

# DENGUE FEVER: ETIOLOGY, DIAGNOSIS, PREVENTION AND TREATMENT

## ABSTRACT

Dengue fever (break-bone fever) is a viral disease transmitted by a species of *Aedes* mosquitos. Dengue fever is caused Dengue virus, a single positive-stranded RNA virus carried by mosquitoes, belonging to the *Flaviviridae* family and genus *Flavivirus*. Most are spread by arthropods (such as mosquitoes or ticks), meaning they are also known as arboviruses (arthropod-borne viruses). Majority of infections are contracted from urban settings. With growth of villages, towns, and cities in locations where it is frequent, as well as greater movement of people, has increased the number of outbreaks and circulation of viruses in recent decades. Dengue, which was once exclusive to Southeast Asia, has now expanded to southern China in East Asia, Pacific Ocean countries. Dengue infections are widespread in various countries across Africa and may be a significant contributor to acute fevers in Nigeria. Clinical manifestation of dengue includes; high fever (40°C/104°F), excruciating headache, eye pain, aches in the muscles and joints, nausea, vomiting, swollen glands, and rash are some of the symptoms. Chronic dengue is more likely to affect people who have already been infected once. The incubation period (the amount of time between exposure and the beginning of symptoms) is typically between 4 and 7 days, but it can be as long as 14 days. If symptoms appear more than 14 days after returning from endemic locations, dengue fever is unlikely to be present in those individuals. intense stomach pain, continuous vomiting, quick breathing, bleeding gums or nose, exhaustion, restlessness, blood in vomit or stool, extreme thirst, pale and chilly skin, and a weak sensation are all severe dengue symptoms that may appear after the fever has subsided. In endemic locations, the screening of dengue is often made clinically, based on the patient's reported symptoms and a physical examination. Tourniquet testing, which involves applying a blood pressure cuff at a pressure between the diastolic and systolic for five minutes, followed by counting any petechial hemorrhages; a higher number increases the likelihood that the patient has dengue, with a cut off of more than 10 to 20 per 1 inch<sup>2</sup> being used as a guide (6.25 cm<sup>2</sup>). Other laboratory methods for dengue screening involves full blood count, cell culture, nucleic acid identification, polymerase chain reaction (PCR), and serology. Microbiological laboratory screening can be employed in the confirmation diagnosis of dengue fever. Control of the vector (mosquito) that spreads the disease and protection from its bites are essential for prevention. Dengvaxia vaccine can also be administered. For treatment, maintaining a healthy fluid balance is crucial as there are no specific antiviral medications for dengue. Dengue fever remains one of the endemic disease in sub-saharan Africa, particularly, in Nigeria. This study is aimed at discussing the current issues of Dengue fever with focus on Nigeria.

**Keywords:** *Dengue, fever, symptoms, virus, Aedes, mosquito, laboratory*

## INTRODUCTION

Dengue fever (break-bone fever) is a viral disease transmitted by a species of *Aedes* mosquitos [1]. It occurs more frequently in tropical and subtropical areas [2]. According to the WHO [2] report, majority of dengue patients are asymptomatic. Yet, those who experience a high temperature, headache, body aches, nausea, and rash are the most typical symptoms. Most people recover within 1 to 2 weeks. Some dengue patients get severe illness and require hospitalization.

Dengue was widespread in more than 120 countries as of 2019 [2]. According to the study conducted by Shepard et al. [3], over 60 million symptomatic infections were reported in 2013; 18% of these led to hospital admissions, and 13,600 people died as a result. Dengue cases are predicted to cost \$9 billion globally [3]. Twelve Southeast Asian nations were expected to have roughly 3 million cases and 6,000 deaths annually throughout the decade of the 2000s [4].

Amarasinghe et al. [5] reported that there have been reports of dengue infection in at least 22 African nations, although it is likely prevalent in all of them, with 20% of the populace at risk. This places dengue among the most widespread vector-borne illness around the globe [6].

The majority of infections are contracted from urban settings [7]. With growth of villages, towns, and cities in locations where it is frequent, as well as greater movement of people, has increased the number of outbreaks and circulation of viruses in recent decades. Dengue, which was once exclusive to Southeast Asia, has now expanded to southern China in East Asia, Pacific Ocean countries, and the Americas according to Gubler [7]. Reiter [8] noted that this could be a danger to Europe. The WHO Territories of Africa, the Americas, the Eastern Mediterranean, South-East Asia, and the Western Pacific are now home to more than 100 nations where the illness is endemic. With Asia accounting for roughly 70% of the global illness load, the Americas, South-East Asia, and Western Pacific are the areas most severely impacted [2]. While serologic evidence showing Dengue infections are widespread in various countries across Africa, the burden of dengue is still relatively poorly reported [9]. According to recent findings, dengue may be a significant contributor to acute fevers in Nigeria [10], despite the fact that many persons who visit medical institutions complaining of fever are administered with an antimalarial drug without further testing. The primary dengue mosquito vectors, *Aedes aegypti* and *Ae. albopictus*, are well documented, and serologic data suggests Dengue virus infections exist in some places [9]. Unfortunately, more thorough and generalizable surveys that would provide data on the incidence of Dengue infection in Nigeria are unavailable [11-13].

