Journal of Namibian Studies, 31 S3 (2022): 924-943 ISSN: 2197-5523 (online)

Deciphering The Global Burden Of Dengue: An In-Depth Look At Transmission Dynamics And Public Health Impact

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Abstract

Dengue fever, a viral infection transmitted by mosquitoes, presents a substantial worldwide public health problem. The incidence of this phenomenon has been consistently rising, propelled by reasons such as the expansion of metropolitan areas, population increase, and changes in climatic patterns. The epidemiology of dengue fever is intricate, characterized by recurring epidemics that are affected by environmental factors and human activity. The disease presents a range of symptoms, ranging from a moderate flu-like sickness to severe consequences including dengue hemorrhagic fever and dengue shock condition, which have the potential to be life-threatening. The diagnosis is based on the patient's symptoms, results from laboratory testing, and serological assays. Treatment mostly involves providing supportive care. Nevertheless, there is currently no targeted treatment available for this particular viral infection, underscoring the need of preventive measures and attempts to reduce the transmission of the virus. Dengue viruses are categorized into four separate serotypes, and immunity acquired by being infected with one serotype may heighten the likelihood of experiencing severe illness when subsequently infected with a different serotype. Efforts to prevent dengue disease include vaccine programs, repellent initiatives, and public health initiatives targeting the reduction of mosquito breeding areas. Continued investigation on dengue vaccines and therapies, together with enhanced surveillance and diagnostic techniques, are crucial for tackling the impact of this illness on global health.

Keywords: Epidemiology- public health, Dengue Fever, Mosquito, burden, Prevalence, Preventive.

INTRODUCTION

Acute febrile sickness known as dengue fever (DF) is on the rise and presents serious health risks to the population worldwide, especially in tropical and subtropical areas. It is from the Swahili phrase "Ka-dinga pepo," which means "cramp-like seizure," that the English term "dengue fever" comes from. Benjamin Rush first described it in 1787, and it was originally known as "break-bone fever" because of the common myalgia and arthralgia symptoms that were seen during epidemic breakouts in Philadelphia in 1780. Epidemics of DF were first recognized clinically in the 1780s, when they were happening in North America, Africa, and Asia at the same time [1-4]. The dengue virus (DENV), which is the causative agent of DF illnesses across the globe, is classified as a flavivirus in the group Flaviviridae. It has four unique serotypes (DENV1-4) that are antigenically related to one another. The virus has a positive sense single-stranded encapsulated RNA genome and consists of seven non-structural (NS) proteins and three structural proteins: membrane-associated (M) protein, envelope (E) glycoprotein, and nucleocapsid or core (C) protein. The bite of a female Aedes mosquito carrying the virus is the main method of transmission to humans [5-6].

The severity of dengue fever (DF) varies, spanning from mild undifferentiated fever to severe conditions such as dengue shock syndrome (DSS) and dengue hemorrhagic fever (DHF) [7, 8]. Although the 1997 WHO classification, which categorized DF into undifferentiated fever, DF, and DHF, is still in use, the 2009 WHO revision reevaluated and classified DF into simple DF and severe DF for case management [8, 9]. Primary clinical indicators across these categories typically include persistent high fever lasting two to seven days, hemorrhagic manifestations (such as petechiae, epistaxis, positive tourniquet test results, or thrombocytopenia), signs of plasma leakage leading to shock (e.g., hemoconcentration or hematocrit above 20%), as well as pleural effusion and ascites [3].

Febrile illnesses among patients are a major public health concern, particularly in areas where DF is endemic or experiencing epidemics, notably in tropical and subtropical regions like Ethiopia [10]. These febrile illnesses in Ethiopia, as well as across Africa, may stem from various infectious microorganisms, complicating the implementation of control and response measures for pandemic and epidemic diseases like COVID-19, Ebola, and malaria [11]. Symptoms of DF and other arbovirus infections often overlap with those of other febrile illnesses [12, 13, 14], yet the prevalence of DF and related arboviral illnesses remains relatively low or poorly understood due to misdiagnosis or undetected cases [13].

