Acta Scientific MICROBIOLOGY (ISSN: 2581-3226)

Volume 5 Issue 6 June 2022

Literature Review

Dengue Fever Epidemiology, Pathogenesis, Prevention and Control in Ethiopia

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DOI: 10.31080/ASMI.2022.05.1079

Received: September 17, 2020

Published: May 18, 2022

Abstract

Dengue fever is a mosquito born viral disease emerging as a global public health threat in many parts of the world. Dengue is among one of the arbo-viral diseases, included in the list of neglected tropical diseases, recommended by World Health Organization. Dengue fever remains to be a major health problem in tropical and subtropical areas. In Ethiopia, Dengue Fever is a newly emerged disease since 2013. Starting from 2014 to 2016 dengue fever outbreak was reported from different part of Ethiopia. Even though the outbreak was reported, the outbreak data was not well documented and recorded, which is very significant for the epidemiological and health information provision as a cornerstone for the health care systems to make possible preventive and curative measures for the coming dengue fever outbreak. An early diagnosis of dengue infection is very important in the management of the disease. Ethiopia, thrive the scope of the existing Malaria Control Program to include Vector-Borne Diseases; initiate dengue and other arboviral diseases surveillance by establishing sentinel sites at health centers and hospitals in the most affected areas of Dire Dawa, Afar and Somali Regions. There is no specific antibiotic (drug) for the treatment dengue fever. Dengvaxia® (CYD-TDV), was the first dengue vaccine, developed by Sanofi and has now been approved by regulatory authorities in 20 countries for use in endemic settings in persons ranging from 9-45 years of age. For dengue fever and sever dengue fever, an experienced physicians and nurses who can give medical care with the effects and progression of the disease can decreasing mortality rates and save lives.

Keywords: Dengue Fever; Dengue Epidemiology; Pathogenesis; Vector; Ethiopia

Introduction

Dengue is a viral disease which has rapidly spread in all regions of the World Health Organization (WHO) in recent years. Dengue virus is transmitted by mosquitoes of *Aedes* species mainly of the *Aedes aegypti* and *Aedes albopictus.* Many arboviral diseases like chikungunya, yellow fever and Zika infection are also transmits by this mosquito. Dengue is widespread throughout the tropics, with local variations in risk influenced by rainfall, temperature and unplanned rapid urbanization [1].

Dengue is a major viral disease which has negative impact worldwide and the most rapidly spread vector borne diseases and [2]. An arthropod-borne flavivirus is the main cause of Dengue, and is currently endemic in several countries worldwide [3,4].

Dengue infection is by one of the four dengue virus serotypes (DENV1, DENV2, DENV3 and DENV4) by the bite of Aedes mosquitoes. World widely, Dengue virus now infects ~230 million people each year, with an estimated 3.6 billion people living in areas

of risk. Dengue fever (DF), more severe dengue hemorrhagic fever (DHF), and life-threatening dengue shock syndrome (DSS) are all diseases symptom which can be caused dengue infection [5,6].

Dengue infections to be classified as either a primary or secondary infection or either a recent or old infection depending on improvements in laboratory tests al. Primary dengue infection is defined as the first experience of a human host with dengue virus and can manifest in one of three clinical forms. In the majority of patients, it presents as an undifferentiated febrile illness, with cold-like symptoms. Other patients develop severe body pain and high fever, which is classic dengue fever. The remaining patients experience a severe form of dengue presenting as dengue hemorrhagic fever (DHF) or dengue shock syndrome. Secondary dengue is defined as contracting dengue virus after an initial exposure and symptoms, and carries an enhanced risk of DHF/DSS/severe dengue fever due to cross-immunity reaction [7,8].

Dengue is a mosquito-borne infection that recently emerged as a major international Public health problem. The disease is endemic in many tropical and sub-tropical regions around the world, predominantly in urban and semi-urban areas. Dengue fever is a severe flu-likes infection which can affect people of all ages, but seldom causes death. Its clinical features vary according to the age of the patient. Infants and young children may have a fever with rash. Older children and adults may have either a mild fever or the classical incapacitating disease with abrupt onset of high fever, severe headache, pain behind the eyes, muscle and joint pains, and rash. Dengue hemorrhagic fever is another severe manifestation of the disease that has potentially lethal complications. In such cases, patients may die within 12 to 24 hours after suffering circulatory failure and a state of shock. Dengue was first recognized in the 1950s during dengue epidemics in the Philippines and Thailand, dengue hemorrhagic fever today affects most Asian countries and is a leading cause of hospitalization and death among children in the region. There are four distinct, but closely related, viruses that cause dengue. Recovery from infection by one provides lifelong immunity against that virus but confers only partial and transient protection against subsequent infection by the other three viruses. There is enough evidence that sequential infection increases the risk of developing dengue hemorrhagic fever [9].

