Dengue Viruses in Brazil

by

Rita Maria Ribeiro Nogueira*#*, Marize Pereira Miagostovich* and Hermann Gonçalves Schatzmayr**

*Laboratory of Flavivirus, Instituto Oswaldo Cruz/FIOCRUZ, Avenida Brasil 4365, 21040-190, Rio de Janeiro, RJ, Brasil
**Department of Virology, Instituto Oswaldo Cruz/FIOCRUZ, Avenida Brasil 4365, 21040-190, Rio de Janeiro, RJ, Brasil

Abstract

Dengue was first recognized in Brazil in 1981-1982. However, the disease became a nationwide public health problem after epidemics occurred in the state of Rio de Janeiro which were caused by DEN-1 and DEN-2 in 1986 and 1990, respectively. Widespread circulation of viruses in the entire country resulted in about 75% of dengue cases notified in the Americas in the last 8 years, with an increased incidence of DHF/DSS. All Brazilian regions have been affected by the epidemics. However, the North-East and South-East have a higher number of notifications.

The more recent introduction of DEN-3 in the state of Rio de Janeiro resulted in the emergence of the largest epidemic with more than 220,000 notified cases of dengue between January-May 2002. The co-circulation of three dengue serotypes has been responsible for the increase in the severe forms of the disease i.e. DHF/DSS.

Keywords: Dengue/Dengue haemorrhagic fever spread, public health problem, epidemics, multivirus circulation, Brazil.

Introduction

The high level of dengue virus activity in the American continent and the reinfestation of Brazil by Aedes aegypti in 1977 contributed to the reintroduction of the dengue (DEN) viruses into Brazil in the 80s[1,2]. From that decade onwards, the country has been responsible for more than 75% of the reported cases of dengue in the Americas (Figure 1).

A dengue outbreak due to DEN-1 and DEN-4 viruses (1981-1982) occurred in the city of Boa Vista, state of Roraima in the Amazon region[3]. This episode was controlled by local measures of vector elimination and no dengue activity was notified during the following four years in the country. It was only in 1986 with the introduction of the DEN-1 virus into the state of Rio de Janeiro that dengue became a nationwide public health problem[4].

# For correspondence: rita@ioc.fiocruz.br
Difficulties in implementing an effective vector control programme resulted in the rapid spread of the virus and consequent occurrence of epidemics in several states. The situation was aggravated in 1990 by the introduction of the DEN-2 virus into the state of Rio de Janeiro (5) and its subsequent spread to other regions in the country. By 2001, 25 of the 27 Brazilian states had reported dengue epidemics, with a total of 3 million cases, resulting from DEN-1 and DEN-2 epidemics in the last 16 years (6).

After complete absence from the Americas for almost 15 years, the DEN-3 virus was reintroduced into the continent in 1994 (7), reaching Brazil in 2000 and causing a large and severe dengue epidemic in the summer of 2001-2002 (8,9). The state of Rio de Janeiro again proved to be the nodal state for the introduction and dissemination of this new serotype in the country.

**Dengue in the state of Rio de Janeiro**

The dengue infection was first confirmed by our laboratory in April 1986, when the DEN-1 virus was isolated from the blood of 8 cases (8/8), collected during an epidemic in the municipality of Nova Iguaçu (10). This municipality belongs to the Greater Metropolitan Area of the state, which includes the capital, Rio de Janeiro, and 20 other municipalities, with 11,151,639 inhabitants out of the 14,768,969 inhabitants in the whole state. This heavy circulation of people in the region facilitated the rapid spread of dengue virus, causing an explosive epidemic, with 92,000 cases reported during the 1986-1987 period (11).
An active surveillance programme by the Health Secretary of Niterói (Greater Metropolitan Area) resulted in the early identification of DEN-2 by April 1990, exactly four years after the DEN-1 virus isolation and during a period of high DEN-1 virus activity. During the epidemic in 1990-1991, which presented two waves, a significantly greater proportion of patients with thrombocytopenia and requiring hospitalization were seen in the DEN-2 predominant phase\(^5\).

Both the DEN-1 and DEN-2 viruses were isolated during a new epidemic recognized in 1995-1996, with a total of 51,465 reported cases of dengue fever. In January 1998, a new epidemic broke out in the Paraíba river valley and quickly spread to other municipalities in the state reaching an important tourist area on the northern coast of the state\(^11\).