Malaria and dengue fever are frequently confused in Nigeria. This might be due to the fact that dengue and malaria both have symptoms that are similar and that malaria is a prevalent endemic disease in the area [14]. According to the study of Chukwuma et al. [15], when the attending clinician sees fit, many feverish individuals in the area are occasionally diagnosed with pyrexia of unknown origin, typhoid fever, or malaria. Even when a test for the malaria parasite is negative or when a patient does not respond to anti-malarial medication, the majority of these patients still lack a diagnosis. According to the aforementioned, dengue patients are frequently mistaken as malaria and go untreated. This has the consequence of creating anti-malaria tolerance in the general population due to the indiscriminate use of anti-malarial drugs [14]. This therefore necessitates for this review on the current level of awareness of the Nigerian populace on Dengue fever.

## **CAUSE**

Dengue fever is caused Dengue virus, a single positive-stranded RNA virus carried by mosquitoes, belonging to the *Flaviviridae* family and genus *Flavivirus* [16]. Yellow fever virus, West Nile virus, Zika virus, Japanese encephalitis virus, tick-borne encephalitis virus, Kyasanur forest disease virus, and Omsk hemorrhagic fever virus are additional relatives of the same genus [17]. According to Howard-Jones et al. [17], since the majority are spread by arthropods (such as mosquitoes or ticks), they are also known as arboviruses (arthropod-borne viruses).

The DNA (genetic material) of dengue virus consists of approximately 11,000 nucleotide bases that code for the three different protein types (C, prM, and E) which make up the viral particles

as well as seven other non-structural protein molecules (NS1, NS2a, NS2b, NS3, NS4a, NS4b, and NS5) that are only present in host's infected cells but are necessary for virus replication [18]. A research carried by Normile [19] reported that there are five different serotypes of the virus, and the first four are known as DENV-1, DENV-2, DENV-3, and DENV-4. In 2013, the fifth strain was revealed [19]. The antigenicity of each serotype is used to distinguish it from the others. [20].

## **SIGNS AND SYMPTOMS**

Studies conducted by Reiter [8] and Whitehorn [21] revealed that most dengue virus infected individuals (80%) are asymptomatic or only experience minor symptoms like a simple fever [8,21]. About 5% of people infected with dengue experience severe more severe illnesses, and only a small percentage of those are life-threatening [21]. The incubation period (the amount of time between exposure and the beginning of symptoms) is typically between four and seven days, but it can be as long as fourteen days [7]. Hence, if symptoms appear more than 14 days after coming home from endemic locations, dengue fever is unlikely to be present in those individuals [22]. Common cold and gastroenteritis-like symptoms have been reported to frequently affect children (vomiting and diarrhea) [23], are more likely to experience serious difficulties noted Simmons et al. [24], although the first few symptoms are typically minor and include a high fever.

Clinical manifestation of dengue includes; high fever (40°C/104°F), excruciating headache, eye pain, aches in the muscles and joints, nausea, vomiting, swollen glands, and rash are some of the symptoms. Chronic dengue is more likely to affect people who have already been infected once [2]. Based on WHO [2] report, intense stomach pain, continuous vomiting, quick breathing, bleeding gums or nose, exhaustion, restlessness, blood in vomit or stool, extreme thirst, pale and chilly skin, and a weak sensation are all severe dengue symptoms that may appear after the fever has subsided. It is important for people to seek professional medical attention right away if they experience these serious symptoms. After recovering, dengue patients may experience fatigue for several weeks.

## **TRANSMISSION**

*Aedes* mosquitoes, especially, *A. aegypti*, are the main carriers of the dengue virus [1-2]. Typically, these mosquitoes inhabit the area between 35° North and 35° South, below an elevation of 1000 meters (3,300 ft) [2]. Although they mainly bite in the morning and the evening, they can bite and spread infection at any time of the day [2]. *Aedes albopictus*, *Aedes polynesiensis*, and *Aedes scutellaris* are other *Aedes* species capable of spreading the disease. The virus's main host are humans [17], although none human primates can play host to the virus also [25]. According to the CDC [26], one bite is enough to spread an infection.