Although comprehensive statistics are currently limited, DF is widely recognized as a significant public health threat prone to epidemics in East African nations [15]. Accurate and multiplex diagnostics are crucial for patient care and epidemiological surveillance to enhance epidemic preparedness and response both domestically and regionally for DF and other arbovirus infections [16]. However, due to constraints such as inadequate personnel, funding, supplies, and technological support for laboratory operations and epidemiological capacity, the current surveillance system struggles to swiftly identify new cases and monitor virus dynamics. Similarly, national discrepancies in diagnosis, diagnostic methodologies, and healthcare systems hinder accurate assessments of the burden and distribution of emerging disorders like DF [17].

These challenges contribute to the 2015 United Nations goal, which includes DF among other arboviral illnesses, appearing distant from achieving its objective of halting emerging or re-emerging neglected tropical disease epidemics by 2030. Since the first known outbreak in 2013, undifferentiated febrile patients in various Ethiopian regions, including Afar, Somali, and Dire Dewa city administration regions, have experienced recurrent outbreaks of dengue fever (DF) [18, 19, 20]. Additionally, serological surveys have indicated the emergence and spread of DF throughout the nation [21-22]. However, the country faces obstacles due to insufficient laboratory diagnostic capabilities and clinical experience to recognize and manage potential DF infections. Consequently, DF cases may go unreported as mild or asymptomatic, be misdiagnosed as other clinical conditions resembling bacterial, viral, or malaria infections, or continue to be classified as unexplained febrile illnesses [13, 23].

Thus, due to the nation's inadequate healthcare infrastructure, inexperienced medical personnel, and economic instability, DF cases, including epidemics, persist as a serious and unaddressed challenge [24]. State-of-the-art reviews typically discuss the current status of Dengue virus (DENV) and DF dynamics. In countries like Ethiopia, where DF cases are not yet recognized as a significant public health concern, critical reflection is necessary when assessing new DF cases for diagnosis and treatment. This review compiles the current understanding of dengue virus infection epidemiology, biology, pathogenesis, clinical symptoms, diagnosis, and trends in Ethiopia.

In conclusion, dengue fever (DF) poses a significant public health challenge globally, particularly in tropical and subtropical regions like Ethiopia. The severity of DF ranges from mild fever to potentially life-threatening conditions such as dengue shock syndrome (DSS) and dengue hemorrhagic fever (DHF). Despite the classification updates by the World Health Organization (WHO), which aimed to streamline case management, the diagnosis and management of DF remain complex due to overlapping symptoms with other febrile illnesses and challenges in surveillance and reporting. Ethiopia, like many other countries, faces various obstacles in addressing DF effectively. Limited resources, including personnel, funding, and technology, hamper surveillance efforts and hinder the prompt identification of new cases and virus dynamics. Furthermore, national discrepancies in diagnostic capabilities and healthcare systems impede accurate assessments of DF burden and distribution.

The United Nations' goal to halt emerging neglected tropical disease epidemics, including DF, by 2030 seems distant, given the persistent challenges in surveillance and diagnosis. Recurrent outbreaks of DF in Ethiopian regions highlight the urgency of strengthening healthcare infrastructure and improving diagnostic capabilities to effectively manage the disease. Serological surveys indicate the emergence and spread of DF throughout Ethiopia, underscoring the need for enhanced surveillance and response measures. However, inadequate laboratory diagnostic skills and clinical experience contribute to underreporting and misdiagnosis of DF cases, exacerbating the burden of the disease. Addressing the challenges posed by DF requires a multifaceted approach, including investment in healthcare infrastructure, capacity building for healthcare professionals, and the implementation of robust surveillance systems. Additionally, raising awareness among healthcare providers and the public about the symptoms and prevention of DF is crucial in controlling its spread. In summary, tackling DF effectively in Ethiopia and other affected regions necessitates concerted efforts from governments, healthcare organizations, and international partners. By addressing the underlying challenges and implementing comprehensive strategies, we can mitigate the impact of DF and move closer to achieving global health goals.

