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SPECIAL ARTICLE

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Dengue is a product of the environment: an approach to the impacts of the environment on the *Aedes aegypti* mosquito and disease cases

A dengue é produto do meio: uma abordagem sobre os impactos do ambiente no mosquito *Aedes aegypti* e nos casos da doença

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ABSTRACT

Dengue is an arbovirus infection whose etiologic agent is transmitted by the *Aedes aegypti* mosquito. Since the early 1980s, when the circulation of the dengue virus (DENV) was confirmed in Brazil, the disease has become a growing multifactorial public health problem. This article presented the main factors that have contributed to the frequent dengue epidemics in recent years, such as the behavior of the vector, climate change, and social, political, and economic aspects. The intersection between these different factors in the dynamics of the disease is highlighted, including the increase in the mosquito population due to higher temperatures and rainy periods, as well as the influence of socioeconomic conditions on the incidence of dengue. Some mosquito control strategies are also addressed, including the use of innovative technologies such as drones and the *Wolbachia* bacterium, as well as the hope represented by the dengue vaccine. Nevertheless, the need for integrated and effective public policies to reduce social inequalities and the impacts of climate change on the spread of dengue is emphasized.

Keywords: Arbovirus infections. Vectors. Climate change. Public policies. Control.

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INTRODUCTION

The term "arbovirus" is derived from Arthropod-borne virus and refers to a diverse group of viruses, typically spherical in shape, with RNA as their genetic material[1]. Arboviruses primarily circulate in enzootic cycles within tropical or temperate regions, where they are transmitted to wild vertebrate animals through the bites of infected hematophagous arthropods, particularly mosquitoes and ticks[2,3].

However, due to human activities, some arboviruses have adapted to environmental changes and initiated an urban transmission cycle, with humans as the vertebrate hosts and urban mosquitoes as vectors[3,4]. While significant arboviruses such as Zika (ZIKV) and chikungunya (CHIKV) are transmitted to humans in urban settings, the dengue virus (DENV), a member of the *Flaviviridae* family and *Orthoflavivirus* genus, has the most significant impact on public health due to its high morbidity and mortality[5].

The dengue virus has four antigenically distinct serotypes, known as DENV-1, DENV-2, DENV-3, and DENV-4[6]. Globally, dengue is considered endemic in over 100 tropical and subtropical countries across the Americas, Africa, Asia, the Middle East, the Pacific Islands, and the Western Pacific Region, with approximately 4 billion people living in these at-risk areas[7]. In 2013, a study estimated that there were roughly 390 million annual DENV infections worldwide, encompassing both symptomatic and asymptomatic cases[8].

In Brazil, although there were some reports of dengue cases in São Paulo and Rio de Janeiro at the beginning of the 20th century, it was only in 1981/1982, following an epidemic in the city of Boa Vista, in the state of Roraima, that the clinical and laboratory diagnosis of the disease was confirmed, including the isolation of serotypes 1 and 4 of the virus[9]. However, the epidemic in Boa Vista was successfully controlled[9], and the DENV-1 and DENV-4 serotypes did not spread to other areas of the country.

After a few years of epidemiological silence, the DENV-1 serotype was isolated again in 1986, this time in the municipality of Nova Iguaçu, Rio de Janeiro, and it quickly spread to nearby cities and states[10,11]. Four years later, in 1990, the DENV-2 serotype was isolated for the first time in the country, also in Rio de Janeiro, in the municipality of Niterói[12]. At that time, there was a significant increase in severe cases of the disease, along with the first recorded deaths related to previous infections[13]. The circulation of DENV-3 in Brazil was first detected in late 2000, once again in Nova Iguaçu, Rio de Janeiro[12,14]. In 2010, the DENV-4 serotype was reintroduced in northern Brazil, detected initially in the state of Roraima[15], and later isolated in Rio de Janeiro[16]. Since then, all four dengue virus serotypes have been circulating in the country.

By the end of May 2024, Brazil had recorded over 5 million probable cases of dengue and more than 3,000 confirmed deaths from the disease[17]. Out of the 27 Federative Units, 10 declared a state of emergency: Amapá, Federal District, Espírito Santo, Goiás, Minas Gerais, Paraná, Rio de Janeiro, Rio Grande do Sul, Santa Catarina, and São Paulo[17]. This was undoubtedly the worst dengue epidemic in the country's history, surpassing the more than 1.6 million cases recorded in 2015 and 2023[18].

As a multifactorial disease, various factors related to the key elements of virus transmission may explain the significant surge in dengue cases observed in the country. Thus, a comprehensive approach that considers the interaction between humans, vectors, pathogens, and the environment is crucial for evaluating the epidemiology of this disease.