In 2018, many Asian countries like Bangladesh, Cambodia, India, Myanmar, Malaysia Pakistan, Philippines, Thailand, and Yemen were reported dengue [1].

Literature Review

Dengue fever remains a major public health problem in tropical and subtropical areas. In terms of morbidity, mortality and economic costs Dengue fever is the most significant emerging arboviral disease in the world By threatening more than 2.5 billion people world widely dengue fever is endemic in Africa, the Americas, eastern Mediterranean, South-East Asia, and the Western Pacific. 50-100 million estimated dengue infections occur each year. Though outbreaks of DF/DHF are poorly documented in Africa, infections were also reported from eastern Africa [9-11].

Pathogenesis of dengue virus

Dengue viruses are members the family Flaviviridae of the genus Flavivirus. There are 4 dengue virus serotypes (DEN-1, DEN-2, DEN-3 and DEN-4), all of which circulate globally, circulation of all 4 serotypes were reported from most endemic countries in recent years [12].

Flaviviruses are single stranded RNA viruses, lipid-enveloped and positive-sense. The structural pre-membrane (prM) and envelope (E) proteins are embedded in the lipid envelope and are displayed on the surface of virions. The 4 DEN serotypes share only about 60%-75% identity at the amino acid level, and are therefore distinct viruses. Upon human inoculation, the virus replicates in local dendritic cells. Subsequent entry into macrophages and activation of lymphocytes is followed by entry into the bloodstream. Dengue viruses primarily infect cells of the myeloid lineage, including macrophages, monocytes, and dendritic cells. There is evidence of infection of hepatocytes and endothelial cells. Haematogenous spread is the likely mechanism for seeding of peripheral organs and the occasionally reported infection of the central nervous system [13].

Dengue virus infection in humans is often clinically indistinguishable and in apparent), but can lead to a wide range of clinical manifestations, from mild fever to potentially fatal dengue shock syndrome [14]. Though outbreaks of DF/DHF are poorly documented in Africa, some eastern Africa countries were reported dengue infections [10].

Factors influencing the emergence of dengue

Despite the overlapping of factors identified, various studies hypothesized general factors to explain the reasons for the emergence of dengue. Firstly, unplanned urbanization

and increased international travel in combination with vector distribution were assumed to result in extensive transmission of dengue virus in Africa. Secondly, urban poverty and minimal capacities for surveillance and control measures remain important precipitating factors of dengue transmission in regions with favorable climate. Thirdly, increases in poor, urban populations, break down in public health measures, especially vector control programs, trade, and environmental disturbances [5].

Adequate evidences are as well available to show the effect of climate change on the global trends of vector borne diseases. Similar to other vector-borne diseases, transmission of the dengue virus is sensitive to climate. For instance, humidity, temperature and rainfall affect the biting rate, breeding cycle and survival of the mosquito vectors (principally *Ae. aegypti*). Higher ambient temperatures favor increase the frequency of blood meals, rapid development of the vector and reduce the extrinsic incubation period. A short incubation period increases the opportunities for virus transmission during the life Time of an infected mosquito. If the ambient temperature is too low, mosquitoes are unlikely to survive long enough to become infectious and pass on dengue. During the past century, surface temperatures have increased by a global average of 0.75°C. Temperature increases of this magnitude may be associated with substantial increases in dengue epidemic potential [15,16].

Classification of dengue virus as per WHO guidelines

The World Health Organization's 2009 classification divides dengue fever into two groups: uncomplicated and severe. This replaces the 1997 WHO classification, which needed to be simplified as it had been found to be too restrictive, though the older classification is still widely used including by the World Health Organization's Regional Office for South-East Asia as of 2011. Severe dengue is defined as that associated with severe bleeding, severe organ dysfunction, or severe plasma leakage while all other cases are uncomplicated [9].

The 1997 classification divided dengue into undifferentiated fever, dengue fever, and dengue hemorrhagic fever. Dengue hemorrhagic fever was subdivided further into grades I-IV. Grade I is the presence only of easy bruising or a positive tourniquet test in someone with fever, grade II is the presence of spontaneous bleeding into the skin and elsewhere, grade III is the clinical evidence of shock, and grade IV is shock so severe that blood pressure and pulse cannot be detected. Grades III and IV are referred to as "dengue shock syndrome" [17].

