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Epidemiological aspects of arboviral diseases in epidemic and non-epidemic years in a brazilian metropolis

Aspectos epidemiológicos das arboviroses em anos epidêmicos e não epidêmicos em uma metrópole brasileira

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ABSTRACT
To describe and analyze the epidemiological aspects of arboviral diseases in epidemic and non-epidemic years in Fortaleza, state of Ceará, Brazil from 2008 to 2017. Ecological, quantitative and descriptive study with secondary data on dengue, chikungunya and zika, confirmed by clinical, epidemiological and laboratory criteria in epidemic and non-epidemic years. Statistical analysis was run in software R®. There were 188,617 confirmed cases of dengue, 79,529 of chikungunya and 1,619 of zika. The epidemic years of dengue were 2008, 2011 and 2012; chikungunya, 2017 and zika, 2016. The critical epidemiological weeks were the 12th to the 18th week and the diagnostic site was the emergency care unit. There was significance of $p<0.05$ for confirmed cases of dengue, clinical criterion and cure. Dengue, chikungunya and zika remain constant in incidence and prevalence in the Brazilian metropolis, constituting a challenge for managers and health professionals.

Keywords: Arbovirus infections. Epidemiology, Descriptive. Epidemics.

RESUMO
Descrever e analisar os aspectos epidemiológicos das arboviroses em anos epidêmicos e não epidêmicos em Fortaleza, Ceará, no período de 2008 a 2017. Estudo ecológico-descritivo com dados secundários sobre dengue, chikungunya e zika, confirmados por critério clinico epidemiológico e laboratorial nos anos epidêmicos e não epidêmicos. A análise estatística foi realizada no *software R*®. Foram confirmados 188.617 casos de dengue, 79.529 de chikungunya e 1.619 de zika. Os anos epidêmicos para dengue foram 2008, 2011 e 2012; chikungunya 2017 e zika 2016. As semanas epidemiológicas críticas são da 12ª a 18ª e o local de diagnóstico foi a unidade de pronto atendimento. Na análise estatística houve significância de $p<0,05$ as variáveis: casos confirmados de dengue, critério clinico e cura. A dengue, a chikungunya e a zika, permanecem constantes em incidência e prevalência na metrópole brasileira, constituindo um desafio para os gestores e profissionais de saúde.

Palavras chave: Epidemias. Epidemiologia descritiva. Infecções por arbovirus.

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INTRODUCTION

Arboviral diseases have been one of the main public health problems in the world, and can cause great economic impact on society. Dengue, chikungunya and zika are transmitted by the same vector, the *Aedes aegypti* mosquito, with increasing

presentation in recent years throughout Brazilian territory, and consequently an increase in cases of severe forms of the diseases, due to its high pathogenicity and rapid territorial spread.[1,2]

Dengue is the urban arbovirus with the highest incidence in the Americas and its etiological agent is the dengue virus (DENV), with four distinct serotypes. It is estimated that three billion people are at risk of getting the disease and that there are 390 million infections and 20,000 deaths annually[1,2].

In Brazil, dengue emerged at the end of the 19th century, in Curitiba, state of Paraná, and at the beginning of the 20th century, in Niterói, state of Rio de Janeiro. The first epidemic occurred in Boa Vista, state of Roraima, in the years 1980 to 1982, caused by serotypes one and four. In 1986, epidemics occurred in the state of Rio de Janeiro and in some capitals in the Northeast region[3].

In 2014, autochthonous transmission of chikungunya was detected in states of Amapá and Bahia, spreading to other Brazilian states. As of April 2015, autochthonous transmission of the Zika Virus (ZIKV) was confirmed in the state of Bahia and then in the states of Rio Grande do Norte, Pernambuco, Rio de Janeiro and São Paulo, with patients presenting a clinical condition of exanthematous fever[4].

Diseases caused by *Aedes Aegypti* present clinically similar symptoms, such as fever, headaches, joint pain, nausea and exanthema (skin rash or red spots on the body), although there are some striking symptoms that distinguish diseases. Federation Units (FUs) register autochthonous transmission of this arbovirus. These can manifest in an atypical and/or severe form, with observation of a high number of deaths[3].

