

## Short Communication

# A major chikungunya epidemic with high mortality in northeastern Brazil

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### Abstract

**Introduction:** Chikungunya causes fever and severe and persistent joint pain. **Methods:** We reported a chikungunya outbreak that occurred in Ceará State, Brazil between 2016 and 2017 with emphasis on epidemiological characterization of cases, high number of deaths, mortality-associated factors, and spatial and temporal spread of the epidemic among municipalities. **Results:** In November 2015, the first autochthonous cases of chikungunya were confirmed in Ceará, Brazil. In 2016-2017, 195,993 cases were reported, with an incidence of 2,186.5/100,000 inhabitants and 244 confirmed deaths. **Conclusions:** Rapid transmission and high mortality rate are serious problems, especially in regions with co-circulating arboviruses.

**Keywords:** Chikungunya. Outbreak. Arbovirus. Dengue. Zika.

In the past 34 years, dengue virus has caused large and geographically wide-ranging epidemics in Brazil<sup>1</sup>. Recent chikungunya virus (CHIKV) and Zika virus outbreaks have affected several million patients<sup>2,3</sup>. Despite this tremendous expansion of both viruses, relatively few cases of chikungunya have been reported in Brazil until 2016, and the current situation is significantly more complex than the previous situation.

CHIKV is an Alphavirus transmitted to humans by *Aedes* mosquito species, particularly *A. aegypti* and *A. albopictus*<sup>4</sup>. It

typically causes fever and severe and persistent joint pain<sup>5</sup>. It was first recognized as a human pathogen in 1952 in Tanzania, and after causing small-scale outbreaks in several African and Asian countries for decades, the disease significantly spread to Indian Ocean islands, resulting in a large-scale disease transmission in Reunion Island, French overseas territory, between 2005 and 2006, which has reemerged globally during the past decade<sup>6-8</sup>.

Autochthonous transmission of CHIKV was first reported in the Americas in December 2013<sup>9</sup> and in Brazil in September 2014. After the introduction of the virus in 2014, CHIKV transmission was evidently restricted to very few municipalities, affecting greater than 47,000 patients<sup>10</sup>.

We reported chikungunya outbreak that occurred in Ceará State, Brazil, between 2014 and 2018 with particular emphasis on epidemiological characterization of the cases, a high number

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**Received** 22 May 2019

**Accepted** 26 July 2019

of deaths, factors associated with mortality, and the spatial and temporal spread of the epidemic among the municipalities. According to the Brazilian Ministry of Health, the disease can manifest in up to three phases (acute, post-acute, and chronic). The acute phase is mainly characterized by a sudden onset of high fever ( $>38.5^{\circ}\text{C}$ ) and intense polyarthralgia for up to 14 days. The post-acute phase can last up to 90 days with the persistence of symptoms. The presence of symptoms for more than 90 days characterizes the chronic phase of the disease<sup>11</sup>. This was a cross-sectional study, and the measure of association used was the prevalence rate (PR) with 95% confidence interval (CI). This study was approved by the ethics committee in Brazil, through n<sup>o</sup>69865717.3.0000.5054/2017.

In early July 2014, the Health Department of the State of Ceará reported the first case of imported chikungunya. This case occurred in the Municipality of Brejo Santo, 504 km away from the City of Fortaleza, capital of Ceará. He was a 25-year-old seminarian resident in the State of Pernambuco, and his probable source of infection was the Dominican Republic, where he was on a religious mission one month prior to the onset of symptoms.

The first imported cases of individuals living in municipalities in the State of Ceará who were infected with CHIKV occurred in July 2014, involving a family who was on vacation in the Dominican Republic (three individuals aged 26, 27, and 56 years). All had high fever, arthralgia, headache, sudden-onset arthritis, myalgias, lumbar polyarthrititis, pruritus, rash, and oral ulcers.

In September 2014, an imported case (49 years old) was reported in the Municipality of Aracoiaba, and in December of the same year, another case (28 years old) was reported in the City of Fortaleza (**Figure 1A**). At that time, local surveillance issued a warning note about the risk of introduction and transmission of CHIKV, considering the high infestation by mosquitoes of the genus *Aedes* and the significant migration of individuals coming from areas with sustained transmission.

The first two autochthonous cases were confirmed in the municipalities of São Gonçalo do Amarante (55 years old) and Fortaleza (49 years old) in November 2015. Another 15 cases were confirmed in December, aged between 30 and 69 years, living in five different municipalities (**Figure 1B**), and 12 of the 15 patients were female. Hence, a sustained transmission started, which ended in 2016-2017 with two epidemic waves that resulted in high incidence and mortality rates.

