

The Dengue Epidemic in Brazil: Mini-Review

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ABSTRACT

Dengue virus (DENV) was first detected in Brazil in 1986, since then dengue fever (DF) became a public health burden, with high morbidity and mortality. The virus is mainly transmitted by *Aedes aegypti* and *Aedes albopictus*. The four DENV serotypes (1-4) have been co-circulating in Brazil for more than 30 years indicating the hyperendemicity of the country for dengue. Climatic factors play a critical role in shaping the epidemic picture mainly in terms of abrupt increase of DF cases and disease severity. In this mini-review, we provide a brief overview of dengue and its epidemiological status in Brazil.

KEYWORDS: *Aedes aegypti* ; Hyperendemicity; Serotypes; Blood transfusion

INTRODUCTION

Dengue is a disease that originates from a zoonotic cycle, and non-human primates are important for the inter epidemic maintenance of the virus [1]. Since the dengue virus (DENV) was first isolated in the summer of 1943, the virus has spread rapidly within other countries and the incidence has increased globally >30-fold over the past five decades [2]. In 2018, the World Health Organization (WHO) stated that nearly half of the global population is exposed to DENV infection and estimated that 100-400 million infections occur annually (WHO. Dengue and severe dengue, Geneva: World Health Organization. Available from: (<http://www.who.int/news>). DENV belongs to the Flavivirus genus and mainly consists of five immunologically related but distinct serotypes (referred to as DENV-1, 2, 3, and 4 with diverse genotypes within each serotype). These serotypes share structural and pathogenic analogies ranging from asymptomatic infection to Dengue Fever (DF) to Dengue Hemorrhagic Fever (DHF) to Dengue Shock Syndrome (DSS) [3]. The virus is a positive-stranded RNA virus composed of three structural genes encoding for the proteins Capsid (C), a membrane-associated protein (M), an envelope glycoprotein (E), and seven non-structural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5) [4]. All four serotypes can cause the full spectrum of disease from subclinical infection to mild self-limiting disease and severe. According to the revised WHO dengue case classifications scheme, affected patients are classified

into dengue without warning signs, dengue with warning signs, and severe dengue ((WHO (World Health Organization), Dengue Guidelines for Diagnosis, Treatment, Prevention, and Control. Geneva; 2009).

DENV is transmitted by infected mosquitoes of the genus *Aedes* including not only *Aedes aegypti* but also *Aedes albopictus*; however, although it is quite rare, the virus transmission can occur via other routes, such as blood transfusion, tissue or organ transplantation, during breastfeeding, and laboratory accidents [5]. Several anecdotal studies documented persistent shedding of DENV-RNA in semen and vaginal secretion [6,7]. DENV was first reported as being sexually transmitted in recent anecdotal reports from Spain (<https://www.who.int>) and South Korea [8]. Under natural conditions, the mosquito usually acquires the virus when they suck the blood from viremic patients, which lasts around five days. From the intestinal tract, the virus goes to the salivary gland, and then the mosquito bite can culminate in infection [9].

DF is endemic in many countries in the Americas, Africa, southern Asia, western Pacific, and the eastern Mediterranean, with a greater tendency to appear in temperate regions [10,11], with the co-circulation of multiple DENV serotypes [12]. In these endemic areas, the incidence of the disease has a seasonal pattern and interannual variation, in addition to the development of notorious epidemics every few years [13]. Moreover, climate change, the unregulated urbanization process,

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the lack of adequate tools to control the vector, irregular water supply, the expansion of global travel, and the movement of viraemic hosts are contributing factors to the dramatic increase of the disease [11].

DENGUE IN BRAZIL

Brazil is the world's fifth-largest country occupies roughly half of the South American continent landmass (>8,500,000 km²) and has the world's longest tropical coast, with extensive forests in the Amazon Region, as well as forests in the east, southeast, and south coast. The country is divided into five geographical macro-regions (North, Northeast, Centre-west, Southeast, South) and has a large swamp region (Pantanal) in the Midwest, a savannah region (Cerrado) in the central plateau area, and a dry region (Caatinga) in the north eastern interior. Thus, the country is a suitable territory for the existence of the vector and, therefore, for the occurrence of Arboviruses.