In the state of Ceará, there have been cases of dengue reported since 1986, especially in the capital, Fortaleza, where the disease has presented endemic and epidemic periods, with the record of seven major epidemics in 1987, 1994, 2001, 2008, 2011, 2012 and 2015. As of 2015, autochthonous transmission of chikungunya and zika viruses was also confirmed. With the endemic circulation of three arboviruses (dengue, chikungunya and zika), new epidemiological scenarios are identified in the state of Ceará in 2017, mainly in cases of chikungunya[6].

Since 1986, 316,583 cases and 275 deaths have been confirmed in the capital Fortaleza. The sum of cases registered in the epidemic years of 1994 (DENV2), 2008 (DENV2), 2011 (DENV1) and 2012 (DENV4) represents 42.1% (133,421/316,583). In the years when DENV3 was the predominant serotype (2003-2007), no major epidemics were recorded. Still in Fortaleza, cases of zika, initially considered as “benign”, changed this status when the zika virus started to be associated with a growing number of microcephaly cases[7].

With climate change and international exchange, arboviruses cause wide dispersion across countries, especially in the last ten years, which makes differential clinical diagnosis difficult[3,8]. The high numbers of morbidity and mortality presuppose direct implications for health services, especially with the lack of vaccines and other protective viral control measures[4,9].

As provided in Consolidation Ordinance 4, of September 28, 2017, dengue, chikungunya and zika are notifiable diseases, whose suspected and/or confirmed case must be notified to the Epidemiological Surveillance Service of the Municipal Health Department (SMS), with ongoing investigation to strengthen health surveillance actions.[3] Thus, the objective of the study was to describe and analyze the epidemiological aspects of arboviruses in epidemic and non-epidemic years in Fortaleza, state of Ceará, Brazil, from 2008 to 2017.

METHOD

This was an epidemiological ecological study, with a descriptive quantitative design, with a time series. Data collected correspond to the period from 2008 to 2017 and include confirmed cases of the arboviruses dengue, chikungunya and zika, in the municipality of Fortaleza, state of Ceará, which is administratively divided into six Regional Executive Secretariats (SER) and 119 neighborhoods[10].

Epidemiological data were obtained from the Notifiable Diseases Information System (SINAN), in its Sinan-Online version, from the Daily Disease Monitoring System (SIMDA), from the Municipal Health Department, and from epidemiological bulletins.

Cases confirmed by clinical-epidemiological and laboratory criteria were included in the study, and then the incidence of the three arboviral diseases per year was calculated, defining as epidemic year the one at which the incidence rate (TI) was greater than one thousand cases per 100 thousand inhabitants, and as non-epidemic year when the incidence was less than one thousand cases per 100 thousand inhabitants. It was classified into epidemic (2008, 2011, 2012, 2015 and 2017) and non-epidemic (2009, 2010, 2013, 2014, 2016) years. Other study variables were: age group (in years), evolution, type of establishment and health regions.

Then, the data of interest were extracted, digitized and analyzed using tables and graphs, built in Microsoft Excel® 2013. In the descriptive analysis of data, variables are represented in the text as absolute and/or relative frequencies.

Data were tested for normality, with subsequent parametric statistical analysis with Student's t-test for normal data, and the Wilcoxon test, for non-normal data, using Software R 4.0.2 for Windows®. In all

cases, the significance criteria of 5% were used.

Independent variables used were related to dengue, zika and chikungunya as they are the arboviral diseases analyzed in the study. Independent variables and outcomes are related to clinical or laboratory diagnosis, age, clinical outcome, and diagnostic site. According to Resolution 510/2016, of the National Health Council, studies including research with information in the public domain do not require approval from the research ethics committee.[11] The study did not present risks to the individuals involved, since it was from a document-based research.

RESULTS

Table 1 lists the annual average of dengue cases (2008-2017), with 18,862 confirmed cases (average incidence rate of 741.3 cases/100,000 inhab.), followed by chikungunya with an annual average of 26,510 cases (average incidence rate of 336.7 cases/100,000 inhab.) and Zika with an annual average of 540 cases (average incidence rate of 20.4 cases/100,000 inhab.). Chikungunya and Zika have records from 2015.