Aedes aegypti as a public health concern

Transmission of all dengue virus serotypes to humans occurs through the bite of infected female mosquitoes of the main vector: *Aedes* (*Stegomyia*) *aegypti* (Linnaeus, 1762), which is prevalent in Brazil and worldwide. This species is also associated with the transmission of ZIKV and CHIKV in several countries, including Brazil[6].

Aedes aegypti is a mosquito native to the African continent. Originally, populations of this mosquito were generalists, utilizing a wide variety of containers as breeding sites and feeding on the blood of various animals, both human and non-human[19,20]. However, recent studies indicate that in the Sahel region of West Africa, some populations of this species have evolved to feed more frequently on human blood and use artificial containers for egg-laying[21]. This domesticated form of the *Aedes aegypti* mosquito has since spread worldwide, particularly in tropical and subtropical regions[22]. The spread across continents was facilitated by the mosquito eggs' high resistance to desiccation, allowing them to remain quiescent for up to a year, which supports the passive dispersal of the species[23,24].

In Brazil, the arrival of *Aedes aegypti* likely occurred during the colonial period, when people were brought from the African continent to be enslaved[25]. By the early 20th century, this mosquito had already become a significant concern for Brazilian public health, as it served as the primary vector in the urban transmission cycle of the yellow fever virus. During this time, the country was experiencing severe yellow fever epidemics, particularly in the state of Rio de Janeiro. In response, President Rodrigues Alves (1903–1906) appointed Oswaldo Cruz as head of the General Directorate of Public Health, tasking him with leading the first public campaign against urban yellow fever and *Aedes aegypti*[26]. Through a policy that included eliminating breeding sites, using larvicides and insecticides, and isolating patients, Oswaldo Cruz succeeded in reducing yellow fever cases in the state. However, the complete eradication of the mosquito was not achieved until 1958[26].

Currently, the eradication of *Aedes aegypti* is highly unlikely, so efforts to mitigate dengue cases are focused on controlling the mosquito population, primarily by eliminating or properly managing containers that can hold water.

Dengue and *Aedes aegypti*

The occurrence of dengue epidemics in Brazil is linked to various factors, including high population density, uncontrolled urban growth, social inequality, and the competence and adaptability of the mosquito vector, among others[27]. The near-constant presence of *Aedes aegypti* in urban environments poses a significant challenge for public health.

The development cycle of *Aedes aegypti* is holometabolous, encompassing aquatic stages of egg, larva, and pupa, followed by the terrestrial adult stage. Female *Aedes aegypti* typically lay their eggs in artificial containers with stagnant water, such as tires, plant pots, water tanks, cans, bottles, etc.[25,28,29]. However, even in urbanized areas, immature forms of *Aedes aegypti* have been found in natural breeding sites like bromeliads, bamboo internodes, and tree holes[30-32], demonstrating the species' plasticity and dominance in human-occupied environments.

The development time from egg to adult *Aedes aegypti* shortens as temperature increases[33]. In the laboratory, it was observed that at 25°C, the average development time from egg to adult for this species was 8.86 days. However, a temperature increase of just two degrees to 27°C reduced this development time to 7.30 days[34]. Temperature can also influence the Extrinsic Incubation Period (EIP) of the virus, which is the time between a female mosquito taking a blood meal and the arrival of the virus in her salivary glands[35]. Laboratory studies have shown that the EIP for the DENV-2 serotype is shorter in *Aedes aegypti* females at temperatures between 32°C and 35°C[36], allowing the virus to reach the mosquito's salivary glands more quickly. In another laboratory study, it was demonstrated that a 2°C increase in temperature could reduce the EIP for both DENV-2 and DENV-4 serotypes in *Aedes aegypti* females[37]. At 28°C, both serotypes were detectable in the females' salivary glands nine days after the blood meal, but this EIP dropped to five days when the temperature was raised to 30°C[37].

Furthermore, the pronounced anthropophilia exhibited by this mosquito is intensified by gonotrophic discordance, which leads the female to feed multiple times within the same oviposition cycle. This behavior increases the likelihood of the mosquito becoming infected and subsequently transmitting the virus to humans[38,39]. These bioecological traits of *Aedes aegypti* offer partial insights into the challenges faced in controlling this mosquito and, consequently, in reducing dengue cases in Brazil.

Climate change and other factors

It is undeniable that the world is experiencing climate change, particularly global warming, driven by human activities over the centuries[5]. According to the Intergovernmental Panel on Climate Change (IPCC), the global surface temperature is now approximately 1.1°C higher than in pre-industrial times, and this warming is expected to reach 1.5°C between 2030 and 2052 if the current rate of temperature increase continues[40].