Epidemiology and Incidence Rates:

According to GBD 2019, there were records of dengue infection in 116 countries or territories. Between 1990 and 2019, the number of dengue episodes worldwide rose by 85.47%, from 30.67 million to 56.88 million. With the exception of Cuba, Thailand, and the US Virgin Islands, among others, dengue episodes have grown throughout the majority of nations and territories. Nearly 60% (34.09 million/56.88 million) of all dengue episodes in 2019 were reported in China (6.10 million) and India (27.99 million). In addition, from 1990 to 2019, China experienced a 291.22% rise in dengue incidents [25].

Dengue infection's annual standardized incidence rate (ASR) varies greatly throughout the world. In 2019, Niue (8749.54 per 100,000), the Northern Mariana Islands (8687.22 per 100,000), and Kiribati (8050.59 per 100,000) had the highest ASRs. ASR grew globally by an average of 1.70% (95% CI 1.62%–1.78%) each year from 557.15 per 100,000 in 1990 to 767.93 per 100,000 in 2011; from 767.93 per 100,000 in 2011 to 740.38 per 100,000 in 2019, it dropped globally by an average of 0.41% (95% CI 0.20%–0.62%) per year. From 2011 to 2019, there was an increase in ASRs in twenty-three nations or territories, the majority of which were in Oceania (Papua New Guinea, Fiji, Solomon Islands, etc.) [26].

Dengue cases witnessed a notable surge in high-middle (181.23%) SDI regions, with high (109.41%), middle (101.70%), low (93.96%), and low-middle (53.71%) SDI regions following suit. In 2019, low-middle SDI regions recorded the greatest ASR (1317.83 per

100,000) and the highest number of dengue events (23.11 million). From 1990 to 2011, the ASR rose in every SDI region; the high-middle SDI regions had the greatest ASR (EAPC 3.96, 95% CI 3.80–4.12). From 2011 to 2019, the ASR trended upward in the middle and high-middle SDI regions but declined in the low- and low-middle SDI regions.

The progressive rise in cases across all age groups was the cause of the increasing frequency of dengue episodes in all SDI regions. Global dengue incidence rates peaked in young adults and adolescents (10–25 years old), then in young children (5–10 years old), middle-aged adults (25–49 years old), and the elderly (> 65 years old) in 2019. Furthermore, in poor and low-middle SDI locations, the incidence of dengue was highest in the elderly (over 65), followed by teenagers and young adults (10–25 years) and small children (5–10 years). According to GBD 2019, there were records of dengue infections in seventeen GBD zones. South Asia accounted for 7.70 million dengue cases in 2019, with East and Southeast Asia following. The number of dengue episodes increased by 559.04% in Oceania, from 63.20 thousand in 1990 to 416.48 thousand in 2019, while throughout the previous three decades, the number of dengue episodes in East Asia more than doubled. Furthermore, Andean Latin America saw the largest increase in dengue occurrences (139.12%), followed by Tropical Latin America (104.50%).

With an ASR > 3173.48 per 100,000 in 2019, Oceania had the greatest risk of dengue infection, whereas South and Southeast Asia also faced a serious threat with an ASR > 1000 per 100,000. ASR was also highest in Tropical Latin America in 2019 (990.10 per 100,000), Central Latin America (771.16 per 100,000), and Andean Latin America (632.56 per 100,000) among the Americas. Around 14 GBD regions (South Asia, Tropical Latin America, Central America, etc.) showed a decreasing ASR trend between 2011 and 2019, but Oceania showed the strongest increasing trend (EAPC 11.01, 95% CI 8.79–13.27), followed by East Asia (EAPC 4.84, 95% CI 2.70–7.03) and Southeast Asia (EAPC 0.38, 95% CI 0.13–0.62) [26].