Table 1. Confirmed cases and incidence of dengue, chikungunya, and zika in Fortaleza, from 2008 to 2017, Fortaleza, state of Ceará, Brazil, 2018

Arboviral diseases	2008-2009	2010-2011	2012-2013	2014	2015	2016	2017
Dengue							
Cases (%)	34,975 (18.5)	38,419 (20.4)	47,844 (25.4)	5,149 (2.7%)	26,816 (14.2)	21,853 (11.6)	13,561 (7.2)
Incidence (100,000/inhab.)	1,412.2	1,551.3	1,874.9	198.7	1,034.9	826.7	513
Chikungunya							
Cases (%)					13 (0.0)	17,789 (22.4)	61,727 (77.6)
Incidence (100,000/inhab.)	-	-	-	-	0.5	673	2,335.3
Zika							
Cases (%)					21 (1.3)	1,329 (82.1)	269 (16.6)
Incidence (100,000/inhab.)	-	-	-	-	0.8	50.3	10.2

Source: Notifiable Diseases Information System and Daily Disease Monitoring System, 2018.

The analysis from 2008 to 2014 referred only to dengue, namely: in 2008, there were 31,550 (16.7%) cases and an incidence of 1,275.5; in 2009, 3,425 (1.8%) cases and 136.70 incidence. In 2010, 3,924 (2.1%) cases and 158.4 incidence. The year 2011 had 34,495 (18.3%) cases and 1,392.84 incidence. For 2012, 39,048

(20.7%) cases and 1,530.21 incidence; in turn, in 2013, 8,796 (4.7%) cases and 344.7 incidence. All incidences were calculated for 100,000 inhabitants. The absolute value and statistical value for arboviral diseases from 2008 to 2017 were: dengue (n=188,617, p=0.001), chikungunya (79,529, p=0.18) and zika (1,619, p=0.37).

Figure 1 illustrates the progression curve of arboviral infections in five epidemic years (2008, 2011, 2012, 2015 and 2017) and five non-epidemic years (2009, 2010, 2013, 2014 and 2016). It is noteworthy that the years 2008, 2011, 2012 and 2015 were epidemic of dengue and the year 2017, of chikungunya.

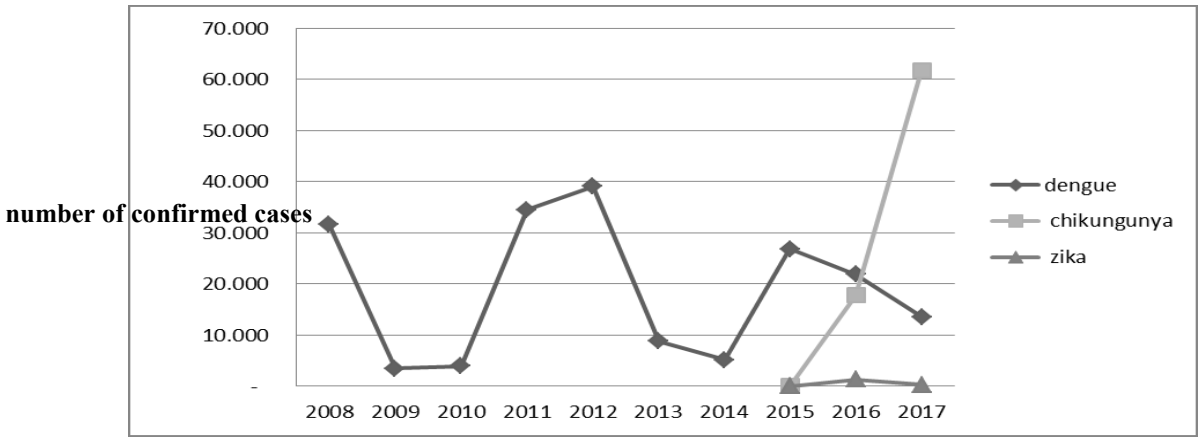

Figure 1: Seasonal variation in years of confirmed cases of arboviral diseases in Fortaleza, state of Ceará, Brazil, 2008 -2017.
Source: Prepared by the authors, 2018.