Exposure to contaminated blood, organs, or other tissues can result in bloodborne transmission due to the about 7-day viremia in humans (such as bone marrow) [26]. Moreover, perinatal dengue transmission happens when the woman contracts the disease right before giving birth. In this case, infection happens through microtransfusions after the placenta separates or through mucosal contact with the maternal blood after delivery. No evidence of congenital transmission

has been found. Breast milk may also be a source of dengue virus transmission. There is no proof that it can be passed via sexual intercourse [26].

## **DIAGNOSIS**

### **Physical Examination**

In endemic locations, in particular, the screening of dengue is often made clinically, based on the patient's reported symptoms and a physical examination [21]. Early sickness, however, might be challenging to distinguish from other viral infections [22]. Fever with alongside nausea and vomiting and any of the symptoms, such as, rash, widespread aches, a low white blood cell count, a positive tourniquet test, or any warning sign in a resident of an endemic area, constitutes a probable diagnosis [27].

### **Tourniquet Screening**

The tourniquet testing, which involves applying a blood pressure cuff at a pressure between the diastolic and systolic for five minutes, followed by counting any petechial hemorrhages; a higher number increases the likelihood that the patient has dengue, with a cut off of more than 10 to 20 per 1 inch<sup>2</sup> being used as a guide (6.25 cm<sup>2</sup>) [27].

Simmons [24] reported that, everyone with a fever within two weeks of being in the tropics or subtropics should be diagnosed, according to the condition's official diagnosis. It can be challenging to differentiate between dengue fever and chikungunya, a closely related viral virus that has a number of identical symptoms as dengue and occurs in comparable geographic locations [28]. Testing are frequently carried out to rule out other disorders that have the same symptoms, such as influenza, measles, leptospirosis, viral hemorrhagic fever, typhoid fever, and meningococcal disease [22,27]. Dengue and zika fever symptoms are identical [29].

### **Full Blood Count Testing**

Ranjit [22] noted that, decreased white blood cell count is the initial change that can be identified through laboratory testing; this is followed possibly by a low platelet count and metabolic acidosis. Reduced platelets and white blood cells are frequently correlated with somewhat high levels of the liver's aminotransferases (AST and ALT). [24]. When a disease is chronic, plasma leakage causes hypoalbuminemia and hemoconcentration, as shown by an increasing hematocrit [22]. Physical examination can reveal pleural effusions or ascites when they are substantial [22], however, the presence of fluid on ultrasound can be helpful with the earlier diagnosis of dengue shock syndrome [21]. The inaccessibility of ultrasonography in many circumstances limits its utilization. A study by Simmons [24] showed that if the peripheral vascular collapse occurs and the pulse pressure falls to or below 20 mm Hg, dengue shock syndrome is present. Children's peripheral vascular collapse can be identified by slow capillary refill, a fast heartbeat, or chilled extremities [27]. Whereas early diagnosis of potentially dangerous diseases is aided by warning signs, the proof for any given clinical or laboratory indicator is poor [6].

### **Cell Culture, Nucleic acid Identification, Polymerase Chain Reaction (PCR), and Serology**

Microbiological laboratory screening can be employed in the confirmation diagnosis of dengue fever [27,30]. This is often accomplished through isolation of virus in cell cultures, nucleic acid identification using PCR, viral antigen detection (such as using NS1), or particular antibodies (serology) [27]. However, WHO [27] noted that whereas virus isolation and nucleic acid detection are more precise than antigen detection, these techniques are less frequently used because of their higher costs. The sensitivity of NS1 identification during the febrile stage of an initial infection may be higher than 90%, but only 60-80% in secondary infection [24]. In the initial phases of the illness, all testing might come back negative [18]. In order to obtain accurate results, Polymerase Chain Reaction and viral antigen detection techniques can be employed [24]. A PCR test that can be conducted on equipment used to diagnose influenza was launched in 2012; this is probably going to make PCR-based diagnosis more accessible [31].

With the exception of serology, these laboratory tests are only useful for diagnosis in the acute stage of the illness. In the later stages of the infection, tests for IgG and IgM antibodies specific to the dengue virus can be helpful in confirming a diagnosis. After 5-7 days, both IgG and IgM are created. IgM is created after reinfection but is identified at its maximum levels (titres) after an initial infection. IgM disappears 30 to 90 days after an initial infection, but sooner after subsequent infections. IgG, in contrast, can still be detected after more than 60 years and, in the absence of symptoms, serves as a reliable sign of previous infection. IgG levels in the blood spike 14 to 21 days after an initial infection. Levels peak early and titres are typically higher in future re-infections. IgG and IgM both offer defense against the viral serotype that is invading cells [7, 18, 28]. Simmons [24] reported that with recent infections or immunizations with the yellow fever virus or Japanese encephalitis, there may be cross-reactivity with other flaviviruses in tests for IgG and IgM antibodies, which could lead to a false positive. Until blood samples are taken 14 days apart and a higher than fourfold increase in levels of particular IgG is identified, the detection of IgG alone is not deemed diagnostic. The presence of IgM is regarded as diagnostic in a patient with symptoms [7].