Fig. 1 shows the percentages of dengue episodes by age group at the GBD regional level in 1990, 2011, and 2019. In 2019, over 80% of occurrences worldwide occurred in individuals under 50 years of age. In 2019, however, more than 10% of occurrences occurred in high-income locations, such as high-income North America and Australasia, among the elderly (≥ 70 years of age). Remarkably, in affluent North America, almost 20% of those impacted were over 70 years old. In most GBD regions, the proportions of dengue episodes in the age category of people over 70 years old increased in 2019 (based on 1990 or 2011 as the baseline) [26].

To the best of our knowledge, this study represents the first utilization of GBD 2019 data to assess dengue infection incidence patterns globally, including long-term trends and regional variations. Between 2011 and 2019, there was a declining trend in the global ASR of dengue infection, despite an upward trend from 1990 to 2011. However, Oceania, East Asia, and Southeast Asia have all witnessed an increase in ASR. Additionally, the ASR trend in the middle and high-middle SDI regions increased from 2011 to 2019. These findings underscore the ongoing challenge posed by dengue worldwide. Across all SDI regions, dengue incidence rates were highest among teenagers and young adults. Conversely, the proportion of dengue episodes among individuals over 70 years old increased in 2019, compared to the baseline years of 1990 or 2011, across most GBD regions, particularly in low and low-middle SDI regions. Meanwhile, compared to 1990, the frequency of dengue occurrences dramatically increased in South, East, and Southeast Asia by 2019. Despite a decreasing ASR trend in most of the Americas from 2011 to 2019, the frequency of dengue episodes surged notably in Andean and Tropical Latin America during the same period. Moreover, in 2019, the ASRs were relatively high in Tropical, Central, and Andean regions of Latin America. Given the complex regional dynamics surrounding this neglected virus, heightened efforts are imperative to combat dengue infection, emphasizing the importance of preventive measures [26].

Our findings highlight that the Southeast, East, and South Asian regions face the greatest threat from the dengue virus. In South Asia, countries such as India, Bangladesh, Pakistan, the Maldives, and Nepal are endemic for dengue fever. East Asia, including

China, Japan, and Korea, has experienced dengue outbreaks in recent years. Similarly, epidemic dengue has been reported in several Southeast Asian countries, except for Brunei. Notably, China and India accounted for approximately 60% of the total worldwide cases of dengue outbreaks.

Unexpectedly, between 2011 and 2019, while ASR decreased globally, it increased in East and Southeast Asia, contributing to the highest dengue incidence rates. China, among the endemic countries in East Asia, witnessed a significant increase in dengue episodes, with a 291.22% rise from 1990 to 2019. This surge in China's dengue outbreaks may be attributed to imported cases from Southeast Asia and Western Pacific nations. Moreover, local dengue infection outbreaks have become more prevalent due to the rise in imported cases. Factors such as climate conditions, the East Asian summer monsoon, and the resilience of Aedes albopictus to insecticides may further contribute to the rising ASR of dengue infection in China. Addressing this situation requires integrated vector management strategies encompassing conventional and novel techniques to reduce mosquito populations and mitigate the dengue burden. Improved travel surveillance and vector-control efforts are also imperative in East Asia to prevent dengue outbreaks. In Southeast Asia, high population concentrations, low public awareness, and inadequate infrastructure have intensified outbreaks in recent years, necessitating enhanced vector-control strategies and improved urbanization and resources [27].

Although ASR trends decreased in most of the Americas between 2011 and 2019, dengue episodes surged in Andean and Tropical Latin America during the same period. Notable ASRs were recorded in various Latin American regions in 2019. Given the persistent challenges posed by poverty, urbanization, and population growth, the Americas require comprehensive strategies, including strengthened national surveillance systems, integrated vector management, and personal behavioral interventions, to address the dengue pandemic effectively. Additionally, a dengue prevention and control management plan may incorporate the development of a future dengue vaccine.