From the epidemic years of dengue, the incidence of cases is also observed per epidemiological week. In this sense, in 2008 the peak of cases occurred between the 12th and the 17th week, with a rapid decline from the 18th week onwards. In 2011, the increase in cases occurred from the 6th to the 14th week, with a decrease in cases from the 15th week onwards. In 2012, there was an increase in the number of cases from the 8th to the 19th week, with stabilization from the 19th to the 20th week, and attenuation from the 21st week onwards. In 2015, there was a significant increase from the 13th to the 19th week, with a reduction in the 20th week. The average, in weeks, of the incidence of dengue cases in the municipality of Fortaleza was 8.5.

In non-epidemic years, the characteristics in the incidence of positions differed from those of epidemic years. In 2009, the epidemic was controlled between the 13th and the 36th week, in 2010, from the 13th to the 34th week, which also occurred in 2014. In 2013, the epidemic was controlled between the 14th and the 34th week, and in 2016, it ranged from the 16th to the 35th week.

The results in Table 2 showed that epidemic years are divided between epidemics of dengue (2008, 2011, 2012 and 2015) and chikungunya (2017). In this sense, there is a prevalence of chikungunya data in 2017 (n=61,727, 87.5%), followed by dengue cases in 2012 (n=39,048, 89.4%), 2011 (34,495, 90.2%) and 2008 (n=31,550, 88.9%), respectively. The clinical diagnostic criterion was the most used in all years, with diagnoses mainly in the age group from 19 to 59 years and evolution favorable to cure.

Table 2. Epidemiological characteristics of dengue and chikungunya in epidemic years in Fortaleza, state of Ceará, 2008-2017

Variables	2008 Dengue		2011 Dengue		2012 Dengue		2015 Dengue		2017 Chikv		p
	n	%	n	%	n	%	n	%	N	%	
Dengue/Chikungunya											
Investigated cases											
Confirmed	31,550	88.9	34,495	90.2	39,048	89.4	26,816	64.3	61,727	87.5	p=0.004
Discarded	3,939	11.1	3,737	9.8	4,620	10.6	14,890	35.7	8,815	12.5	
Criterion											
Clinical	27,100	86.0	30,777	89.2	35,282	90.4	21,522	80.3	50,092	81.2	p=0.003
Laboratory	4,421	14.0	3,718	10.8	3,766	9.6	5,294	19.7	11,635	18.8	
Age group (years)											
0-9	7,549	23.9	7,218	18.9	3,946	10.1	2,341	8.7	3,632	4.6	p=0.37
10-18	7,042	22.3	8,786	23.0	8,308	21.3	6,010	22.4	8,801	11.1	
19-59	15,560	49.4	20,303	53.1	24,666	63.2	17,047	63.6	53,902	67.8	
≥ 60	1,370	4.3	1,932	5.1	2,128	5.4	1,418	5.3	13,181	16.6	
Evolution											
Death	17	0.1	26	0.1	21	0.1	31	0.1	144	0.2	p=0.69
Cure	30,494	97.1	31,841	92.3	37,369	95.7	26,740	99.7	61,241	99.2	
Ignored/blank	905	2.9	2,628	7.6	1,658	4.2	45	0.2	342	0.6	

Source: Notifiable Diseases Information System and Daily Disease Monitoring System, 2018.

Regarding the establishment where the disease was confirmed, there were seven places qualified to diagnose arboviral diseases between 2008 and 2017, as presented in Table 3. In relation dengue, there were 164,269 diagnoses, mainly in emergency care units (UPAs), primary health care units (UAPs) and State or Federal hospitals, respectively. Considering chikungunya and zika, the UPAs and UAPs prevailed.

