Experience of the Arbovirus Death Investigation Committee in Ceará, Brazil, in 2017: advances and challenges

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Abstract

Objective: to describe the experience and preliminary results of the Arbovirus Death Investigation Committee in Ceará, Brazil, in 2017. **Methods:** the Committee investigates and discusses all suspected cases of arbovirus deaths reported by the epidemiological surveillance service. **Results:** a total of 443 suspected arbovirus deaths were reported, 220 (49.7%) of which were confirmed; of these, 88.2% were from chikungunya and 11.8% from dengue; the median age of chikungunya deaths was higher when compared to dengue (77 versus 56 years) and the time until death was also longer when compared to dengue (38 versus 12 days); median time for case closure was 54.5 days; in 2017, Ceará confirmed 80.4% of Brazilian chikungunya deaths. **Conclusion:** the investigation of deaths showed that CHIK viruses were responsible for the majority of arboviral deaths in the state of Ceará, in 2017.

Keywords: Arboviruses; Dengue; Chikungunya Virus; Surveillance; Mortality.

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Introduction

The triple arbovirus epidemic scenario in the Northeast Brazilian region poses many challenges for health services.[1,2] This scenario emerged following isolation of the dengue virus (DENV) as long ago as the 1980s, and more recently, with the detection of the chikungunya fever virus (CHKV) in 2014 and the Zika fever virus (ZIKV) in 2015.

DENV circulation was confirmed in Brazil in 1982 and the first epidemic occurred in 1986-1987,[3] while the first severe cases began with effect from 1990[4-6] In Northeast Brazil, the state of Ceará stands out owing to the number of cases since 1986, as well as the number of severe cases and high lethality.[7,8]

> *The Brazilian Ministry of Health, in face of the first chikungunya and Zika deaths in 2015, adapted its dengue death investigation protocols for arbovirus death investigation.*

The first autochthonous chikungunya cases were confirmed in Brazil, in Oiapoque, in the state of Amapá, during the second half of 2014,[9] following confirmation of the introduction of CHKV in Central America the year before.[10,11] CHKV was also detected in a further six Brazilian states in 2014 and in 2015 it spread to more than 690 municipalities.[12,13] The first autochthonous cases in the state of Ceará were confirmed in 2015. Two large epidemics were confirmed in 2016 and 2017, with incidence rates of 320.2/100,000 inhabitants and 1,149.2/100,000 inhabitants, respectively.[14]

Autochthonous ZIKV transmission was confirmed in Brazil in May 2015,[13,15,16] following isolation of the virus in suspected dengue cases.[15] Its association with microcephaly cases was subsequently confirmed,[17] and shortly afterwards classified as congenital Zika virus syndrome (CZS),[18] with great impact on Public Health, especially in the Northeast, where 83.6% of all Brazilian cases were reported in 2015 and 2016.[19]

Even 30 years after detection of dengue in Brazil, despite all government efforts since then, dengue lethality has remained above the suggested maximum level of 1%.[20] In turn, prior to the epidemic on Reunion Island, chikungunya fever had not been associated with high mortality rates;[21] however, recent publications have challenged the conventional view of CHIKV infection not being deadly.[21-23] While severe or atypical manifestations of CHIKV infection reach 1%, the overall lethality rate of these complications can reach 30%.[24]

After more than 30 years of DENV surveillance in Brazil, notwithstanding the progress made, it was only with effect from 2016 that more robust evidence was found of dengue-associated deaths which had not been detected by passive surveillance services. In cities where death investigation services are sensitive and articulated with surveillance teams and laboratories, lethality can increase threefold, suggesting that dengue deaths may be underestimated in many places.[25,26]

The Brazilian Ministry of Health, in face of the first chikungunya and Zika deaths in 2015, adapted its dengue death investigation protocols for arbovirus death investigation.[13]

In 2017, the state of Ceará reported Brazil's largest chikungunya epidemic, with 137,424 (73.9%) cases. In addition, Ceará notified 80.1% of Brazil's chikungunya deaths in 2017. Dengue and Zika also circulated in Ceará, with 24,879 and 2,343 confirmed cases, respectively.