In a small proportion of cases, the disease develops into the life-threatening dengue hemorrhagic fever, resulting in bleeding, low levels of blood platelets and blood plasma leakage, or into dengue shock syndrome, where dangerously low blood pressure occurs [18].

Dengue in Ethiopia

Dengue is one of the arbor-viral diseases considered or suspected to be endemic in Ethiopia. Although dengue was first reported from Wollo, Hararghe and Addis Ababa during the 1940s by Italian physicians; the identification of the viruses causing dengue fever syndromes in human was identified done during and since 1960-62, yellow fever epidemic). It was in the past, from 1975 to 1996 that Ethiopia was considered as dengue endemic since 1975 to 1996 with other countries [19].

In Ethiopia, considerable but incompletely documented numbers of arboviral diseases are endemic. However, infections remain under reported due to lack of laboratory facilities and inaccessibility of some of the endemic areas. The disease was reported between 1985 to 1987 in refugees around Hargeysa in Somali. In Dire Dawa, 9258 people were suspected of dengue fever (DF) and, of these, 40 were confirmed as dengue fever cases in 2013 [20].

It is estimated that more than 390 million dengue virus (DENV) infections occur every year, and it is endemic across more than 100 countries (Figure 1), including 34 countries in Africa (Figure 2). In Ethiopia, there were no reports of DENV prior to 2013, but the virus has emerged in multiple regions since. Studies have also indicated that there are many febrile illnesses of unknown causes in Ethiopia, many of which may be attributed to DENV. In the new work, Getachew F., *et al.* of the University of Gondar, Ethiopia, and colleagues performed a cross-sectional study of all febrile patients visiting Metema and Humera hospitals in Northwest Ethiopia between March 2016 and May 2017. Blood samples from each patient were tested for anti-DENV and risk factors for the virus were assessed of 600 blood samples tested, the overall prevalence of anti-DENV detected was 33.3%, with slightly higher

rates in Metema (40%) compared to Humera (27.5%) (Getachew F., *et al.* 2018).Furthermore, the overall prevalence of IgM and IgG antibodies against DENV infection was 19% and 21% respectively. The highest prevalence of antibodies was found in the spring and summer, with a peak in August. Residence, occupation, the presence of uncovered water, and lack of mosquito net use were all associated with DENV infection or antibody status. This study showed that the presence of antibodies against DENV infection indicates dengue as one of the causes of undifferentiated febrile illness in the study areas, suggesting prevention and control measures should be designed considering the risk factors identified in the study [21].

At the end of 2013, in Dire Dawa, 9258 people were suspected of dengue fever (DF) and, of these, 40 were confirmed as dengue fever cases (Ethiopia Humanitarian Bulletin, unpublished data). The dengue fever that occurred in Dire Dawa varied from mild to severe with symptoms of sudden onset of fever which lasted for 2-3 days (extended to 4-5 days in some cases), headache (typically located behind the eyes), mild to severe muscle and joint pains (general body pain in some cases), feeling cold, and arthritis-like symptoms/pain (Getachew D., *et al.* 2015). Nose bleeding and vomiting were also reported in few cases. Some of the patients were also hospitalized. According to the preliminary information gathered from some of the recovered patients, it was mentioned that they lose their appetites and feel weak especially after recovery [21].

Dengue occurred in eastern Ethiopia. Thus, since 2013, Ethiopia has reported more than 12 000 dengue fever cases to the World Health Organization Most African countries lack such established reporting mechanisms and only sporadic outbreaks and individual case reports have been documented. In addition, the frequently non-specific clinical presentation of dengue may be difficult to distinguish from the myriad other infectious diseases present in Africa, since dengue diagnostic assays are not widely available. Thus, the burden of dengue remains largely unknown in Africa [22].

Figure 1: Global geographic distribution of DEN viruses [23].

In Ethiopia, DF was diagnosed only among travelers that return to countries to which dengue was not endemic but never reported as occurring locally and it is also not included among the lists of national reportable diseases. On September 12, 2013 Dire Dawa town administration health bureau reported non malaria febrile cases of unknown etiology. All the cases were examined for malaria parasites by microscopy by health centers in one of malaria parasites while the patients were sick. The number of cases had grown and even doubled over the weeks. The regional health bureau carried out an outbreak investigation, but they could not identify the source and the underlying agent by local capacity and therefore requested the national team for further investigation. Hence, the current investigation was carried out to identify and determine the etiology, source and magnitude of the outbreak that can be used to design control and prevention measures [22].

Figure 2: Dengue risk in Africa and the Middle East [24].