The unexpected increasing trend of ASR in middle and high-middle SDI regions from 2011 to 2019 underscores the urgency of global efforts to combat dengue. Oceania, comprising nations like Papua New Guinea, Fiji, and the Solomon Islands, showed a growing ASR trend in the medium and high-middle SDI zones. The tropical or subtropical environment in these nations hastens dengue outbreaks, while poverty continues to disproportionately affect populations, contributing to the persistence of dengue. Integrated monitoring and evaluation of dengue outbreaks are essential to contain this growing threat in Oceania [27].

Furthermore, our analysis reveals that dengue predominantly affects teenagers and young adults globally, with a notable increase in incidence among individuals over 70 years old. This underscores the need for tailored treatment approaches for older adults and underscores the importance of vaccine safety and effectiveness in this population. While this study leveraged GBD 2019 data to provide insights into global dengue trends, limitations include potential bias in the data due to differences in surveillance systems and the absence of information on dengue genotypes. Future research should focus on addressing these limitations to enhance the accuracy and reliability of dengue incidence estimates.

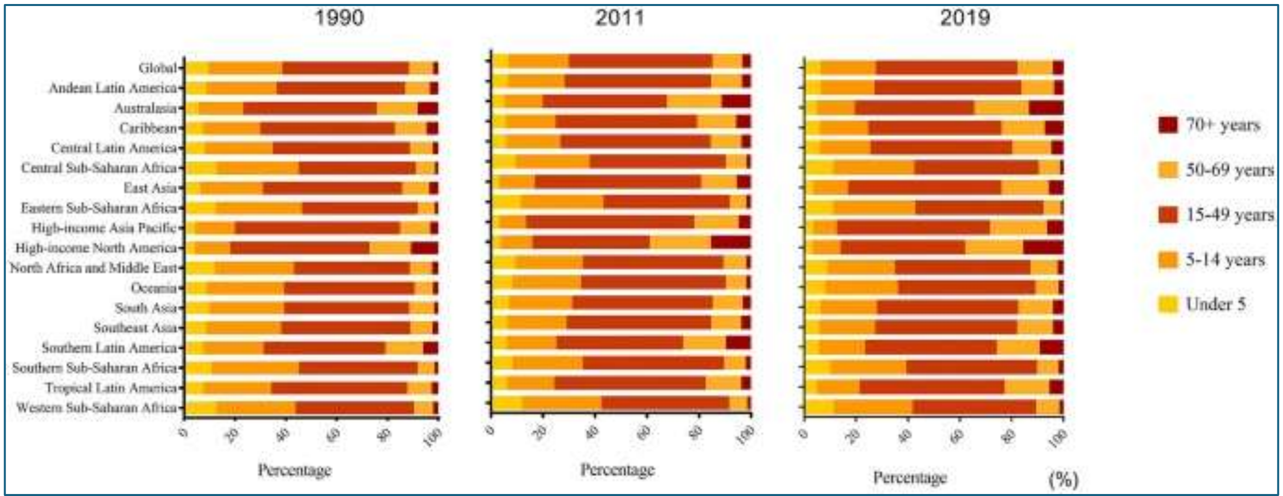

Figure 1: Incidence of Dengue Fever.

Clinical Symptoms and Signs:

Based on data, fever was the most commonly reported clinical symptom or sign, with a pooled proportion of 98.1% (95% CI: 97.2–98.7%), followed by malaise (76.0%, 95% CI: 64.1–84.9%), headache (75.7%, 95% CI: 69.5–81.0%), and asthenia (74.3%, 95% CI: 45.8–90.8%). Hemorrhagic symptoms were present in 25.8% of patients (95% CI: 21.0–31.1%), with petechiae being the most prevalent at 22.3% (95% CI: 16.5–29.3%). The dengue-infected group exhibited significantly higher rates of myalgia, chills, rash, eye/retro-orbital pain, petechiae, exanthema, lethargy, lymphadenopathy, thrombocytopenia, leukopenia, conjunctival injection, and positive tourniquet test results compared to the laboratory-negative group (all $P < 0.05$). However, laboratory-negative patients were more likely to experience coughing, sore throat, and nasal congestion, attributed to influenza infection, which was more prevalent among them (all $P < 0.05$).

