TIME SERIES ANALYSIS OF INCIDENCE OF DENGUE AND AEDES AEGYPTI IN CEARÁ

Série histórica da dengue e do Aedes aegypti no Ceará

Serie historica de la dengue y el Aedes aegypti en Ceará

ABSTRACT

Objective: To analyze the epidemiological behavior of dengue in the state of Ceara and the control of Aedes aegypti. **Methods**: This is a documentary study that used as data source the epidemiological bulletins published by the Ceara State Department of Health and other complementary documents from 1986 to 2011. A descriptive analysis of the incidence of dengue in this period was carried out according to age, severe forms, deaths and circulation of DEN-V virus. The study analyzed the vector control program and the evolution of infestation and dengue transmission in the same period. **Results**: It was found that, from 1986 to 2011, Ceara had five dengue epidemics with high incidence rates, and from 2008 to 2010, children were the most affected group. On average, there was Aedes aegypti infestation in 120 municipalities and transmission in 84 of them annually. The circulation of more than one serotype resulted in a large number of deaths almost every year, more than that estimated by the World Health Organization. **Conclusion**: The epidemiological behavior of dengue in Ceara justifies the classification made by the Ministry of Health that acknowledges the State as a Very High Risk-area with vulnerability to the disease. In recent years, the rate of severe cases has increased, probably because of the simultaneous circulation of three serotypes and the population's sensitization due to previous infections. This situation is aggravated by the vector presence in nearly the entire State and a deficient vector control policy.

Descriptors: Dengue; Aedes; Vector Control.

RESUMO

Objetivo: Analisar o comportamento epidemiológico da dengue no Ceará e o controle do Aedes aegypti. Métodos: Trata-se de um estudo documental, com base na consulta aos boletins epidemiológicos divulgados pela Secretaria Estadual de Saúde do Ceará referentes ao período de 1986 a 2011 e outros documentos complementares. Realizou-se análise descritiva da incidência de dengue no Ceará nesse período, segundo faixa etária, formas graves, óbitos e circulação do vírus DEN-V. Analisou-se o programa de controle vetorial e a evolução da infestação e transmissão da dengue no mesmo período. Resultados: Constatou-se que, de 1986 a 2011, ocorreram cinco epidemias de dengue no Ceará, com elevada incidência, sendo que, de 2008 a 2010 as crianças foram as mais acometidas. Em média, houve infestação pelo Aedes aegypti em 120 municípios e transmissão em 84, anualmente. A circulação de mais de um sorotipo culminou em um grande número de óbitos quase todos os anos, superior ao aceitável pela Organização Mundial de Saúde. Conclusão: O comportamento epidemiológico da dengue no Ceará justifica a classificação de "área de vulnerabilidade de risco muito alto" feita pelo Ministério da Saúde. Nos últimos anos, a proporção de casos graves tem aumentado, decorrendo, provavelmente, da circulação simultânea de três sorotipos virais e da população sensibilizada por infecções anteriores. Essa situação é agravada pela presença do vetor em quase todo o estado e pela deficiência da política de controle vetorial.

Descritores: *Dengue; Aedes; Controle Vetorial.*

Estelita Pereira Lima[1]
Marília Oliveira Fonseca Goulart[2]
Mário Ronaldo Albuquerque[1]
Fernanda Moura Victor[1]
Natália Bitu Pinto[1]

1) Federal University of Ceará
(*Universidade Federal do Ceará – UFC*) -
Fortaleza (CE) - Brazil

2) Federal University of Alagoas
(*Universidade Federal de Alagoas – UFAL*)
- Maceió (AL) - Brazil

