting, myalgia, and joint pain. Other common symptoms include changed taste sensations, colicky belly pain, constipation or diarrhoea, and dysuria are all common symptoms. Cough, sore throat, and rhinorrhoea are all other common symptoms.

The critical period begins around day 3–6 of sickness and lasts 48–72 hours. During this stage of the illness, a variety of systemic issues may arise. An unexplained "vasculopathy," in which a rise in vascular permeability causes capillary leakage syndrome, is the most feared consequence. In a small percentage of instances, severe plasma losses result in potentially lethal hypovolemic shock (severe blood loss that renders the heart unable to pump blood).

In some cases, Dengue infection can lead to a more deadly form of the disease called Dengue Haemorrhagic fever or DHF. Dengue haemorrhagic fever begins with the normal dengue signs and symptoms listed above. The fever might continue anywhere between two and seven days. Following the onset of the fever, symptoms related to increased permeability of the capillary blood vessels appear. Severe abdominal discomfort, continuous vomiting, and breathing difficulties are all possible symptoms.

A secondary infection with a different virus serotype causes severe dengue. Increased vascular permeability, combined with cardiac dysfunction and dehydration, can lead to shock and multiorgan failure. The onset of dengue shock can be dramatic, and the disease's course can be unrelenting.

If the patient does not develop any fatal complications, or does not experience DHF or DSS, recovery is likely to occur. The recovery phase occurs around Days 6–8 of Illness, this phase begins. The increased vascular permeability and impaired haemostasis are just temporary and normally go away after 48–72 hours. However, adults may endure extended convalescence, with symptoms such as extreme weariness, asthenia, and depression persisting for several weeks following recovery. Hair loss has also been noted during convalescence. Specific organ dysfunction (e.g., hepatic failure or myocarditis) can last for weeks after the vasculopathy has resolved.

6. Diagnosis and Treatment of Dengue

A. Diagnosis of Dengue

1) Overview

Because the body's immunological response to the virus is dynamic and complex, dengue fever is usually diagnosed using a combination of blood tests. Laboratory tests include Molecular testing for dengue virus (PCR) which detect the presence of the virus itself. These tests can diagnose dengue fever up to 7 days after the onset of symptoms and can be used to determine which of the four dengue virus serotypes is causing the infection. IgM and IgG antibody tests detect antibodies produced by the immune system after a person has been exposed to a virus. These tests are most efficient if performed at least 4 days following infection.

Molecular testing (polymerase chain reaction, PCR) detects dengue virus genetic material in blood within the first week after symptoms (fever) manifest and can be used to determine which of the four serotypes is causing the infection. RT–PCR assays are sensitive in general, but they necessitate specialised equipment and technical training for those doing the test, therefore they are not always available in all medical facilities. RT–PCR results from clinical samples can be used to genotype the virus, allowing for comparisons with virus samples from different geographical locations.

Antibody tests are primarily used to diagnose a current or recent infection. They look for IgG and IgM antibodies, which are produced by the body in response to a dengue fever infection. Because the body's immune system creates different quantities of antibodies over the course of a disease, a diagnosis may require a combination of these tests.

IgM antibodies are the first to be generated, and tests for these should be done at least 7-10 days after exposure. For a few weeks, levels in the blood increase, then gradually decline. IgM antibodies are no longer detectable after a few months. In response to an infection, IgG antibodies are generated more slowly. With an acute infection, the level of IgG usually rises, stabilises, and then persists for a long time. Individuals who have been exposed to the virus before the present infection have a higher amount of IgG antibodies in their blood, which can impact how diagnostic results are interpreted.

Complete blood counts (CBCs) are used to check for low platelet counts, which are common in the later stages of the illness, as well as to detect changes in haemoglobin, haematocrit, and red blood cell (RBC) count (evidence of anaemia) caused by blood loss from severe dengue fever. A basic metabolic panel (BMP) is used to check kidney function and look for signs of dehydration, which can happen when someone is sick.