During 2000, a Virological Surveillance Programme was carried out in Nova Iguaçu during an inter-epidemic period. This resulted in the isolation of the DEN-3 virus from a case with classical dengue fever and from the vector \textit{Aedes aegypti} collected in the field\(^8,12\). The introduction of the DEN-3 virus increased the number of notified cases to 69,269 in 2001 and during the summer of 2002, caused the most severe epidemic in the state of Rio de Janeiro so far observed\(^9\). The number of reported cases exceeded the epidemic of 1990-1991 in which more than 100,000 cases, with 462 cases of dengue haemorrhagic fever/dengue shock syndrome (DHF/DSS) and 8 deaths were reported. In 2002, until the 21st epidemiological week, a total of 224,684 cases had already been reported with 1,728 cases of DHF/DSS and 61 confirmed deaths. The higher notification of the disease was observed in the Greater Metropolitan Area which has been the most heavily affected area with respect to dengue outbreaks (Figure 2).

\[\text{Figure 2: Dengue reported cases in the state of Rio de Janeiro and the Greater Metropolitan Area}\]

\[\text{Source SES-RJ/SUS/CE/ADTVZ}\]

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Laboratory studies carried out on 1,478 suspected dengue cases in the same period confirmed a 54.5% infection rate by serology and/or virus isolation and reverse transcriptase-polymerase chain reaction (RT-PCR). Three DEN-1, one DEN-2 and 320 DEN-3 virus strains were detected, showing that this new serotype represented 98.7% of the circulating viruses during the 2002 epidemic in the state. Forty fatal cases were confirmed in the laboratory, 20 of them were shown to be positive by at least two different methodologies, and the DEN-3 virus was the only serotype detected in these cases.

DEN-1, DEN-2 and DEN-3 spread to Brazilian states
The South-East and the North-East are the most affected regions by dengue infections, with epidemics occurring almost yearly. In the South-East region besides the state of Rio de Janeiro, the states of Minas Gerais and Espírito Santo have also been reporting epidemics in both the capital cities and inland municipalities. In the state of São Paulo, dengue viruses activity is mainly observed in inland municipalities and sporadically in coastal localities. The North-eastern region, which is composed of nine states, has suffered successive dengue epidemics and it has been responsible for the highest number of dengue notifications during the later 90s. In 1991, a dengue epidemic caused by the DEN-2 virus occurred in the state of Tocantins and in 1995 in the state of Pará, both in the Northern region. The state of Roraima confirmed dengue activity in 1996, 14 years after the first outbreak occurred in the state. In 1998, the state of Amazonas notified a dengue epidemic with 23,910 cases. In 2001 all states in that region, including Acre and Amapá, were affected by epidemics of variable magnitude.

In the Southern region, the state of Parana had been the only one notifying dengue since 1995. No indigenous cases had been notified so far by the states of Santa Catarina and Rio Grande do Sul.

Figure 3 shows the distribution of dengue reported cases, according to the Brazilian regions. It should be pointed out that dengue infections in the country, according to the available epidemiological data, are in general found in all age groups.

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Table: Number of DHF/DSS and deaths reported in Brazil, 1990-2001

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<tr>
<td>DHF</td>
<td>274</td>
<td>188</td>
<td>–</td>
<td>–</td>
<td>25</td>
<td>114</td>
<td>69</td>
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<td>Deaths</td>
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<td>11</td>
<td>2</td>
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<td>9</td>
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Source: National Center of Epidemiology, Ministry of Health, Brazil
– = indicates no notified DHF/DSS and deaths

The co-circulation of DEN-1 and DEN-2 viruses in Brazil led to the appearance of DHF/DSS (Table), initially in Rio de Janeiro and afterwards in other states\(^5,21,22,23\). The increase in the number of more severe cases in the country, like in many others in the Americas, was coincidental with the introduction of the DEN-2 south-east Asian genotype into the continent\(^24\).

Analysis by the sequencing of the genome, performed on DEN-1 and DEN-2 viruses isolated in Brazil, identified the Caribbean and the south-east Asian genotypes for the DEN-1 and DEN-2 viruses, respectively\(^25,26,27,28\). The partial sequence of the junction from E/NS1 of DEN-2 Brazilian isolates, during 1990 to 2001, showed that this genotype is still the only one circulating in Brazil (data not published).

The DEN-3 virus genotype introduced into the continent has been associated with major DHF/DSS epidemics in Sri Lanka and India and with DHF/DSS cases and deaths in Mexico and Central American countries\(^29,30\). The molecular characterization of DEN-3 viruses isolated from autochthonous cases in Rio de Janeiro, by the sequencing of structural proteins, showed that our strain belonged to the same genotype\(^31\).

Unusual manifestations such as the involvement of the central nervous system were first reported during the 1986-1987 epidemic in Rio de Janeiro and later in different states, including one case in the state of Rio Grande do Norte, where immunohistochemistry detected dengue antigen in neurons\(^32,33,34,35\).

High levels of serum amino-transferases have also been observed. In the more severe cases, yellow fever infections were occasionally suspected; however, epidemiological investigations and laboratory results confirmed dengue infection in all these cases.

During the DEN-3 epidemic in Rio de Janeiro, we were able to detect by RT-PCR, viral RNA in cerebrospinal fluid, liver, brain, lung, spleen, and kidney from fatal cases.

In summary, the dengue viruses activity in Brazil during the past 16 years is demonstrated by the high number of notified cases and the number of states involved in the epidemics. The high dengue endemicity besides the co-circulation of three serotypes have been responsible for the increase of the severe forms of the disease such as DHF/DSS in the country.
Acknowledgments

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