RESUMEN

Objetivo*: Analizar el comportamiento epidemiológico de la dengue en Ceará, y el control del Aedes aegypti.* **Métodos***: Se trata de un estudio documental basado en revisiones de boletines epidemiológicos divulgados por la Secretaria Estadual de Salud de Ceará, correspondientes al periodo entre 1986 y 2011 y otros documentos complementares. Se realizó un análisis descriptivo de la incidencia de dengue en Ceará nesse periodo según la franja etaria, formas graves, muertes y circulación del virus DEN-V. Se analizó el programa de control vectorial y la evolución de infestación y trasmisión de la dengue en el mismo periodo.* **Resultados***: Se constató que entre 1986 y 2011 ocurrieron cinco epidemias de dengue en Ceará con elevada incidencia, siendo que, entre 2008 y 2010 los niños fueron los más acometidos. Hubo una media de 120 municipios con infestación por el A. aegypti al año y transmisión en 84 de ellos. La circulación de más de un serotipo dio lugar a un gran número de muertes casi cada año, más del aceptable por la Organización Mundial de la Salud.* **Conclusión***: El comportamiento epidemiológico de la dengue en Ceará justifica la clasificación hecha por el Ministerio de la Salud, en Área de vulnerabilidad de Riesgo Muy Elevado para la aparición de la enfermedad. En los últimos años la proporción de casos graves ha aumentado probablemente en consecuencia de la circulación simultánea de tres serotipos virales y de la población sensibilizada por infecciones anteriores. Esta situación está peor por la presencia del vector en casi todo el Estado y por la deficiencia de la política de control vectorial.*

Descriptores*: Dengue; Aedes; Control de Vectores.*

INTRODUCTION

Dengue is an arbovirus disease whose vectors are the mosquitoes of the genus *Aedes*. It has an acute febrile evolution and its etiologic agent is composed of four serotypes of the dengue virus (DENV), namely: DENV-1, DENV-2, DENV-3 e DENV-4, belonging to the *Flaviviridae*[1] family.

Over the last 50 years, the incidence of dengue increased by 30 times with an increasing geographic expansion to new countries and, in the last 10 years, to small towns and rural areas[2]. A recent study estimates that about 390 million DENV infections occur annually, a number three times higher than estimated by the World Health Organization[3]. Approximately 500 thousand new cases of dengue hemorrhagic fever (DHF) are registered worldwide[4].

Studies in Asian and American countries, including Brazil, revealed that dengue epidemics cost the public coffers about U$ 1.8 billion just with ambulatory and hospital expenses, not including the cost of surveillance activities, vector control and social mobilization[5].

Aedes aegypti is the only DENV vector of epidemiological importance in the Americas[6], where it found favorable climate and conditions for its rapid expansion into cities created disorderly, deficient in water supply and urban sanitation. Added to these factors is the use of disposable containers that serve as breeding grounds for the mosquito[4].

In Brazil, the *Aedes aegypti* mosquito is found nationwide. Out of the four serotypes of the DENV virus, three were circulating (DENV-1, -2 and -3) and at the end of 2010 DENV-4 was reintroduced in the state of Roraima[7], a situation which increased the risk of occurrence of the severe forms of this disease, lethality and deaths[5].

In Ceará, the *Aedes aegypti* mosquito was found in the 1950s, as a vector of yellow fever. After the eradication of this disease, the mosquito was only reintroduced in the state in 1984, in the municipality of Aquiraz[8,9], from where it became widespread. In 2011, its presence was registered in 87.5% of the territory of Ceará and dengue transmission occurred in 96% of the municipalities[10].

Dengue has been endemic in Ceará for 25 years and with high incidence. Since 2011, three viral serotypes have been circulating within the state (DENV-1, -3 and -4) and approximately 47% of the municipalities are considered "vulnerable areas ranging from high to very high risk" of transmission of the disease[10].

Based on the above, the objective of this study is to analyze the epidemiological behavior of dengue in Ceará and the control of the *Aedes aegypti* mosquito.

METHODS

A documentary descriptive study was conducted about dengue in the state of Ceará from 1986 to 2011. Epidemiological bulletins published weekly by the State Health Secretariat were used as a source of data along with nine documents (including articles, dissertations and monographs) that were used to complement the information gathered.