The purpose of this article was to describe the experience and the preliminary results of the Arbovirus Death Investigation Committee in Ceará, Brazil, in 2017.

Methods

This is an experience report on the creation of a death investigation committee, the objective of which was to investigate all suspected arbovirus deaths reported to the health services in Ceará. In face of the increasing number of suspected arbovirus deaths, Ceará State Health Department convened a group of professionals and created a multidisciplinary and interinstitutional arbovirus death investigation committee through Ordinance No. 2,099, dated November 29, 2016. The group is comprised of specialists in infectious diseases, epidemiology, pathology, general practice, pharmacy, nursing, physiotherapy and biology, working in sectors such as epidemiological surveillance, health care, infectious diseases reference hospitals, Public Health laboratories, universities and death investigation services.

This committee has weekly meetings, on Tuesdays, to present and discuss all suspected cases of arbovirus deaths notified by the epidemiological surveillance

system in Ceará. Notification may be done via the Notifiable Diseases Information System (SINAN), the Death Investigation Service (SVO) or even by health centers. A Committee secretary convenes the weekly meeting by e-mail sent to all members and informing of cases to be discussed.

The Committee members present available information on each case, based on investigations carried out in households, outpatient services, hospitals and laboratories, as well as by the SVO when autopsies are performed. Each case is presented by the practitioner who conducted the investigation and is then discussed based on the available information. After this presentation and discussion between Committee members, the case may be closed for not being an arbovirus case, confirmed for chikungunya, dengue or Zika, or confirmed for another arbovirus; or may even remain under investigation, according to the Ministry of Health case definition. In cases that remain under investigation, searching for complementary information is recommended as this is needed to conclude the investigation and to close the case.

Ministry of Health recommendations for laboratory diagnosis of arboviruses comprise serology tests (rapid test and/or Elisa), NS1, RT-qPCR, virus isolation or post mortem examinations such as immunohistochemistry. In these cases, serum, blood or viscera are used.

Results

In 2017, 443 suspected cases of arbovirus deaths were reported. Among these notified deaths, 312 (70.4%) were suspected cases of chikungunya and the remaining (131; 29.6%) were suspected dengue cases. No suspected cases of Zika deaths were notified that year. Of the notified deaths, 220 (49.7%) were confirmed, 222 (50.1%) were ruled out and one (0.3%) remains under investigation.

Among the confirmed cases, 179 (81.4%) were laboratory-confirmed with a positive result for at least one among the available techniques, while the other 31 (18.6%) cases were confirmed by clinical-epidemiological criteria. The main causes of the non-arbovirus deaths were leptospirosis, influenza and bacterial meningitis, among others.

Of the notified chikungunya deaths, 194 (62.2%) were confirmed in 29 (15.8%) different municipalities.

The municipality of Fortaleza stands out, with 144 (74.2%) of the state's confirmed deaths. Taking confirmed chikungunya deaths, 103 (53.1%) were male, with median age of 77 years (<1 to 105). The median time between the first symptoms and date of death was 14 days, with 75.0% of deaths occurring within up to 38 days (post-acute phase of the disease). The average time for chikungunya death investigation closure by the Committee was 81 days, with median time of 55 days (Table 1).

Regarding dengue, 26 deaths (19.8%) were confirmed in seven municipalities. Fortaleza stands out with 19 (73.1%) of these deaths. Thirteen women died (50.0%), with median age of 56 years (<1 to 93). Among the confirmed dengue deaths, median time with the disease was 6 days, with up to 12 days for 75.0% of confirmed cases. However, considering investigation difficulties, average time for dengue death investigation closure was 96 days, with a median time of 53 days (Table 1).

Deaths in which clinical suspicion of arbovirus occurred during autopsy, notified by the Ceará State Death Investigation Service (SVO/CE) as suspected dengue or chikungunya cases, had positive cerebrospinal fluid sample laboratory results. 27.0% of confirmed cases had positive IgM and/or AgNS1 cerebrospinal fluid results for dengue. 35.0% of confirmed chikungunya deaths had positive Ac IgM and/or RT-qPCR cerebrospinal fluid results.