Blood manifestations (OR: 9.57, 95% CI: 4.78–19.15), pleural effusion (OR: 12.44, 95% CI: 7.07–21.91), ascites (OR: 13.91, 95% CI: 8.03–24.11), and mortality (OR: 11.46, 95% CI: 4.16–31.56) were more common in DHF patients than in DF patients. Conversely, body pain was significantly less frequently reported by DHF patients compared to DF patients (OR: 0.60, 95% CI: 0.36–0.99). The odds of death were notably higher for individuals experiencing shock symptoms (OR: 308.09, 95% CI: 42.56–2230.53). Conversely, headaches showed a negative correlation with death (OR: 0.46, 95% CI: 0.22–0.95) [28].

Serotyping and Discussions:

Data on dengue serotypes was given by studies of 174 outbreaks that happened between 1990 and 2015. DENV-2 (36, 20.7%) was the virus that caused the most monoinfection outbreaks, followed by DENV-1 (29, 16.7%), DENV-3 (19, 10.9%), and DENV-4 (7, 4.0%). Outbreaks involving all four serotypes were the most prevalent (25, 14.4%), followed by coinfection with DENV-1 and DENV-2 (16, 9.2%) and coinfection with DENV-1, DENV-2, and DENV-3 (12, 6.9%). Coinfection with more than one DENV serotype was observed in 47.7% of the outbreaks. In the six outbreaks that were reported between 1990 and 1994, DENV-2 was the most often identified serotype (5/6, 83.3%). The most common serotype found in dengue epidemics between 1995 and 1999 and between 2000 and 2004 was DENV-2 monoinfection (11/20, 55.0% and 10/45, 22.2%) [29].

Subsequent outbreaks (2005–2009) were dominated by co-infection (12/23, 52.2%), particularly co-infection with all four serotypes (4/23, 17.4%). Following 2010, co-infection with all four serotypes continued to dominate the coinfection outbreaks (17/46, 37.0%), whereas DENV-1 led the monoinfection outbreaks (17/34, 50.0%). Following 2010, different serotypes predominated in different WHO regions: coinfection with all four serotypes was most common in Southeast Asia; DENV-1, DENV-2, and DENV-3 were most frequently observed in the Eastern Mediterranean region; DENV-1 was predominant in the Western Pacific region; and DENV-1 and DENV-2 were most common in the African and American regions.

The epidemiology, clinical features, serotype distribution, and risk factors for global dengue epidemics that affected people between 1990 and 2015 are presented in this paper. Of the 262 outbreaks, most happened in developing nations including China, Brazil, and India. These high figures may be explained by the insufficient control mechanisms and sparse laboratory facilities in these nations. The transmission of DENV may also be aided by the high population density, low socioeconomic position, and perfect habitat for mosquitoes found in developing nations. Following 2010, the Western Pacific area was responsible for the bulk of dengue outbreaks and patients, with cases primarily reported from China, Singapore, and Malaysia. On the other hand, the Europe area only recorded a small number of dengue outbreaks, and those that did occur exclusively concerned France and Portugal. Its low frequency of dengue outbreaks may have something to do with Aegypti's absence from the European Basin between the 1950s and 2005. It is significant to remember that the dengue epidemics in adjacent or close-by countries had an impact on numerous dengue outbreaks. According to Wang et al., the dengue virus that caused the 2013 outbreaks in Xishuangbanna and Dehong, China, was brought in from Southeast Asian nations. There have been reports of imported dengue epidemics in southern China as a result of the increasingly frequent interactions between the populations of China and Southeast Asian nations. Furthermore, it was reported that passengers to Madeira were most likely the source of the first significant dengue outbreak in Europe (Wilder-Smith et al., 2014). In order to stop future disease outbreaks and their spread to other areas, border regions of dengue epidemic zones must implement integrated vector control and a valid laboratory-based disease surveillance system (Guo et al., 2015) [30-31].