The following aspects were taken into consideration by this prescriptive analysis of the incidence of dengue in the state of Ceará during the period under investigation: group age, severe forms of viral manifestation, deaths and the circulation of the DENV virus. In addition to these variables, the performance of insecticide and vector control programs put into practice by the state was analyzed, as well as the evolution of the infestation and transmission of dengue in this period. The incidence (IR/100,000 inhab.) and lethality (LR) rates expressed in the bulletins along with the other variables analyzed helped Excel tables and graphics be built.

RESULTS

The first cases of dengue in Ceará occurred in 1986 with the notification of 4,419 people infected with DENV-1. The following year, the number of cases rose to 22,519, registering the first epidemic (Tables I and II).

Tabela I - Serotypes of DENV in circulation. Ceará, 1986-2011.

Year	Serotype of DENV in circulation
1986-1993	DENV-1
1994-2001	DENV-1 e 2
2002	Introdução em circulação do DENV-3
2003	DENV-1, 2 e 3
2005	DENV-1 e 3
2006-2008	DENV-2 e 3
2009	DENV- 2
2010	DENV-1 e 2
2011	DENV-1, 3 e 4

Sources: Coordination for Health Promotion and Protection / Center for Epidemiological Vigilance, State Health Secretariat of Ceará (*Secretaria de Saúde do Estado do Ceará - SESA-CE*), Central Laboratory of Ceará (*Laboratório Central do Ceará - LACEN-CE*).

Tabela II - Number of cases and dengue incidence rate per age group. Ceará, 1986-2011.

Year	No. of cases	Incidence 100.000 inhab.	predominant age group (age)
1986	4.419	75.6	***
1987	22.518	378.9	***
1988	385	6.3	***
1989	4.126	67.1	***
1990	15.725	231.7	***
1991	6.709	105.4	***
1992	165	12.5	***
1993	8	0.1	***
1994	47.789	732.3	***
1995	66	0.9	***
1996	789	11.3	***
1997	1.264	18.4	***
1998	3.581	51.0	60 and older
1999	9.757	138.9	60 and older
2000	13.645	189.5	20-59
2001	34.390	455.6	20-59
2002	16.465	218.1	20-59
2003	23.796	306.7	20-59
2004	3.094	39.5	20-59
2005	22.817	234.4	60 and older
2006	25.569	305.0	60 and older
2007	25.026	304.5	20-59
2008	44.508	533.9	< 1 year
2009	5.144	60.1	< 1 year
2010	13.817	161.6	< 1 year
2011	56.714	670.9	20-59

***Data not available Coordination for Health Promotion and Protection / Center for Epidemiological Vigilance, State Health Secretariat of Ceará (*Secretaria de Saúde do Estado do Ceará - SESA-CE*), Central Laboratory of Ceará (*Laboratório Central do Ceará - LACEN-CE*), Cavalcanti *et al*., 2011[23].

Between 1986 and 1993, 54,055 cases of classic dengue were reported. In 1994, there was another epidemic process, with 47,789 notifications (incidence rate of 732.31 / 100,000 inhab.) and with the introduction of DENV-2 in the state, the lethality rate (LR) for dengue hemorrhagic fever (DHF) reached 48% (Tables I, II and III).

The incidence of dengue from 1997 to 2001 is presented in ascending order. In 2000, however, the incidence rate was considered low, but, out of the four DHF cases reported, three died (75% LR) (Tables II and III).

In 2001, 34,390 cases were reported, among which, 78 were DHF cases, with a proportion of 10.2% of deaths. In 2002, there was the introduction of DENV-3 and the simultaneous circulation of three serotypes (Tables I and II).

The fourth epidemic took place in 2008, when the highest number of cases of severe forms of the disease was recorded: 639 cases with complications and 448 cases of DHF. A total of 44,244 cases were registered, corresponding to an incidence rate of 530.77/100,000 inhab. The children were the most affected group, especially those younger than one year (Table II).