Table 3. Health facility-confirmed cases of dengue, chikungunya, and zika from 2008 to 2017, Fortaleza, state of Ceará, Brazil, 2018

Variables	Dengue		Chikungunya		Zika	
	n	%	n	%	n	%
Facility						
Emergency care unit	82,909	50.5	29,369	36.9	480	30.0
Uaps	42,834	26.1	32,781	41.2	956	59.8
State/Federal Hospital	20,431	12.4	5,032	6.3	6	0.4
Municipal Hospital	13,430	8.2	6,689	8.4	144	9.0
Private/Philanthropic Hospital	3,327	2.0	2,458	3.1	2	0.1
Laboratory	43	0.0	2,674	3.4	-	-
Ignored/Other municipalities	262	0.2	53	0.1	-	-
Others	1,033	0.6	460	0.6	10	0.6

Source: Sinan Online, 2019

Figure 2 shows the distribution of confirmed cases from 2008 to 2017, according to the Coordination of Regional Health Units (CORES), in which dengue reached 192,242 cases, chikungunya, 77,491 and zika, 1,571 cases.

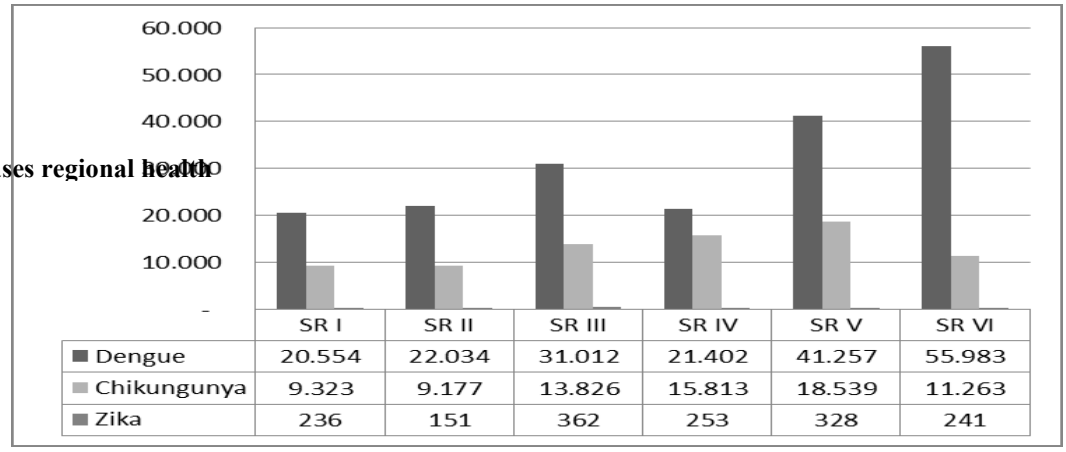

Figure 2. Confirmed cases of dengue, chikungunya and zika per regional health (SR) unit in Fortaleza, state of Ceará, Brazil, from 2008 to 2017.
Source: Prepared by the authors, 2019.

Dengue showed the highest number of cases in regional units VI (n=55,983, 29.1%) and V (n=41,257, 21.5%), chikungunya in regional units V (n=18,583, 23.8 %) and IV (n=15,813, 20.3%) and zika in regional units III (n=362, 23.0%) and V (328, 20.9%).

Regarding statistical analysis, data referring to the univariate analysis with the dengue variable and dependent variables were significant, namely: confirmed cases of dengue (p=0.001), clinical criteria (p=0.002), cure (p=0.003), according to Student's t- test. The variables analyzed

with wilcox were: laboratory criteria (p=0.06), deaths (p=0.06) and ignored (p=0.06), with significance for those related to the place of diagnosis for dengue (p=0.007), chikungunya (p=0.007) and zika (p=0.03). The bivariate analyses were described in tables with significant values in the Student's t-test for confirmed and discarded cases (p=0.004), clinical and laboratory criteria (p.0.003). Ages had p≥0.37 and were not significant.