Life cycle of dengue parasite and the dengue vector

The *Ae. aegypti* mosquito is the primary vector of dengue. The virus is transmitted to humans through the bites of infected female mosquitoes. After virus incubation for 4-10 days, an infected mosquito is capable of transmitting the virus for the rest of its life. Infected symptomatic or asymptomatic humans are the main carriers and multipliers of the virus, serving as a source of the virus for uninfected mosquitoes. Patients who are already infected with the dengue virus can transmit the infection (for 4-5 days; maximum 12) via Aedes mosquitoes after their first symptoms appear. Like most arboviruses, DENV infect different organs of the mosquito, including the salivary glands and the central nervous system. Mosquito infection elicit behavioral changes including increase of the probing time which lead to host interruption that might lead to wider spread of the virus [25].

The adult *Ae. aegypti* prefers to rest indoors and feed on humans during daylight hours. Its peak biting periods are early in the morning and before dark in the evening. Once contracted the virus, the mosquito remains infected during its entire life and may transmit the virus during blood meals. The viruses are maintained in an *Ae. aegyptihuman - Ae. aegypti* cycle with periodic epidemics. Most females of *Ae. Aegypti* may spend their lifetime in or around the houses where they emerge as adults [9].

The *Ae. aegypti* mosquito lives in urban habitats and breeds mostly in man-made containers. Unlike other mosquitoes *Ae. aegypti* is a day-time feeder, its peak biting periods are early in the morning and in the evening before dusk. Female *Ae. aegypti* bites multiple people during each feeding period. *Ae. albopictus*, a secondary dengue vector in Asia, has spread to North America and more than 25 countries in the European Region, largely due to the international trade in used tyres (a breeding habitat) and other goods (e.g. lucky bamboo). *Ae. albopictus* is highly adaptive and, therefore, can survive in cooler temperate regions of Europe. Its spread is due to its tolerance to temperatures below freezing, hibernation, and ability to shelter in microhabitats. Dengue viruses are primarily maintained in a human to-mosquito-to-human cycle (Figure 3). The primary vector is the *Ae. aegypti* mosquito, which is highly adapted to human habitations. *Ae. albopictus* can also sustain dengue virus transmission in humans. Other species maintain a monkey-mosquito cycle in south-east Asia and western Africa. Dengue virus transmission from non-human primates to humans appears to be rare. The spread of vectors following urbanization and the decline in vector-control efforts has partially contributed to the increased incidence of dengue virus infections. However, dengue is not confined to urban settings and is increasingly reported from rural areas. Additionally, factors such as population growth, globalization and travel, and climate change facilitate increased transmission of dengue viruses. Dengue exhibits substantial temporal and geographic variability [1].

Comparative analysis of the salivary gland transcriptomes of native and DENV-infected *Ae. aegypt*i identified a number of

Figure 3: Route of transmission [26].

differentially expressed genes related to sugar/protein digestion enzymes, immunity related genes and blood meal acquisition enzymes that might have an impact on the efficiency of viral replication or mosquito feeding behavior. This study showed that DENV infection alters the expression of key host-seeking genes in the mosquito's main olfactory organs and the antennae [26].

Diagnosis, control and prevention

Diagnosis

An early and accurate laboratory diagnosis of dengue infection is of paramount importance in the management of the disease. It has been estimated that the number of misdiagnosed dengue cases could reach a record ratio of 50% of all cases, mainly due to a large disparity of dengue signs and symptoms which overlap with the symptoms of other viral infections, especially for persons living in or traveling to endemic areas of tropical infectious diseases. Dengue fever should be distinguished from other illnesses which share similar symptoms such as chikungunya, Mayaro fever, Ross River fever, West Nile fever, Zika fever, yellow fever and viral hemorrhagic fevers [27].

The diagnosis of dengue is typically made clinically, on the basis of reported symptoms and physical examination; this applies especially in endemic areas. However, early disease can be difficult to differentiate from other viral infections. A probable diagnosis is based on the findings of fever plus two of the following: nausea and vomiting, rash, generalized pains, low white blood cell count, positive tourniquet test, or any warning sign in someone who lives in an endemic area. Warning signs typically occur before the onset of severe dengue. The tourniquet test, which is particularly useful in settings where no laboratory investigations are readily available, involves the application of a blood pressure cuff at between the diastolic and systolic pressure for five minutes, followed by the counting of any petechial hemorrhages; a higher number makes a diagnosis of dengue more likely with the cut off being more than 10 to 20 per 1 inch2 (6.25 cm^2) [17].