In 2009, the second lowest incidence rate of dengue within the last 12 years (60.18/100,000 inhab.) and the circulation of only one serotype (DENV-2) were registered. However, despite the lower number of cases of severe forms (97), the DHF lethality rate was 34.6% and the rate of cases with complication was 48% (Tables I, II and III).

The serotype DENV-1 was isolated again in 2010, which had not circulated within the state since 2005. Dengue incidence rate was kept low, below 200/100,000 inhab., but with an undesirable lethality rate. In all, 22% of the cases presenting complications led to death and so did 11% of DHF cases (Tables I, II and III).

The fifth dengue epidemic took place in 2011, with a record of 56.714 cases, mainly in the age group ranging from 20 to 59 (Table II). When DENV-4 was introduced in the state of Ceará, three serotypes (DENV-1, DENV-3 and DENV-4) began circulating simultaneously (Table I). In terms of lethality, 62 deaths were registered, which showed that this epidemic had been more lethal than the previous one (Table III).

The control of Aedes aegypti mosquito in Ceará has been primarily chemical. From 1986 to 2011, larvicides and adulticides belonging to the organophosphates and pyrethroids groups, biological agents, such as *Bacillus thuringiensis israelensis* (Bti) and growth regulators

Tabela III - Number of DHF cases, dengue cases with complications and Lethality rate. Ceará, 1994-2011.

Year	DHF Cases Lethality (%)	Dengue cases with complications/lethality
1994	25 (48.0)	-
1995	-	-
1996	-	-
1997	-	-
1998	4	-
1999	3	-
2000	4 (75.0)	-
2001	78 (10.2)	2
2002	71 (12.6)	-
2003	291 (6.8)	65 (18.4)
2004	14 (7.1)	31 (3.2)
2005	199 (12.0)	164 (4.2)
2006	172 (8.7)	170 (11.7)
2007	300 (4.0)	410 (4.4)
2008	448 (5.1)	639 (3.2)
2009	26 (34.6)	71 (48.0)
2010	63 (11.1)	105 (22.0)
2011	174 (7.5)	457 (10.7)

Sources: Coordination for Health Promotion and Protection / Center for Epidemiological Vigilance, State Health Secretariat of Ceará (*Secretaria de Saúde do Estado do Ceará - SESA-CE*), Central Laboratory of Ceará (*Laboratório Central do Ceará - LACEN-CE*).

(diflubenzuron) were used. Between 1986 and 2000, organophosphates were used in vector control programs in most parts of the state. From 2001 to 2009, there has been a partial substitution of this larvicides for Bti and the

adulticides for pyrethroids in all municipalities. In 2010, there was the substitution of two products: the larvicide for diflubenzuron and the adulticides for malathion (Figure 1).
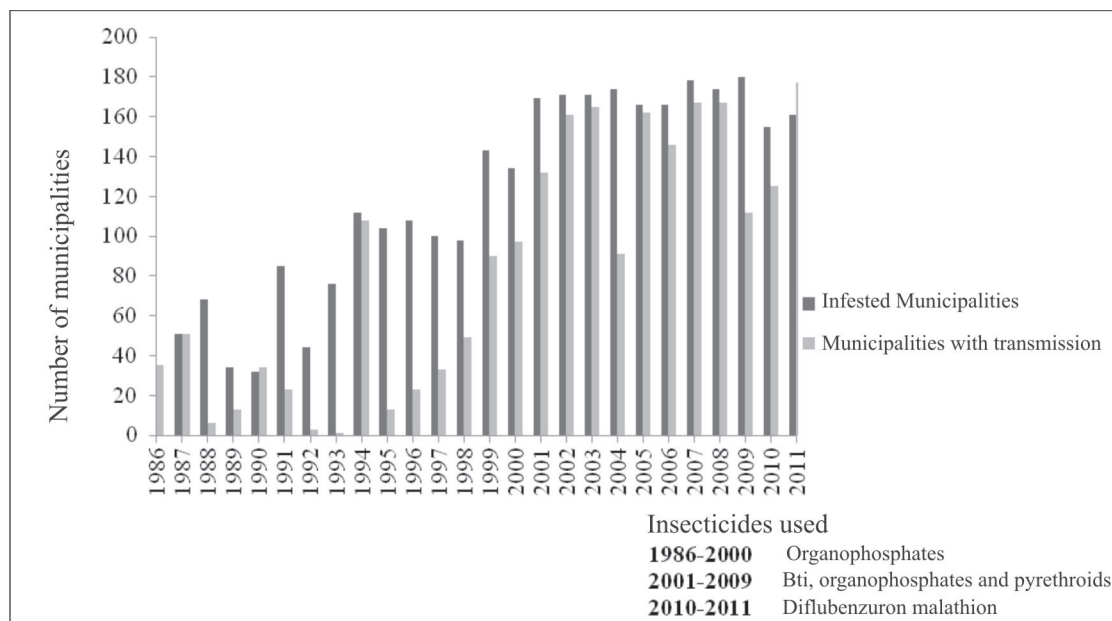