The increase in the *Aedes aegypti* population is primarily associated with higher temperatures[41-43] and periods of rainfall[41,44]. Similarly, the incidence of dengue cases is higher during the hottest and rainiest months[43,45-47]. Since temperature and rainfall influence the dynamics of the *Aedes aegypti* vector, and dengue is a disease closely tied to these climatic variables, it is expected that climate change, particularly global warming, is impacting the epidemiology of this disease both in Brazil and globally[48,49].

Many studies suggest that climate change will impact the geographic distribution of mosquito vectors and the diseases they transmit[50-52]. Some models predict that with global warming, the distribution of *Aedes aegypti* could expand, and by 2080, this species may be present in approximately 159 countries worldwide, with its presence reported for the first time in at least three of them[50]. The introduction of diseases into countries where the population has had little or no previous exposure to these pathogens can lead to significant epidemics, as seen with Zika and chikungunya[53,54].

A recent study evaluated climatic and demographic indicators in Brazil between 2000 and 2020 to explain the expansion of dengue fever and the increase in the number of cases nationwide[55]. The study revealed that the number of microregions with incidence rates exceeding 300 per 100,000 inhabitants has been rising over the years, particularly in the western and southern parts of the Southeast and Central-West regions, respectively. Additionally, in the Central-West and South regions, an increase in the number of excessively hot days was observed between 2014 and 2020 compared to 2007 to 2013[55]. The rise in the number of hot days, with temperatures above the regional norm, is one of the consequences of climate change that may help explain the observed increase in dengue incidence across the country[55].

A review study highlighted the effects that climate change, along with human behavior, can have on vector-associated diseases like dengue fever[56]. Periods of heavy rain, whether they cause flooding or not, as well as periods of drought, can influence the dynamics of pathogen transmission by vectors[56]. Increased rainfall can fill artificial containers left exposed in the environment, turning them into breeding sites for *Aedes aegypti*[49,57]. Conversely, during droughts, people may store water in urban areas with irregular supply[58]. This water storage often occurs in improvised containers, such as buckets, barrels, and tanks, which are frequently not properly sealed, attracting *Aedes aegypti* females to lay their eggs[56].

However, it is important to emphasize that, in addition to climate change, social, political, and economic factors can also facilitate the DENV transmission cycle. Rapid and unplanned urbanization, coupled with inadequate sanitary conditions, insufficient public health infrastructure, limited access to healthcare, and inadequate efforts to control the mosquito vector, also contribute to the occurrence of dengue epidemics[59].

A study evaluated the spatio-temporal evolution of dengue cases in Brazil between 2001 and 2012, analyzing the relationship between reported records and sociodemographic factors[60]. The occurrence of dengue cases in Brazil between 2001 and 2012 was inversely associated with the proportion of people living in rural areas, that is, the greater the human population in cities, the greater the risk of dengue fever[60]. A direct and inverse association, respectively, was also observed between the Gini index and the presence of a sewage system with the risk of dengue fever[60]. In another study, it was demonstrated that the incidence of dengue presented a heterogeneous pattern in the Northeast of Brazil between 2014 and 2017, with social indicators such as human population density, education and social vulnerability showing a positive correlation with the disease[61]. For example, access to piped water had a negative correlation with the incidence of dengue fever[61].

Human behavior plays a crucial role in the occurrence of dengue epidemics in Brazil, particularly in the elimination of *Aedes aegypti* breeding sites within homes, which relies heavily on societal mobilization. For example, a study conducted in a neighborhood in São José do Rio Preto, São Paulo, demonstrated that despite extensive educational efforts, including distributing leaflets to households, posting posters in public and commercial areas, holding meetings with mothers in daycare centers, and giving lectures in schools, there was no reduction in the number of breeding sites found in homes before and after the awareness program[62].

In contrast, preventive actions against dengue in Catanduva, São Paulo, yielded positive results[63]. Between 1999 and 2001, two areas on the outskirts of Catanduva were evaluated: one as a study area and the other as a control area. In the study area, vector control agents implemented preventive measures without applying larvicides or eliminating mosquito breeding sites. Educational materials were used to explain the *Aedes aegypti* life cycle, and recreational activities, such as theater and scavenger hunts, were conducted[63]. As a result, the study area experienced a significant reduction in the proportion of households with potential containers or standing water compared to the control area. Additionally, there was a notable decrease in the average number of potential containers with stagnant water in households within the study area[63].