The earliest change detectable on laboratory investigations is a low white blood cell count, which may then be followed by low platelets and metabolic acidosis. A moderately elevated level of aminotransferase (AST and ALT) from the liver is commonly associated with low platelets and white blood cells. In severe disease, plasma leakage results in hemo-concentration (as indicated by a rising hematocrit) and hypoalbuminemia. Pleural effusions or ascites can be detected by physical examination when large, but the demonstration of fluid on ultrasound may assist in the early identification of dengue shock syndrome. The use of ultrasound is limited by lack of availability in many settings. Dengue shock syndrome is present if pulse pressure drops to ≤ 20 mm of Hg along with peripheral vascular collapse. Peripheral vascular collapse is determined in children via delayed capillary refill, rapid heart rate, or cold extremities. While warning signs are an important aspect for early detection of potential serious disease, the evidence for any specific clinical or laboratory marker is weak [28].

The diagnosis should be considered in anyone who develops a fever within two weeks of being in the tropics or subtropics. It can be difficult to distinguish dengue fever and chikungunya, a similar viral infection that shares many symptoms and occurs in similar parts of the world to dengue. Often, investigations are performed to exclude other conditions that cause similar symptoms, such as malaria, leptospirosis, viral hemorrhagic fever, typhoid fever, meningococcal disease, measles, and influenza. Zika fever also has similar symptoms as dengue [28].

Overall, there is an urgent need to reduce dengue morbidity and mortality by improving the diagnosis and two diagnostic modalities have been applied to detect the disease at an early stage. The first one is a direct method targeting the acute phase of dengue disease, which is based upon detection of genomic RNA by qPCR or soluble NS1 by antigen capture in blood samples from viremic patients. The second is the indirect method that relies on serological tests to detect dengue related immunoglobulin par Mac-ELISA for the capture of specific IgM or indirect ELISA for the capture of anti-DEN IgGs [29].

The diagnosis of dengue fever may be confirmed by microbiological laboratory testing. This can be done by virus isolation in cell cultures, nucleic acid detection by PCR, viral antigen detection (such as for NS1) or specific antibodies (serology).Virus isolation and nucleic acid detection are more accurate than antigen detection, but these tests are not widely available due to their greater cost. Detection of NS1 during the febrile phase of a primary infection may be greater than 90% sensitive however only 60-80% in subsequent infections. All tests may be negative in the early stages of the disease. PCR and viral antigen detection are more accurate in the first seven days. In 2012 a PCR test was introduced that can run on equipment used to diagnose influenza; this is likely to improve access to PCR-based diagnosis [30].

These laboratory tests are only of diagnostic value during the acute phase of the illness with the exception of serology. Tests for dengue virus-specific antibodies, types IgG and IgM, can be useful in confirming a diagnosis in the later stages of the infection. Both IgG and IgM are produced after 5-7 days. The highest levels (titers) of IgM are detected following a primary infection, but IgM is also produced in reinfection. IgM becomes undetectable 30-90 days after a primary infection, but earlier following re-infections. IgG, by contrast, remains detectable for over 60 years and, in the absence of symptoms, is a useful indicator of past infection. After a primary infection, IgG reaches peak levels in the blood after 14-21 days. In subsequent re-infections, levels peak earlier and the titers are usually higher. Both IgG and IgM provide protective immunity to the infecting serotype of the virus. In testing for IgG and IgM antibodies there may be cross-reactivity with other flaviviruses which may result in a false positive after recent infections or vaccinations with yellow fever virus or Japanese encephalitis. The detection of IgG alone is not considered diagnostic unless blood samples are collected 14 days apart and a greater than fourfold increase in levels of specific IgG is detected. In a person with symptoms, the detection of IgM is considered diagnostic [31].

Control and prevention

Ethiopia, expand the scope of the existing Malaria Control Program to include Dengue Fever and other Vector-Borne Diseases; initiate dengue surveillance by establishing sentinel sites at health centers and hospitals in the most affected areas of Dire Dawa, Afar and Somali Regions; strengthen capacity for laboratory diagnosis and case management; develop an integrated vector management strategy and plan of action; establish a coordination mechanism with relevant sectors, including establishment of a multi-sectorial task force; work with partners such as WHO, CDC and AFENET for capacity building in case management, integrated vector management and surveillance; actively engage in Advocacy, communication and social mobilization [9].