Figure 1 – Number of municipalities infested by *Aedes aegypti* with dengue transmission and insecticides used in vector control program in Ceará from 1986 to 2011.
Sources: Coordination for Health Promotion and Protection / Center for Epidemiological Vigilance, State Health Secretariat of Ceará (*Secretaria de Saúde do Estado do Ceará - SESA-CE*), Central Laboratory of Ceará (*Laboratório Central do Ceará - LACEN-CE*).

Figure 1 shows that, from 1986 to 2011, there was an upward evolution of both the dispersal of Aedes aegypti mosquito by the state as well as the transmission of dengue. On average, annually, the presence of the vector was reported in 120 municipalities and the transmission of the disease in 84 of them.

DISCUSSION

Fortaleza, the capital of Ceará, and neighboring municipalities that make up Ceará's coast are among the main tourist routes of the country. This keeps the doors open for the entry of diseases and the passive circulation of disease-transmitting agents. That is how the introduction of DENV-1 happened in 1986 and, consequently, the first cases of dengue in Aracati and then, in Fortaleza, imported by tourists from Nova Iguaçu, RJ, where there was an epidemic of dengue[11,12] at the time.

The permanence of the *Aedes aegypti* mosquito in Ceará and dengue epidemics caused by it in the state are explained

hypothetically. Only two years after its reintroduction in 1984, effective controlling measures were implemented, a late decision, for the infestation rates were already sky-high. When Dengue first appeared in 1986, there was no way to control it because there was little knowledge about it in Brazil and in Ceará. Dengue found the population and health authorities of Ceará completely unprepared, which led to the first epidemic[13]. Although there are records of 54,055 dengue cases reported in the state between the years 1986 and 1993, health officials estimate that about one million people were affected by the infection[14].

The epidemic in 1994 is considered the one with the highest proportion ever recorded in North and Northeast of Brazil. The State Health Secretariat notified 47,789 dengue cases distributed among 108 out of the 184 municipalities in Ceará. However, a seroepidemiological survey conducted in Fortaleza estimated that 660,000 people were affected by the disease during this epidemic, a larger number of cases compared to the numbers reported by the competent agencies[14]. That year, 84% of dengue cases nationwide[15,16] occurred in Ceará.

These numbers could be explained due to a six months interruption of the vector controlling activities in late 1993, because that year the focus of combat was cholera which was an epidemic in Ceará[17]. With no actions to combat the vector, the infestation rates in Fortaleza exceeded 20%[15]. The high pluviometric index, the high density of the vectorial population, the introduction of a new serotype (DENV-2) and the inadequate destination given to garbage, mainly in areas with no proper sewage system, are the main reasons for the proliferation of dengue in the state capital[14].

From 1994, with the emergence of DHF and lethality caused by it, dengue became a national concern, prompting the Ministry of Health to develop the Plan for the Eradication of *Aedes aegypti* (*Plano de Erradicação do Aedes aegypti - PEAa*) in 1996. This plan consisted of integrated actions with several other ministries, divided into nine areas: entomology; field operations to combat the vector; surveillance at ports, airports and borders; sanitation; information, education and social education; epidemiological surveillance and an information system; laboratories; development of human resources; and supporting legislation.