Continuous outbreaks most likely indicate inadequacies in vector prevention and control. Due to its increased capacity for viral duplication, which raises the likelihood of viral transmission, A. aegypti, which originated in Africa and spread to tropical nations in the seventeenth and eighteenth centuries, has been identified as the main dengue vector. Our meta-analysis contained sixty publications that discussed mosquitoes. As expected, Aegypti was the most common mosquito, accounting for 76.7% of cases, followed by A. albopictus (43.3%). Furthermore, compared to outbreaks linked to A. albopictus mosquitoes (0.4, 95% CI: 0.1–2.5%), the pooled death rate in A. aegypti mosquito outbreaks (0.7, 95% CI: 0.3–1.7%) was greater. A. albopictus often causes moderate, transient dengue outbreaks, rainfall combined with the hot weather was a contributing factor in the mosquito population's sharp rise [32].

Temperature has an impact on the survival of dengue transmission vectors as well as their rate of development and reproduction. Rainfall provides breeding locations and encourages egg hatching (Johansson et al., 2009). Ae. aegypti mosquitoes have been shown to have a significantly increased dengue virus infection rate at high temperatures by Chepkorir et al. (2014) and Watts et al. (1987), indicating a potentially important role for temperature in the dynamics of dengue transmission. Dengue outbreaks may be on the rise as a result of the high temperature, which may enhance virus reproduction to high titers and shorten the time needed for the virus to establish itself inside the vector (Lambrechts et al., 2011). In addition to the conventional approaches to vector control, a promising new approach has been developed in the past ten years: scientists have released Aegypti or Albopictus mosquitoes infected with Wolbachia, which may prevent the insects from spreading the dengue virus and prevent them from infecting humans [33-36]

According to our study's findings, dengue outbreaks that happened prior to 2000 were primarily caused by the DENV-2 serotype, but outbreaks that happened between 2000 and 2009 were primarily caused by the DENV-3 serotype. Global dengue epidemics after 2010 were mostly caused by DENV-1, with DENV-4 being the least common serotype to be discovered. Since prior exposure to a single virus could not confer protection against possible infections with other serotypes, it is noteworthy that at least two serotypes were detected in over half of the outbreaks (Rahim and Sikder, 2005). Additionally, the new DENV serotype can bind cross-reactive and non-neutralizing antibodies from the original infection, which will let the virus enter vulnerable cells. According to Simmons et al. (2007) and Wang Y. et al. (2015), there existed a phenomena called antibody-dependent enhancement of infection (ADE), which was thought to be the most logical reason for severe dengue. This may possibly account for the substantial correlation our investigation found between DHF and secondary infection (OR: 1.86, 95% CI: 1.46–2.37) [37-39].

Furthermore, we discovered that outbreaks dominated by DENV-2 had the greatest pooled fatality rate (2.0%), and that this serotype was associated with much higher mortality rates than other serotypes. Liu et al. previously discovered several mosquito galactose-specific C-type lectins (mosGCTLs) that promoted dengue infection, despite the lack of dengue vaccines or treatments. These mosGCTLs were induced in the tissues of mosquitoes infected with DENV-2 and directly interacted with the DENV-2 surface envelope (E) protein and virions both in vitro and in vivo. Immunization against mosGCTLs may be a workable strategy for avoiding dengue infection, as membrane blood feeding of antisera against mosGCTLs has been shown to effectively limit DENV-2 infections among mosquitoes (Liu et al., 2014). Furthermore, during outbreaks, it is important to guarantee the use of early clinical and laboratory diagnosis, intravenous rehydration, staff training, and hospital rearrangement in order to lower the mortality rate among dengue patients (Lo et al., 2007; WHO, 2012) [40].