Attempts are ongoing to infect the mosquito population with bacteria of the genus Wolbachia, which makes the mosquitoes partially resistant to dengue virus. While artificially induced infection with Wolbachia is effective, it is unclear if naturally acquired infections are protective. Work is still ongoing as of 2015 to determine the best type of Wolbachia to use. Prevention depends on control of and protection from the bites of the mosquito that transmits it. The World Health Organization recommends an Integrated Vector Control program consisting of five elements:

- Advocacy, social mobilization and legislation to ensure that public health bodies and communities are strengthened.
- Collaboration between the health and other sectors (public and private).
- An integrated approach to disease control to maximize use of resources.

- Evidence-based decision making to ensure any interventions are targeted appropriately.
- Capacity-building to ensure an adequate response to the local situation [9].

The primary method of controlling *Ae. aegypti* is by eliminating its habitats. This is done by getting rid of open sources of water, or if this is not possible, by adding insecticides or biological control agents to these areas. Generalized spraying with organophosphate or pyrethroid insecticides, while sometimes done, is not thought to be effective. Reducing open collections of water through environmental modification is the preferred method of control, given the concerns of negative health effects from insecticides and greater logistical difficulties with control agents. People can prevent mosquito bites by wearing clothing that fully covers the skin, using mosquito netting while resting, and/or the application of insect repellent (DEET being the most effective).However, these methods appear not to be sufficiently effective, as the frequency of outbreaks appears to be increasing in some areas, probably due to urbanization increasing the habitat of *Ae. aegypti*. The range of the disease appears to be expanding possibly due to climate change [32].

At present, the main method to control or prevent the transmission of dengue virus is to combat vector mosquitoes through:

- Preventing mosquitoes from accessing egg-laying habitats by environmental management and modification.
- Disposing of solid waste properly and removing artificial man-made habitats.
- Covering, emptying and cleaning of domestic water storage containers on a weekly basis.
- Applying appropriate insecticides to water storage outdoor containers.
- Using of personal household protection such as window screens, long-sleeved clothes, insecticide treated materials, coils and vaporizers.
- Improving community participation and mobilization for sustained vector control.
- Applying insecticides as space spraying during outbreaks as one of the emergency vector- control measures.

Active monitoring and surveillance of vectors should be carried out to determine effectiveness of control interventions. Careful clinical detection and management of dengue patients can significantly reduce mortality rates from severe dengue [1].

Vaccine

The first dengue vaccine, Dengvaxia® (CYD-TDV) developed by Sanofi Pasteur was licensed in December 2015 and has now been approved by regulatory authorities in 20 countries for use in endemic areas in persons ranging from 9-45 years of age. In April 2016, WHO issued a conditional recommendation on the use of the vaccine for areas in which dengue is highly endemic as defined by seroprevalence of 70% or higher. In November 2017, the results of an additional analysis to retrospectively determine serostatus at the time of vaccination were released. The analysis showed that the subset of trial participants who were inferred to be sero-negative at the time of first vaccination had a higher risk of more severe dengue and hospitalizations from dengue compared to unvaccinated participants. The live attenuated dengue vaccine CYD-TDV has been shown in clinical trials to be efficacious and safe in persons who have had a previous dengue virus infection (sero-positive individuals), but carries an increased risk of severe dengue in those who experience their first natural dengue infection after vaccination (sero-negative individuals). For countries considering vaccination as part of their dengue control program, pre-vaccination screening is the recommended strategy. With this strategy, only persons with evidence of a past dengue infection would be vaccinated (based on an antibody test, or on a documented laboratory confirmed dengue infection in the past). Decisions about implementing a pre-vaccination screening strategy will require careful assessment at the country level, including consideration of the sensitivity and specificity of available tests and of local priorities, dengue epidemiology, country-specific dengue hospitalization rates, and affordability of both CYD-TDV and screening tests. Vaccination should be considered as part of an integrated dengue prevention and control strategy. There is an ongoing need to adhere to other disease preventive measures such as well-executed and sustained vector control. Individuals, whether vaccinated or not, should seek prompt medical care if dengue-like symptoms occur [9].

Dengvaxia is based on a weakened combination of the yellow fever virus and each of the four dengue serotypes. Two studies of

a vaccine found to be 60% effective and prevented more than 80 to 90% of severe cases. In 2017, the manufacturer recommended that the vaccine only be used in people who have previously had a dengue infection as otherwise there was evidence it may worsen subsequent infections [2].

There are ongoing programs working on a dengue vaccine to cover all four serotypes. Now that there is a fifth serotype this will need to be factored in. One of the concerns is that a vaccine could increase the risk of severe disease through antibody-dependent enhancement (ADE). The ideal vaccine is safe, effective after one or two injections, covers all serotypes, does not contribute to ADE, is easily transported and stored, and is both affordable and cost-effective [9].