7. Treatment of Dengue

A. Overview

Dengue fever does not have a specific therapy. Fever reducers and painkillers can be used to treat muscle aches and pains as well as fever. For severe dengue, medical care provided by physicians and nurses who are familiar with the symptoms and development of the disease can save lives, lowering fatality rates from more than 20% to less than 1%. The patient's bodily fluid volume must be maintained during severe dengue treatment. Patients with dengue fever should seek medical help as soon as symptoms arise.

Other than supportive measures and judicious hydration therapy, there is no specific treatment for dengue fever. Over the last 50 years, clinical trials have evaluated a variety of therapy options with varying degrees of success. Dengue fever has a relatively short danger phase, or so-called "critical period," during which the patient's condition may rapidly deteriorate. It lasts 48–72 hours. The chances of a fatal outcome are slim if the patient is properly handled throughout this stage. Even so, fluid management must be closely monitored and frequently reviewed. In simple dengue fever, there are no long-term consequences if the patient recovers (rare complications of dengue, such as orchitis, oophoritis, keratitis, and encephalitis, can have a long-term impact in a small minority of cases).

During the febrile phase, a large amount of oral fluid should be given, as well as antipyretic treatment with paracetamol as needed. Nonsteroidal anti-inflammatory medicines (NSAIDs) should be avoided as well. If the patient has easy access to a nearby health care institution, he or she can be handled at home with daily full blood counts. Excessive vomiting or diarrhoea that causes dehydration, severe prostration, or early bleeding symptoms are all signs that one should be admitted to the hospital and monitored closely.

In the case of a severe infection, there are no clear strategies for predicting outcome and advancement. The mainstay of management is careful fluid management and supportive therapy. Corticosteroids and intravenous immunoglobulins have been shown to be ineffective. There hasn't been any evidence that a specific therapy improves survival.

8. Dengue Vaccine

A. Overview

The first licenced dengue vaccine is CYD-TDV. It was first approved in Mexico in December 2015 for use in people aged 9 to 45 who live in endemic areas, and it has since been approved in 20 countries. Sanofi Pasteur developed CYD-TDV, a live recombinant tetravalent dengue vaccine that is given in a three-dose series every 0/6/12 months.

Dengvaxia® (CYD-TDV) was approved by regulatory bodies in 20 countries in December 2015. The findings of an additional investigation to identify serostatus at the time of immunisation were disclosed in November 2017. When compared to unvaccinated participants, the subset of trial participants who were inferred to be seronegative at the time of initial immunisation had a greater risk of more severe dengue and hospitalizations from dengue. As a result, the vaccine is intended for those aged 9 to 45 who live in endemic areas and have previously experienced at least one documented dengue virus infection.

Dengvaxia® was authorised by the US Food and Drug Administration (FDA) in May 2019 for use in children aged 9 to 16 years who have had a past laboratory-confirmed dengue virus infection and who live in a dengue-endemic area (common).

9. Conclusion

Dengue fever (DF) is a vector-borne disease caused by four dengue viruses (DENV 1–4) that are closely related.20 It is caused by the Aedes aegypti mosquito, and the Aedes albopictus mosquito.4 Dengue is common in most tropical and subtropical areas, where populations of A. aegypti and A. albopictus are widespread. The 4 viruses that cause dengue are closely related serotypes from the family Flaviviridae. The symptoms of dengue fever usually appear four to seven days after the initial infection. Symptoms will be minimal in many cases. They could be confused for flu or other illness symptoms. In young children and people who have never been infected the illness may be milder, than in older children and adults.4 Common symptoms include vomiting and nausea, rashes and pains and aches (eye pain, typically behind the eyes, muscle, joint, or bone pain). In the case of dengue fever, plenty of fluids should be taken, along with paracetamol to relieve pain. However, in certain cases (usually if the patient has had dengue previously), severe dengue may occur. It may cause shock, internal haemorrhage, and even death. The only treatment is fluid therapy. However, there is a vaccine, known as Dengvaxia, produced by Sanofi Pasteur. It is intended for those aged 9 to 45 who live in endemic areas and have previously experienced at least one documented dengue virus infection.

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