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.
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°C) and intense polyarthralgia for up to
14 days. The post-acute phase can last up to 90 days with the
presence of symptoms. The prevalence of symptoms for more
than 90 days characterizes the chronic phase of the disease.11
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 nº69865717.3.0000.5054/2017.

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,
myalgia, lumbar polyarthralgia, 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 infection 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 Pentecosté (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
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 cases. 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.9 However, in recent
years, several studies have challenged the conventional view of
the nonlethal nature of CHIKV8,12-13. The association between
the incidence of chikungunya and increase in all mortality
causes supports the possibility that CHIKV has an impact on
mortality rates.

The 2016/2017 chikungunya fever outbreak in Ceará
occurred in the same area where dengue outbreaks have
occurred since 198614. High-density mosquito populations and
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\textsuperscript{15}. 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

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**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.
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.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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