Treatment

There is no specific treatment for dengue fever. For severe dengue, medical care by physicians and nurses experienced with the effects and progression of the disease can save lives - decreasing mortality rates from more than 20% to less than 1%. Maintenance of the patient's body fluid volume is critical to severe dengue care [33].

There are no specific antiviral drugs for dengue; however, maintaining proper fluid balance is important. Treatment depends on the symptoms. Those who are able to drink, are passing urine, have no "warning signs" and are otherwise healthy can be managed at home with daily follow-up and oral rehydration therapy. Those who have other health problems, have "warning signs", or cannot manage regular follow-up should be cared for in hospital. In those with severe dengue care should be provided in an area where there is access to an intensive care unit [26].

Invasive medical procedures such as nasogastric intubation, intramuscular injections and arterial punctures are avoided, in view of the bleeding risk. Paracetamol (acetaminophen) is used for fever and discomfort while NSAIDs such as ibuprofen and aspirin are avoided as they might aggravate the risk of bleeding. Blood transfusion is initiated early in people presenting with unstable vital signs in the face of a decreasing hematocrit, rather than waiting for the hemoglobin concentration to decrease to some predetermined "transfusion trigger" level. Packed red blood cells or whole blood are recommended, while platelets and fresh frozen plasma are usually not. There is not enough evidence to determine if corticosteroids have a positive or negative effect in dengue fever [9].

During the recovery phase intravenous fluids are discontinued to prevent a state of fluid overload. If fluid overload occurs and vital signs are stable, stopping further fluid may be all that is needed. If a person is outside of the critical phase, a loop diuretic such as furosemide may be used to eliminate excess fluid from the circulation [9].

Apart from attempts to control the spread of the Aedes mosquito there are ongoing efforts to develop antiviral drugs that would be used to treat attacks of dengue fever and prevent severe complications. Discovery of the structure of the viral proteins may aid the development of effective drugs. There are several plausible targets. The first approach is inhibition of the viral RNA-dependent RNA polymerase (coded by NS5), which copies the viral genetic material, with nucleoside analogs. Secondly, it may be possible to develop specific inhibitors of the viral protease (coded by NS3), which splices viral proteins. Finally, it may be possible to develop entry inhibitors, which stop the virus entering cells, or inhibitors of the 5′ capping process, which is required for viral replication. Research efforts to prevent and treat dengue include various means of vector control, vaccine development, and antiviral drugs [9].

Conclusion and Recommendation

Dengue fever is a serious public health problem and is newly emerging threat in affected town of Ethiopia. This seminar paper highlights as dengue appearing cyclic every year's mainly affecting adult population of reproductive age group. It also shows the sign of expanding too many part of the country, there is an urgent need to enhance dengue surveillance and control, especially for the high-risk populations in high-risk areas in dengue affected areas of the country. In the absence of vaccination and effective drugs, the only intervention is vector control to contain the current outbreak and ensure prevent future prevention. Environmental management should be undertaken by emphasizing on artificial manmade mosquito breeding sites. To monitor the trend of the disease and point out public health significance, DF needs to be included in the existing disease surveillance system in Ethiopia [34].

The control of most Dengue fever in Ethiopia is in its infancy and mostly underfinanced. The key to control of dengue lies

in understanding the geographical distribution of disease in a given country. Only a few NTDs have been adequately mapped in Ethiopia. This indicates the need for integrated mapping to better understand the distribution of particular diseases and areas of overlap for treatment and control.

Resource mobilization for conducting integrated surveys should be prioritized. Once the mapping is completed and disease distribution is known, cost estimates for the control of common NTDs within Ethiopia will enable resource mobilization and guide donors and partners.