Fever (98.1%), malaise (76.0%), headache (75.7%), and asthenia (74.3%) were the most common symptoms of dengue infections; nevertheless, in certain instances, hemorrhage (25.8%), plasma leakage (8.3%), and organ damage (such as hepatosplenomegaly, 17.5%) were also noted. Despite the fact that dengue was often moderate and self-limiting in this study, there may be enough time for virus transmission and outbreak growth if cases are misdiagnosed by inexperienced medical professionals (Huang Xue et al., 2014). Apart from the typical dengue symptoms and indicators, DHF patients were often found to have manifestations such as bleeding (OR: 9.57), pleural effusion (OR: 12.44), and ascites (OR: 13.91). As a result, doctors should keep an eye out for signs of bleeding and capillary leakage in their patients, as these could be signs of DHF or DSS (Trofa et al., 1997). Our study's findings indicated that dengue outbreaks that occurred after 2010 had considerably lower rates of DHF, secondary infection, and mortality than outbreaks that occurred before 2010, indicating a potential decline in the severity of dengue infection worldwide after 2010. Much work has gone into reaching the target set by the World Health Organization in 2012 through the use of prompt, appropriate clinical management, global outbreak surveillance, and sustainable vector control; nonetheless, these efforts still face a difficult environment (WHO, 2012) [41-43].

It is noteworthy, in our opinion, that dengue patients diagnosed after 2010 were substantially older than those diagnosed prior to 2010 (mean pooled age: 34.0 vs. 27.2). This finding could have two possible explanations: first, younger people spend more of their days in air-conditioned, enclosed spaces and are therefore less likely to be exposed to mosquitoes (Lin et al., 2012); second, older people with chronic illnesses visit the doctor more frequently, which increases the likelihood of detecting an existing dengue infection (Lee et al., 2006) [44-45].

Our study still has several shortcomings. First off, some dengue outbreaks might not have been documented because our investigation and analysis were dependent on published publications; as a result, the findings of our study should be evaluated cautiously. Due to the fact that dengue is a self-limiting illness, and the majority of cases are asymptomatic (Bordignon et al., 2008), some dengue patients may go unrecognized during epidemics. It's possible that far more instances than were officially reported were connected to these outbreaks. Notwithstanding these drawbacks, we think that the information provided by our systematic review and meta-analysis about the global epidemiology of dengue epidemics is valuable. In order to target prevention and early identification efforts in dengue outbreaks worldwide, our study identified the countries and WHO regions most severely affected by dengue outbreaks, as well as the risk factors for and clinical characteristics of dengue infection, DHF and mortality, as well as the global distribution of dengue serotypes [46].

Conclusion:

Dengue fever remains a significant global health concern due to its widespread prevalence, complex epidemiology, diverse symptoms, and multiple serotypes. With its transmission primarily mediated by the Aedes mosquito, dengue fever affects millions of people annually across tropical and subtropical regions. The disease's epidemiology is characterized by periodic outbreaks, often associated with environmental factors, urbanization, and population movement. The prevalence of dengue fever has been on the rise, attributed to factors such as climate change, increased travel, and urbanization, leading to expanded mosquito habitats and viral transmission. Symptoms of dengue fever can vary widely, ranging from mild flu-like manifestations to severe and potentially life-threatening complications. Classical symptoms include fever, headache, muscle and joint pain, rash, and fatigue. However, severe cases can progress to dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS), characterized by vascular leakage, thrombocytopenia, and hemorrhagic manifestations, posing significant challenges to clinical management.

Serotyping of dengue viruses further complicates the understanding and control of the disease. Dengue viruses are classified into four distinct serotypes (DENV-1 to DENV-4), with each serotype capable of causing infection. Serotype-specific immunity following infection provides partial protection against homologous serotypes but may enhance the risk of severe disease upon subsequent infection with a different serotype, a phenomenon known as antibody-dependent enhancement (ADE). In conclusion, dengue fever represents a multifaceted public health challenge, characterized by its increasing prevalence, complex epidemiology, diverse clinical manifestations, and the presence of multiple serotypes. Efforts to combat dengue fever require a comprehensive approach, including vector control measures, early diagnosis, and prompt clinical management. Furthermore, ongoing research into dengue vaccines and therapeutics, as well as improved surveillance and public health interventions, are essential for mitigating the burden of this mosquito-borne disease on global health.

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