Discussion

The characteristics of chikungunya deaths were very distinct from those of dengue deaths in terms of time with the disease until death and the median age of the cases. Whereas dengue deaths frequently occurred during the first week of the disease, this pattern was not repeated in chikungunya cases. Most chikungunya deaths seem to occur during the post-acute or even chronic phase of the disease. This poses yet another challenge for investigation of these deaths since infection generally decompensates underlying diseases, hindering investigation of the real cause of death and case closure.[27] Age at which death occurs also stands out: in Ceará, with regard to dengue, in recent years the age at which death occurs has tended to decrease,[6,20] while most chikungunya deaths occurred in the elderly or older adults.

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Table 1 – Main characteristics associated with deaths analyzed by the Arbovirus Death Investigation Committee in Ceará, 2017

Deaths investigated in 2017	Dengue fever	Chikungunya	Zika
Reported	131	312	–
Confirmed	26	194	–
Female sex	13	103	–
Median Age (from the youngest to the oldest)	56 (<1 to 93)	77 (<1 to 105)	–
Median disease time	6	14	–
Median investigation time	53	55	–

Moreover, the tendency of the cause of these deaths among the elderly to be more overlooked draws attention, considering the fact that their families rarely allow autopsies to be performed to confirm the cause. Another interesting finding was proof of central nervous system infection, given the positivity of Ac IgM, Ag and viral genome in the cerebrospinal fluid of many of these patients who died. An earlier study, carried out with patients referred by the Ceará Death Investigation Service, showed that dengue positivity in cerebrospinal fluid reached 48.8% for the DENV-2 and DENV-3 serotypes circulating at the time of the study.[28] In 2017 DENV-1 was in circulation, suggesting the possibility of this serotype having infected the central nervous system less than the serotypes studied earlier. With regard to the chikungunya virus, past studies showed neurological manifestations in India and on Reunion Island.[29,30] The results of the death analysis strongly suggest that these arboviruses play an important role in deaths of patients with central nervous system infection.

The relatively excessive time taken to close some cases involving death is due to the poor structure of some services and the lack of immunohistochemical tests in Ceará, showing an important limitation of death surveillance.

Given this new scenario, surveillance services struggle to close chikungunya death cases, because of doubts especially in cases with underlying disease decompensation, such as diabetes.[27] Frequently, issues such as whether chikungunya decompensated underlying diseases that led to death, or whether chikungunya evolved in an unsatisfactory way owing to the presence of some underlying disease, are part of Committee's routine when discussing cases. Another aspect to be considered is excessive medication absorbed by patients with chikungunya, mostly with no medical guidance, and whether there was any type of iatrogenic procedure during care for these patients.

The work of the Ceará Arbovirus Death Investigation Committee has shown that deaths associated with CHIKV infection are not brought to light by health authorities for many reasons, including : (i) shortcomings in the service offered to patients; (ii) association of chikungunya with the exacerbation of other existing diseases, resulting in deaths attributed exclusively to previous existing diseases, because of the lack of a thorough investigation that could classify CHIKV infection as the primary or secondary cause of death; (iii) the fact that severe chikungunya cases affect elderly patients, requiring a long stay in hospital, facilitating lethal hospital infections rarely associated with the initial infection condition; and (iv) the clinical expression of the disease with nonspecific symptoms and the occurrence of cases with atypical manifestations, especially neurological ones (encephalitis, meningitis), may confuse diagnosis.[23,27]

Authors' contributions

Cavalcanti LPG, Escóssia KNF, Simião AR, Linhares PMC, Lima AAB, Lopes KW, Braga DNM, Ramalho ILC, Mello LMS, Vale RLS, Barreto FKA, Oliveira RMAB, Lima Neto AS and Araújo FMC contributed with the study conception and design, case investigation, writing and critical review of the manuscript's intellectual content.All the authors have approved the final version and declared themselves to be responsible for all aspects of the study, ensuring its accuracy and integrity.

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