DISCUSSION

In the municipality of Fortaleza, arboviral diseases of greatest concern to public health are dengue, chikungunya and zika. The emergence of chikungunya and zika in the municipality increased the problems related to combating diseases transmitted by *Aedes aegypti*.[10]

This study evidenced that, from 2008 to 2017, the three arboviral diseases totaled 269,765 confirmed cases in the municipality of Fortaleza, state of Ceará. In this period, there were four dengue epidemics, the main one in 2012 and one chikungunya epidemic in 2017. A study carried out in Natal, state of Rio Grande do Norte, in 2007 - 2012, states that the year 2008 was considered epidemic in most Brazilian municipalities, as it had a high incidence of dengue cases.[12]

According to the Ministry of Health, the capitals: Rio de Janeiro (state of Rio de Janeiro), Fortaleza (state of Ceará) and Goiânia (state of Goiás) for two consecutive years (2011 and 2012) had the highest number of dengue cases among the Brazilian municipalities. However, some federation units showed an increase in the number of cases and incidence in 2012, such as in the states of Roraima (182.5 cases per 100 thousand inhabitants), Sergipe (184.4 cases per 100 thousand inhabitants), Bahia (200.9 cases per 100 thousand inhabitants), Alagoas (207.2 cases per 100 thousand inhabitants), Pernambuco (311.4 cases per 100 thousand inhabitants), Mato Grosso (454.7 cases per 100 thousand inhabitants) and Tocantins (837.7 cases per 100 thousand inhabitants) per 100,000 inhabitants).[3] This corroborates the data of this study.

In Manaus, state of Amazonas, studies carried out from 2000 to 2012 showed the largest dengue epidemic in 2011 with an incidence of 1,612.4 per 100 thousand inhabitants.[13] In this study, 2011 was an epidemic year of dengue with the second highest incidence per 100 thousand inhabitants in the years studied.

A study carried out in São Luís, state of Maranhão, between 2002 and 2012, revealed that in 2011 there was the introduction of DENV-4, with an epidemic explosion with high incidence rates and a

large number of cases.[14] In this study in 2011, there was 34,495 cases of dengue in Fortaleza, state of Ceará, with an increase of 4,553 cases for the same period of the following year.

Cases in epidemic years, even within the same geographic region as the Northeast, fluctuate significantly. This is due to the time of introduction of dengue in the region, diversity of circulating serotypes, differences in susceptibility to different serotypes, simultaneous presence of these serotypes, in addition to the installed capacity of local epidemiological surveillance and vector control actions developed.[15]

The distribution of probable cases, in the time window studied, highlights epidemic years, the first being in 2008 with the circulation of DENV2. Subsequently, Brazil faced epidemics in the years 2010, 2013, 2015 and 2016, marked by the reintroduction of new serotypes (2010 and 2013), as well as the introduction of the new arboviruses chikungunya and zika viruses, respectively, marked in the 2015 and 2016 epidemics.[3] These findings corroborate the data described here and also the epidemics in other Brazilian cities, such as Manaus (state of Amazonas), Rio de Janeiro (state of Rio de Janeiro), Natal (state of Rio Grande do Norte), São Luiz (state of Maranhão) and Goiânia (state of Goiás).

With respect to the age group, there was a predominance of the age group 19-59 years old for all epidemic years of this study, totaling 131,478 people infected with dengue and chikungunya. Several studies revealed a similar age group and point to losses regarding the economically active age group, which may lead to absences from work activities, sequelae and deaths.[16]

In Mato Grosso, a research carried out from 2007 to 2017 for dengue showed cumulative cases in the age group from 31 to 54 years.[2] In a multicenter study conducted from 2008 to 2013 in all regions of the country, the highest rates were observed in the age group that comprises 15 to 59 years of age.[16] In São Luís, state of Maranhão, from 2002 to 2012, the most affected age group was 20 to 49 years, affecting mainly females.[14] These studies corroborate the age group found in the present study.

In Fortaleza, during the epidemics, there were 144 deaths from chikungunya in 2017, showing the highest number of deaths in the world and causing several sequelae in the most serious cases considered chronic cases of the disease. Epidemiological aspects point to an increasing number of people affected by chikungunya in the last 10 years. Of these, the cumulative number of infected individuals suffering from disabling or long-term pain is estimated to

be approximately 1 to 2 million, generating high costs for health systems.[17]

In Brazil, the year 2015 concentrated the highest number of deaths (863), caused by dengue, with a reduction in the following years. In the period from 2003 to 2019, the mortality rate in Brazil was 3/100 thousand inhabitants, with emphasis on the states of Goiás, Mato Grosso, Ceará, Mato Grosso do Sul and Espírito Santo, with average mortality rates up to three times greater than the national. Regarding chikungunya, the highest concentration of cases and deaths occurred in the Northeast region, with emphasis on Ceará in 2017 with 61.4% cases and 80% deaths in the country (incidence of 1,264.2 cases per 100 thousand inhab.).[3] In the present study, in 2015, there were 31 deaths, the second highest number in ten years.