In 2016, 56,264 suspected cases were reported, of which 32,766 were confirmed. The incidence of the disease in Ceará was 365.5/100,000 inhabitants, with 11 (6.0%) municipalities having an incidence of greater than 1,000 cases/100,000 inhabitants, particularly the municipalities of Pentecoste (4,568.3/100,000 inhabitants), Nova Russas (3,805.5/100,000 inhabitants), and Hidrolândia (2,021.3/100,000 inhabitants). Of the total number of cases, the female sex (64.1%), the age group between 20 and 59 (67.2%) years, and the brown color (86.8%) predominated. The most prevalent symptoms were fever (83.8%), polyarthralgia (70.5%), headache (65.4%), and myalgia (61.5%). Among those who reported underlying diseases, hypertension (58.4%) and diabetes (23.5%) predominated.

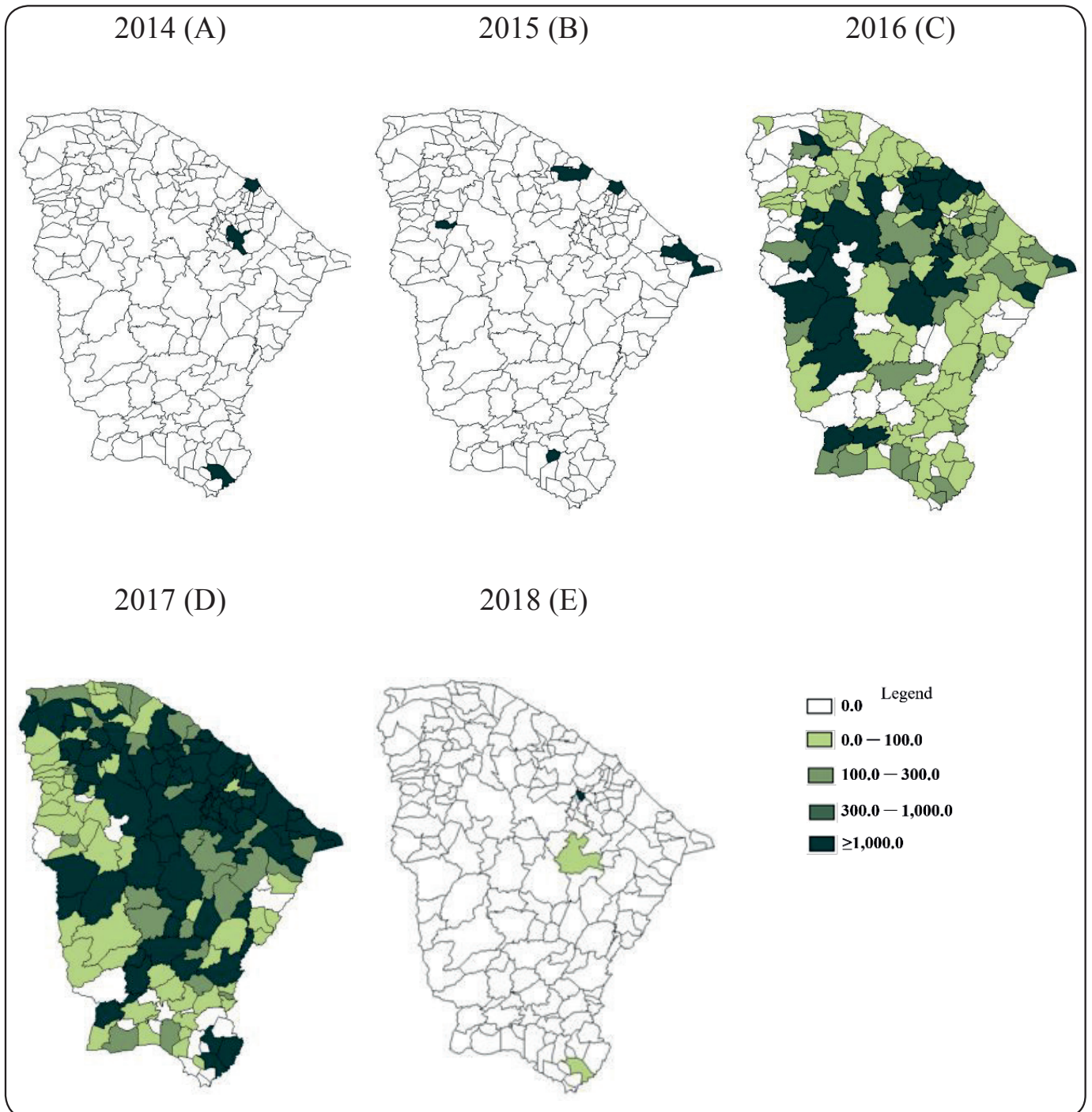
In 2017, 139,729 cases were reported, with 105,312 confirmed cases. The incidence of the disease was 1.174,9/100.000 inhabitants, with 41 (22.8%) municipalities having an incidence of greater than 1,000 cases/100,000 inhabitants, most notably the municipalities of Aracati (3.109,8/100.000 inhabitants), and Catarina (2,669.1/100,000 inhabitants). The female sex (62%), the age group between 20 and 59 years (65.9%), and the brown color (85.5%) predominated. The most frequent symptoms were fever (90.8%), headache (76.1%), arthralgia (75.6%), and myalgia (66.7%). Peak transmission occurred between April and May. Among those who reported baseline diseases, hypertension (59%) and diabetes (25%) predominated. After these two epidemic waves, there was a significant reduction in the number of cases in 2018, with 1,396 cases being confirmed, presenting a similar clinical and epidemiological profile.