The implementation of the actions of the PEAa program began in 1997. The Ministry of Health invested more than one billion *reais* in structuring the vector control program in the insured municipalities. These funds were invested in hiring and training staff, purchasing of vehicles and equipment[18]. Important areas were left aside due to lack of resources to carry out two out of the three key components (sanitation, education and social mobilization), reducing the plan almost exclusively to the chemical vector control between 1997 and 2001. This allowed the continued expansion of the area inhabited by the vector and the maintenance of high levels of household infestation, especially in larger, more complex urban centers[6].

Despite the efforts to stop the spread of *Aedes aegypti* in Ceará, every year, there was infestation by the vector in more than 50% of the municipalities of Ceará, reaching almost 92% of the entire state in 2001, culminating in the third epidemic. Several factors contributed to the dengue epidemic in 2001, because, although there was continuity to the actions, the vector control program was going through administrative changes. Until 1997, these actions were the responsibility of the National Health Foundation (*Fundação Nacional de Saúde – FUNASA*), but from 1998 to 2001, this agency was gradually unstructured and the actions decentralized by transferring the vector control program to the responsibility of the states and municipalities[17]. However, shortly after, it was confirmed that the vector's resistance to temephos[19], larvicide used continuously for years, also contributed to the epidemic.

About the decentralization, it is important to reinforce that one of the principles of the Brazilian National Health System, also known as the Unified Health System (*Sistema Único de Saúde – SUS*), is to increase the efficiency and effectiveness of the actions, as they have to fit into different local realities[20]. Regarding the control of dengue, the main criticism of the vertical action of the former Superintendency of Public Health Campaigns (*Superintendência de Campanhas de Saúde Pública – SUCAM*) was making technical decisions at the national level with the uncritical implementation of activities throughout the country. Years after the so-called "decentralization", the same criticism could still be made. What happened was the municipalization of uncritical implementation of actions whose standards were still coming from the federal level.

With the failure of PEAa program and simultaneous circulation of three viral serotypes (DEN-1, DEN-2 and DEN-3) in several Brazilian states, in 2002, a new program was implemented in Brazil, the National Dengue Control Program (*Programa Nacional de Controle da Dengue – PNCD*). The goal was to reduce to less than 1% the households infestation rates and DHF lethality in all priority municipalities, and reduce by 50% the number of cases in 2003 compared to 2002, and in subsequent years by 25% each year[4].

According to reviews[18] conducted in 2002, the Ministry of Health invested R$ 1,033,817,551.00 in dengue control and 85% of this amount was employed in the surveillance and vector control. In 2003, about R$ 790 million were invested primarily in costing, purchasing of equipment, insecticides, maintenance and staff training and social communication actions.

Despite the efforts and investments, the PNCD did not fully achieve its goals. According to a study[21] that evaluated the program in the priority municipalities in the Southeast and Midwest regions, there was not a 50% reduction in the number of cases in 2003 compared to 2002 – or in the following years (25% each year) – in 143 (49%) of the priority municipalities analyzed.

In Ceará, the PNCD also failed to reduce the incidence of dengue, which kept growing. Considering the years 2003 to 2008, there was a reduction in 2004 only. In other years, all infestation rates remained above 200/100,000 inhab. and the ratio between classical and DHF cases dropped from 82 to 46. The mortality rate remained well above the proposed target, being 3.2%[10] the lowest rate recorded in that period.

As to the chemical control, even with the introduction of Bti replacing temephos, success was not attained in the municipalities where the larvicide was used. Perhaps because within the insecticide control policy itself there are several operational failures, among them, not to

consider the period of residual effect of the products on the home visits and the treatment of deposits. Bti has a 15 day residual effect[20], "being, therefore, irrational that its deposit be made in domestic breeding grounds which cannot be eliminated – drains, water tanks etc. – by health agents whenever possible (Ministry of Health standard, every three months)"[20:308].