## **PREVENTION**

According to the WHO [27], control of the vector (mosquito) that spreads the disease and protection from its bites are essential for prevention. The World Health Organization (WHO) suggests a five-part integrated vector control approach which includes; ensuring that public health organizations and communities are strengthened through advocacy, social mobilization, and legislation; collaboration between the public and private sectors in the health sector; a coordinated strategy for disease prevention that makes the best use of available resources; and building capacity and using evidence-based decision-making to ensure that any interventions are targeted effectively and appropriately [27].

Eradicating the habitats of *A. aegypti* is the main strategy of management [27]. This is accomplished either by eliminating open water sources or, if that is not practicable, by spraying insecticides or biological control agents on the affected areas. Although it is occasionally done, generalized spraying with organophosphate or pyrethroid insecticides is not believed to be successful [8]. Given the potential harm that pesticides may cause to human health and the greater logistical challenges presented by control agents, reducing open water collections by

environmental change is the preferred way of management [27]. Wearing clothes that completely covers the skin, sleeping with mosquito netting, and/or applying insect repellent are all ways that people can avoid getting bitten by mosquitoes (DEET being the most effective) [26]. Normile [19] reported that the incidence of outbreaks appears to be increasing in some places, most likely as a result of urbanization expanding the habitat of *A. aegypti*. While these steps can be successful at lowering an individual's risk of exposure, they do little to mitigate this trend. Additionally, it seems like the disease is spreading farther, perhaps as a result of climate change [19].

Susie [32] reported that dengue fever vaccine with mixed results went on sale in the Philippines and Indonesia in 2016. Mexico, Brazil, El Salvador, Costa Rica, Singapore, Paraguay, most of Europe, and the United States have all given their approval for its use [33]. Only those with a prior dengue illness or groups where the majority (>80%) of people have been exposed before age 9 are advised to get the vaccination [34]. There is indication that it may exacerbate subsequent infections in people who have never had one [33]. Due to this, even in locations where the disease is prevalent, Prescrire does not deem it appropriate for widespread immunization [35].

The WHO [2] recommends rest, drinking of lots of fluids, use of acetaminophen (paracetamol) for discomfort, avoidance of non-steroidal anti-inflammatory medicines like ibuprofen and aspirin, watching for severe symptoms, and getting in touch with your doctor right immediately as a way to manage dengue infection. Dengvaxia vaccine has so far received approval and licensing in several nations. Nevertheless, this vaccination can only provide protection to people who have a history of dengue infection. There are other dengue vaccine candidates being investigated [2]. According to Guy et al. [36], Dengvaxia vaccine is centered on a weakened mixture of the four serotypes of dengue and the yellow fever virus. The vaccination was 66% successful in studies conducted by Torres [34], preventing more than 80 to 90% of chronic cases. For some people, this is less than ideal noted Pollack [37].

## **TREATMENT**

Although there are no specific antiviral medications for dengue, maintaining a healthy fluid balance is crucial according to Simmons [24]. Symptoms determine the course of treatment [27]. With regular monitoring and oral rehydration therapy, patients who are able to drink, are passing urine, have no "warning signals," and are generally healthy can be treated at home. People who require hospital treatment include those who have additional health issues, exhibit "warning signs," or are incapable of managing routine follow-up [22]. Patients who have chronic dengue cases should receive care in a location with access to an Intensive Care Unit (ICU) [27].

Usually, intravenous hydration is only necessary for one or two days, if at all it is needed [27]. A quick dose of 20 mL/kg is appropriate for children with dengue shock [38]. Following the stabilization of vital signs, normalization of the hematocrit, and a urinary output of 0.5–1 mL/kg/h, the rate of fluid delivery is adjusted [22]. It is advised to use the least amount of fluid necessary to accomplish this [27].

## CONCLUSION

Dengue fever remains one of the endemic disease in sub-saharan Africa, particularly, in Nigeria. It is even of great threat seeing that it shares similar symptoms with malaria and other mosquito borne disease and as a result calls for greater awareness and measures towards it minimum control in the Nigerian nation. Professionals should also be trained and equipped to detect dengue especially when diagnosis do not reflect malaria and sickness persists in a patient.

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