A total of 245 deaths caused by CHIKV were confirmed in the laboratory, 50 in 2016, 194 in 2017, and one in 2018. The mean time between onset of symptoms and death was 28 days, with a median of 15 days. Most of these deaths occurred during the acute (49.0%) and post-acute (45.3%) phases of the disease. Another 5.7% were recorded greater than 90 days after the onset of symptoms (chronic phase). Among the confirmed deaths, 79 were necropsied and presented respiratory failure (36.7%), septic shock (8.9%), and hypovolemic shock (7.6%), considered as the main immediate causes of death. The organ with the greatest damage, macroscopically and microscopically, was the lungs, manifested by moderate to intense congestion in 75.6% and edema in 47.4% of cases. Hemorrhage was insignificantly prevalent.

Fever and vomiting were significantly prevalent in all cases ( $p < 0.05$ ), whereas headache and back and retro-orbital pain were significantly associated with protective factors to deaths ( $p < 0.001$ ). The median age among the cases (37 years old) was lower than the median age of the deaths (75 years old) ( $p < 0.001$ ). Elderly men (aged greater than 60 years) with comorbidities were the group with the highest prevalence of death among all the groups from chikungunya-related causes. Patients with leukopenia presented a twofold higher prevalence of progression to death (PR, 2.42; CI, 1.24-4.70;  $p = 0.007$ ) than patients with no leukopenia. Previous comorbidities such as renal disease (PR, 13.9; CI, 7.86-24.76;  $p < 0.001$ ), diabetes (PR, 9.75; CI, 7.25-13.10;  $p < 0.001$ ), and arterial hypertension (PR, 7.65; CI, 5.90-9.91;  $p < 0.001$ ) had significantly higher prevalence of death compared to cases [**Supplementary data (Table 1)**].

Before the outbreak on Reunion Island, this disease was not associated with high mortality rates<sup>8</sup>. However, in recent years, several studies have challenged the conventional view of the nonlethal nature of CHIKV<sup>8,12-13</sup>. The association between the incidence of chikungunya and increase in all mortality causes supports the possibility that CHIKV has an impact on mortality rates<sup>13</sup>.

The 2016/2017 chikungunya fever outbreak in Ceará occurred in the same area where dengue outbreaks have occurred since 1986<sup>14</sup>. High-density mosquito populations and



**FIGURE 1:** Municipalities with imported cases registered in 2014 (A) and autochthonous cases in 2015 (B), incidence of chikungunya in 2016 (C), 2017 (D), and 2018 (E) in Ceará, Brazil.

immunologically naive population were two contributing factors in this outbreak. Along with Zika and dengue viruses, CHIKV has become a substantial global public health threat not only because of the high magnitude of the epidemics but also because of its highly debilitating clinical symptoms, including intense joint pain that can last for years and a significant number of deaths<sup>15</sup>.

CHIKV was not endemic in Ceará, Brazil, before 2015. We reported an outbreak that occurred less than 2 years (2016/2017) after the introduction of the CHIKV, resulting in two epidemic waves.

The key finding of chikungunya outbreak in Ceará were the high incidence and high mortality rates among elderly patients with preexisting medical conditions (comorbidities such as



hypertension, diabetes, kidney disease). All causes of mortality during chikungunya epidemics could be monitored as a strategic tool, beyond individual case reporting to the epidemiological surveillance system, to estimate mortality rate and the overall burden of chikungunya.

Despite considerable improvements of quality since the 1990s, the data shown in the present study have limitations with regard to the coverage and the insufficient variables and low quality of the databases used by the Ministry of Health of Brazil. The use of these data could lead to the underestimation of the real number of cases during the epidemics. For example, the highest number of cases of chikungunya in women is probably due to their higher demand for health services than men, and consequently, reports of chikungunya are predominant in women.

### ACKNOWLEDGMENTS

We offer our deepest thanks to the Secretaria de Saúde do Ceará that provided technical support for the development and implementation of this study.

### Conflict of Interest

The authors declare that there is no conflict of interest.

### Financial Support

LPGC is a class 2 research fellow at the National Council for Scientific and Technological Development (CNPq/Brazil). Fundação Cearense de Apoio ao Desenvolvimento Científico e Tecnológico (FUNCAP) financially supported this study through the call 01/2017-SUS/PPSUS-CE FUNCAPSESA-Decit/SCTIE/MS-CNPq and National Council for Scientific and Technological Development (CNPQ) through the call MCTIC/CNPq 28/2018.

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