It is essential for society to feel a sense of responsibility in mosquito control efforts to successfully reduce breeding sites within homes. However, information and education must be complemented by coordinated public policies across all levels of government, focusing on effective basic sanitation measures, such as regular solid waste collection[64]. The link between dengue and social determinants underscores the need for specific public policies aimed at addressing inequalities to reduce the incidence of the disease in the most vulnerable regions.

The multisectoral nature of dengue highlights the challenges in controlling the disease within the country. The dominant tropical climate, characterized by hot and rainy months, naturally supports the establishment, expansion, and proliferation of *Aedes aegypti*. Additionally, this mosquito species possesses ecological and behavioral traits that enhance its vector capacity.

The current control methods appear to be insufficient in reducing vector density. For chemical control, the development of resistance in mosquito populations to certain classes of insecticides and larvicides poses a significant challenge[65]. In mechanical control, the elimination and proper management of potential *Aedes aegypti* breeding sites can be difficult, particularly in hard-to-reach areas. As an alternative, drones have been identified as a valuable tool to address this limitation, as they can provide high-resolution images for identifying *Aedes aegypti* breeding sites in areas inaccessible to entomological surveillance agents[66,67].

Wolbachia is an endosymbiotic bacterium found in various insect species, including *Aedes* (*Stegomyia*) *albopictus*[68], a mosquito species considered a potential vector for DENV, ZIKV, and CHIKV in Brazil[69]. *Wolbachia* is not naturally present in *Aedes aegypti*, and its introduction into this mosquito species reduces its competence to transmit dengue, Zika, and chikungunya viruses, potentially helping to decrease cases of these arboviruses in the country[70,71]. Additionally, the bacteria are transmitted to subsequent generations through eggs[72]. This control method involves releasing adult mosquitoes infected with the bacteria into target areas over several months. In Niterói, Rio de Janeiro, the release of these adult mosquitoes has demonstrated positive results[72]. However, when implementing this biological control method, it is crucial to consider the genetic diversity of Brazilian *Aedes aegypti* populations and the country's varying ecological and epidemiological contexts[73].

The QDENGA® vaccine represents a promising advancement in reducing dengue cases and mortality, particularly following the recent epidemic in Brazil, notably that of 2024. The vaccination regimen consists of two doses, and after 18 months, the overall effectiveness of QDENGA® is 76.1% in seropositive individuals — those who have had previous exposure to the dengue virus — and 66.2% in seronegative individuals, who have not been exposed to the virus[74]. The vaccine's overall efficacy against different DENV serotypes ranges from 95.1% (DENV-2) to 48.9% (DENV-3)[74]. Previously, the Dengvaxia® vaccine was approved and introduced in Brazil in 2015 for individuals aged 9 to 44 years. However, this vaccine proved beneficial only for seropositive individuals[75]. Since QDENGA® was only introduced in 2024 and a limited number of doses have been administered, its full protective impact on the Brazilian population remains to be determined.

Even with the introduction of vaccination, political-social, and climatic factors must be addressed, as they present significant challenges for controlling both the mosquito vector and the disease. Implementing public policies for regular garbage collection and ensuring equitable access to piped water across the Brazilian population can substantially aid in reducing mosquito infestation and cases of arboviruses associated with *Aedes aegypti*. Additionally, effective measures to mitigate the impacts of climate change are essential to prevent increases in periods of drought and major flooding, which can affect the transmission dynamics of arboviruses and other infectious diseases impacting public health in Brazil.

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RESUMO

A dengue é uma arbovirose cujo agente etiológico é transmitido pelo mosquito *Aedes aegypti*. Desde o começo dos anos 1980, quando a circulação do vírus dengue (DENV) foi confirmada no Brasil, a doença passou a ser um crescente problema multifatorial para a saúde pública. Neste artigo, apresentamos os principais fatores que contribuíram e contribuem para as frequentes epidemias de dengue ocorridas nos últimos anos, como o comportamento do vetor, as mudanças climáticas e os aspectos sociais, políticos e econômicos. Destaca-se a interseção entre esses diferentes fatores na dinâmica da doença, incluindo o aumento da população do mosquito devido a temperaturas mais altas e a períodos chuvosos, bem como a influência das condições socioeconômicas na incidência da dengue. Também são abordadas algumas estratégias de controle do mosquito, incluindo o uso de tecnologias inovadoras, como drones e a bactéria *Wolbachia*, bem como a esperança representada pela vacina contra a dengue. Ainda assim, enfatiza-se a necessidade de políticas públicas integradas e eficazes para reduzir as desigualdades sociais e os impactos das mudanças climáticas na propagação da dengue.

Palavras-chave: Arboviroses. Vetores. Mudança climáticas. Políticas públicas. Controle.

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