Still from an epidemiological point of view, another variable analyzed in this study was the health units that confirmed the arbovirus infection by dengue, chikungunya or zika in Fortaleza. The UPAs and UAPS confirmed most cases treated in these units. It is worth mentioning that both types of units are public services of the municipality, configuring the certainty of the diagnosis through emergency and/or outpatient care provided to the population, mostly by the Unified Health Service.[10] In the UPAs, 112,758 were confirmed, and in the UAPS, 76,571 of the three arboviral diseases dengue, chikungunya and zika, respectively.

Study carried out in ten capitals, all of them located in endemic areas, demonstrated the difficulties of their surveillance systems in detecting hospitalized cases, the SINAN and SIH-SUS databases identified an additional 69,935 hospitalizations from dengue, which is equivalent to 50.3% more hospitalized records computed in the SINAN.[16] In this study, dengue was diagnosed in the UPAs with 82,909 cases.

To better identify the areas of disease caused by arboviruses, this study identified the health units where the territorial areas in the municipality of Fortaleza were concentrated in the period from 2008 to 2017. From this idea, it was observed that regional health units V and VI, considered the most populous in the capital of Ceará totaled 97,240 confirmed cases of dengue. Chikungunya cases were identified in greater numbers in health units V and zika in health unit III, the study revealed simultaneous circulation of mosquitoes in all areas, but in areas with poorer population levels, sanitation, among other social conditions, there was greater contamination by the virus causing arboviral diseases.

The municipality of Fortaleza adopted, through Municipal Law 8000 of January 29, 1997, the municipal

administrative organization with the objective of decentralizing management. Thus, the municipality had its territory divided into 06 (six) administrative regions. Precarious areas are concentrated in regional health units I, IV, V and VI, for the most part, they are located in unhealthy and risky areas, mainly on the banks of rivers and streams and subjected to periodic floods.[10]

In addition to the interference and modification of ecosystems by human action, other factors are also related to the emergence of arboviruses in large centers, such as disordered urban population growth, the process of globalization and expansion of international exchange with climate change.[18-19]

CONCLUSION

The study reveals the epidemiological aspects that interfere with the prevention and control of arboviral diseases in Fortaleza, accentuated by the increase of dengue, chikungunya and zika, mainly in epidemic years.

In the period from 2008 to 2017, 269,765 cases of arboviral diseases and 239 deaths were confirmed, 245,382 were attended in public and private health services, with epidemics (2008, 2011-2012 and 2015) of dengue and (2017) of chikungunya, in addition to four non-epidemic years (2009-2010 and 2013-1014, 2016). In epidemic years, the incidence was always higher than 1,000 cases/100 thousand inhabitants. The most populated areas and considered precarious in terms of sanitation and unfavorable environmental and social characteristics also contributed to the increase in these values.

As limitations to the study, it is inferred the underreporting of cases, the incompleteness of data in the information systems and the need to update and train the servers that feed these research sources.

In this way, it is understood that dengue, chikungunya and zika remain constant in the metropolis of the state of Ceará, being a challenge for managers and health professionals, especially in epidemic years, increasing epidemiological indices and the precariousness of health services. It is expected that new studies can elucidate the cases of arboviral diseases in all Brazilian capitals with a multilevel design, bringing effective alternatives to reduce the diseases caused by arbovirus.

PRACTICAL AND/OR EPIDEMIOLOGICAL APPLICATIONS OF THE STUDY

The study allows the identification of the territory and helps in referencing the areas of vulnerability to arboviruses in the municipality of Fortaleza. In addition, it

analyzes the diseases epidemiologically, highlighting the need to know the relationship between epidemic and non-epidemic years with meteorological and management variables, so that strategies are applied to minimize the risks of contagion for the population.

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