A similar situation occurred with temephos. When tests proved the decrease of their residual effect and the existence of *Aedes aegypti* populations with high levels of resistance to it, the routine visits and building treatments remained as before (four to six cycles per year). A resistance level superior to 10 (RR >10) can jeopardize the insecticide efficiency[22].

As to the chemical control policy, the criticisms are as follows: "The use of larvicides and adulticides by health agents will not result in a complete vector control, but only in a temporary reduction of its density. Larvicides are central tools for vector eradication, not for controlling it. To focus the control on health agents' job only, as it was in the beginning of the 20th century, when Oswaldo Cruz lived, had not been and will not be effective"[20:308].

In the state of Ceará, independently of the strategies and insecticides adopted, dengue, in the last 25 years, has repeated a standardized cycle of epidemics, repeating the process every six years. However, from 2008 on, there has been a break in this cycle, reducing the interval between epidemics to three years. At the same time, there has been a change in the group age standards[23], a tendency found in other Brazilian states[6,24].

This change had been happening less visibly in the hospitalizations due to DHF[6]. During the 2008 epidemic in Rio de Janeiro, it was noticed a sudden elevation of classic dengue and DHF among people under fifteen year of age. Almost half the DHF cases reported happened in this age group and the risk of dying was increased by five times in children. In Manaus-AM, the increase of the incidence of dengue in this group was noticed in 2006. Infants under one year of age showed a higher risk of getting sick in 2006 as well as in 2007, with an incidence of 114.1/100,000 inhab. and 210.7/100,000 inhab., respectively[24].

As to dengue lethality, Ceará has shown alarming statistics. From 1994 to 2011, the lethality rate was never under 1%, which would be accepted by the World Health Organization. Throughout this period, the rates varied from 3.2% (dengue with complications) to 75% (DHF), higher numbers than the ones found in Brazil as a whole, except for the period comprising 1995 to 1999 and the years of 2004 and 2007[5, 25].

Such a high lethality suggests that either the agent presented itself in a more virulent form or there were failures in the victims' assistance. In this respect, it is stated that "this issue solely relates to the health sector. It is necessary that every city has a strategic plan to assist suspected dengue patients, making it easier for them to access health services"[26:870].

The service should have competent personnel for the classification of cases and to adopt appropriate conducts, from patient monitoring at home to hospitalization in intensive care units. "It is necessary to organize referral services for patients, reserve hospital beds, maintain the required inputs and personnel capable of meeting the different levels of complexity of medical assistance"[26:870]. Along with these measures, the population needs to be advised about the possibility of the occurrence of severe forms of the disease, which could cause the patient's death, and about the warning signs and symptoms, stimulating them to seek medical assistance as early as possible.

It becomes evident that the dengue control focused on combating *Aedes aegypti* has failed. It is necessary that environmental sanitation actions, which are state duty, such as drainage, supplying drinking water, collecting and disposing the garbage produced, are seen as priorities, rather than as complementary actions. Equal importance should be given to domestic health education, since the population must assume the leading role in their homes, as in Brazil, about 90% of the breeding grounds of the mosquito are found in homes[25].

CONCLUSIONS

The analysis of the historical series of dengue in Ceará shows that its epidemiological behavior in the state justifies the classification made by the Ministry of Health "area of vulnerability of very high risk" for the occurrence of this disease, and hence requires constant vigilance. In recent years, the proportion of severe cases has increased, probably due to the simultaneous circulation of three viral serotypes and population weakened by previous infections. The policy focused on combating *Aedes aegypti*, prioritizing chemical control, has proved ineffective and the challenge seems to increase every year, because even in endemic periods, the risk of getting sick and dying from dengue has been high.

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Mailing address:
Estelita Pereira Lima
Rua Ivani Feitosa, 123
Bairro: Tiradentes
CEP: 63031-140 - Juazeiro do Norte - CE - Brazil
E-mail: estelitaplima@hotmail.com