The DF very first report in Brazil was way back in 19th from Curitiba, capital of the State of Paraná (Southern region), and in 20th from the Niteroi, a city in the State of Rio de Janeiro (Southeastern region) [14]. However, the first confirmed report dates back to the 1980's in the State of Roraima (North region), according to the Brazilian Ministry of Health. Still, in the same decade, epidemics occurred in Rio de Janeiro and capitals of the Northeast region [15]. Brazil contributed to 55% of the 18 million cases of dengue reported all over the American continent during 1995-2015. Despite mandatory notification, many patients (95%) are still not notified to the SINAN, country-wide disease notification system, or incorrectly classified [16]. The dengue outbreak occurred in Roraima in the 1980's was caused by DENV-1 and DENV-4 viruses and was successfully contained by local vector control measures a few months later. No known cases of DF reported anywhere in Brazil for the next four years of that outbreak [17]. By 1986, Rio de Janeiro was hit hard by DENV-1 and since then dengue has continued to increase and spread to new areas all over the country with the introduction of DENV-2 in 1990, DENV-3 in 2000, and the de novo emergence of DENV-2 and DENV-1 in 2008 and 2009, respectively, replacing of DENV-2 and DENV-3 [18]. In 2011, DENV-4 was identified in the city of Niteroi in Rio de Janeiro, which spread throughout the state [19,20]. Recent data from the Pan American Health Organization published in 2019 showed a simultaneous circulation of the four serotypes of DENV in Brazil (PAHO/WHO) P-A-H-O, Epidemiological Update Dengue. 2019). Altogether, these data reveal the spatial and temporal dispersion of simultaneous cocirculation of DENV serotypes with alternation in the prevalence of viral serotypes in the epidemic years [21].

Due to climatic conditions and the large population, Brazil registered the highest incidence of DF in South America [22] in three explosive national epidemics reported in 2002, 2008, and 2010 [23]. For instance, the outbreak that affects Rio de Janeiro alone between January and April in 2008, caused more than 235000 reported cases, more than more 260 deaths, and over 12900 hospital admissions [24]. This devastating epidemic called on the local authority to seek the help of military force to help in improving the health-care and vector control operations. In

Latin America, the disease is prevalent in adults; however, in Brazil, there was a change in the aspect of the disease: the infection is associated with more severe cases and with the younger population [25]. Also, the Atlantic coast and the interior of the state of São Paulo have the highest number of cases of dengue development [26]. In the last 20 years, the incidence of the disease has increased, affecting the North, Northeast, Midwest, and Southeast regions of the country [26]. According to the General Coordination of Arbovirus Surveillance report issued in 2019 until week 49, Brazil has reported 1,527,119 suspected dengue cases, increases were greatest in the Midwest region (1,318.3 cases/100 thousand inhabitants); the states with the highest number of suspected cases were Minas Gerais, Espírito Santo, and São Paulo, all located in the south eastern region of the country (Ministério-da-Saúde. Boletim Epidemiológico 38. 2019). DF cases are reported throughout the year, but a greater number of cases occur during January to June, a period during which there is a large amount of rain and temperature rise, contributing to the existence of a seasonal pattern of outbreaks and hospitalization [27].

Concerning the DF severity and death, Brazil has reported 1,388 and 18,328 cases of severe dengue and alarm signs, respectively, including 754 deaths in 2019. The number of cases with severe dengue and alarm signs was only 321 and 3,616, respectively, including 155 deaths reported in the same period in 2018.

Currently, in week 2020-36, a total of 928,282 suspected dengue cases were reported throughout the country. According to the Ministry of Health, the epidemic curve of suspected cases this year is higher than the previous year (2019); however, around week 12, there was a reduction in suspected cases when also compared to the previous year. A justification for this probably attributed to the COVID-19 pandemic, which led to the mobilization of epidemiological surveillance teams, resulting in delay or underreporting for cases of Arboviruses, including dengue (Ministério-da-Saúde. Boletim Epidemiológico 38. 2020).

The seriousness of the on-going dengue epidemic in Brazil cannot be underscored by the country's authorities. Urgent efforts such as health awareness campaigns that target both the general public and health professionals with particular focus on earlier and more consistent recognition and supportive clinical management of dengue cases are needed.

Abbreviations

DENV: Dengue Virus

DF: Dengue Fever

DHF: Dengue Hemorrhagic Fever

DSS: Dengue Shock Syndrome

AUTHORS' CONTRIBUTIONS

AN, AJSD, and SSS performed the literature review and wrote the manuscript

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The authors declare that they have no competing interests.

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