Bibliography

1. WHO. "Dengue and severe dengue". September (2018).
2. WHO. "Global Strategy for Dengue Prevention and Control 2012 - 2020". WHO, Geneva, Switzerland, (2012).
3. Kyle JL and Harris E. "Global spread and persistence of dengue". *Annual Review of Microbiology* 62 (2008): 71-92.
4. Wilder-Smith A., *et al*. "Update on dengue: epidemiology, virus evolution, antiviral drugs, and vaccine development". *Current Infectious Disease Reports* 12.3 (2010): 157-164.
5. Gubler DJ. "The economic burden of dengue". *American Journal of Tropical Medicine and Hygiene* 86.5 (2012): 743-744.
6. Halstead Scott B. "Dengue". London: Imperial College Press, (2008): 180-429.
7. Abdallah TM., *et al*. "Epidemiology of dengue infections in Kassala, Eastern Sudan". *Journal of Medical Virology* 84.3 (2012): 500-503.
8. Malik A., *et al*. "Dengue hemorrhagic fever outbreak in children in Port Sudan". *Journal of Infection and Public Health* 4.1? (2011): 1-6.
9. WHO. "Dengue Guidelines for Diagnosis, Treatment, Prevention and Control (PDF)". Geneva: World Health Organization (2009).
10. Amarasinghe A., *et al*. "Dengue Virus Infection in Africa". *Emerging Infectious Diseases* 17.8 (2011): 1349-1354.
11. Guillena J B., *et al*. "Prevalence of dengue fever (DF) and dengue hemorrhagic fever (DHF): a description and forecasting". in Proceedings of the 11th National Convention on Statistics (NCS '10) (2010): 16.
12. Messina JP., *et al*. "Global spread of dengue virus types: mapping the 70 year history". *Trends in Microbiology* 22.3 (2014): 138-146.
13. Guzman MG., *et al*. "Dengue: a continuing global threat". *Nature Reviews Microbiology* 8 (2010): S7-16.
14. Cameron P Simmons., *et al*. "Dengue: Current concepts (Review article)". *The New England Journal of Medicine* 366.15 (2012): 1423-1432.
15. Van Kleef E., *et al*. "Review: The geographic distribution of dengue fever and the potential influence of global climate change". (2009).
16. Morin CW., *et al*. "Climate and dengue transmission: Evidence and implications". *Environmental Health Perspectives* 121.11,12 (2013).
17. Whitehorn J and Farrar J. "Dengue". *British Medical Bulletin* 95 (2010): 161-173.
18. Kularatne SA. "Dengue fever". *BMJ* 351 (2015): h4661.
19. M Mekonnen and H Kloos. "Yellow fever and other arboviral diseases". in Epidemiology and Ecology of Health and Disease in Ethiopia, Y. Berhane, D.H. Mariam, and H. Kloos, Eds., pp. 635- 645, Shema Books, Addis Ababa, Ethiopia (2006).
20. Dejene Getachew., *et al*. "Breeding Sites of Aedes aegypti: Potential Dengue Vectors in Dire Dawa, East Ethiopia". *Interdisciplinary Perspectives on Infectious Diseases* (2015).
21. Getachew Ferede., *et al*. "A serologic study of dengue in northwest Ethiopia: Suggesting preventive and control measures". *PLOS Neglected Tropical Diseases* 12.5 (2018): e0006430.
22. Were F. "The dengue situation in Africa". *Paediatrics and International Child Health* 32 (2012): 18-21.
23. Centers for Disease Control and Prevention. "National Center for Emerging and Zoonotic Infectious Diseases (NCEZID); Division of Vector-Borne Diseases (DVBD)". (2014): 888-232-634.
24. Jentes., *et al*. "Evidence-based risk assessment and communication: a new global dengue-risk map for travelers and clinicians". *Journal of Travel Medicine* 23.6 (2016).
25. Platt KB., *et al*. "Impact of dengue virus infection on feeding behavior of Aedes aegypti". *American Journal of Tropical Medicine and Hygiene* 57.2 (1997): 119-125.

26. Simmons CP., *et al*. "Dengue". *The New England Journal of Medicine* 366.15 (2012): 1423-1432.

27. Malavige GN., *et al*. "Dengue viral infections". *Postgraduate Medical Journal* 80 (2004): 588-601.

28. Yacoub S and Wills B. "Predicting outcome from dengue". *BMC Medicine* 12.1 (2014): 147.

29. Alcon-LePoder S., *et al*. "Secretion of flaviviral non-structural protein NS1: From diagnosis to pathogenesis". *Novartis Foundation Symposia* 277 (2006): 233-247.

30. New CDC test for dengue approved. Centers for Disease Control and Prevention (2012).

31. Chen LH and Wilson ME. "Dengue and chikungunya infections in travellers". *Current Opinion in Infectious Diseases* 23.5 (2010): 43844.

32. Center for Disease Control and Prevention. "Chapter 5 - dengue fever (DF) and dengue hemorrhagic fever (DHF)". Yellow Book (2010).

33. Brady OJ., *et al*. "Refining theglobal spatial limits of dengue virus transmission by evidence-based consensus". *PLOS Neglected Tropical Diseases* 6 (2012): e1760.

34. Bekele Woyessa., *et al*. "The first acute febrile illness investigation associated with dengue fever in Ethiopia". *Journal of Health Development* 28.3 (2014): 155-161.