Short Communication

Factors related to severe dengue during an epidemic in Vitória, State of Espírito Santo, Brazil, 2011

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ABSTRACT

Introduction: The prognosis of dengue depends on early diagnosis and treatment, which can help prevent severe forms whose characteristics were evaluated here. **Methods:** A cross-sectional study was conducted involving dengue cases in Vitória, State of Espírito Santo, Brazil, in 2011. **Results:** Two health regions registered 56.3% of 371 cases of severe dengue. Of these cases, 21.3% presented with dengue hemorrhagic fever. There were associations between dengue hemorrhagic fever with younger ages and a longer time before receiving care. **Conclusions:** There was a greater involvement of dengue hemorrhagic fever in young people. Delay in care, poor urban quality and high endemicity were identified as possible risk factors for dengue severity.

Keywords: Dengue hemorrhagic fever. Age distribution. Socioeconomic factors.

Dengue is a systemic disease that is caused by a virus from the *Flaviviridae* family. The virus is transmitted to humans through the bite of an infected mosquito of the genus *Aedes*. Dengue can cause a wide spectrum of clinical symptoms, including severe forms of the illness.

Hemorrhagic fever typically appears between the fourth and sixth day after the onset of clinical manifestations. Medical treatment at an early stage can substantially modify the prognosis of severe dengue, but it is difficult to predict which patients will develop this form of the disease. As a consequence, the mortality associated with dengue hemorrhagic fever (DHF) remains high because patient care is not always timely or appropriate. This cross-sectional study is based on data from dengue cases reported to the Municipal Health Department of Vitória and evaluates potential factors related to the development of severe dengue.

Vitória is located in the southeastern region of Brazil and is the capital of the State of Espírito Santo. Its health system is divided into six regions and 27 territories.

The data regarding dengue fever (DF) cases were obtained from the Information System for Notifiable Diseases (SINAN). The data regarding severe dengue, which included all of the cases classified as dengue with complications (DWC) and DHF, were collected from data sheets for the severe cases used by the Service of Epidemiological Surveillance of Vitória. The information was collected from January 1, 2011, to December 5, 2011.

The patient age was considered as both a continuous and a categorical variable. The patients were divided into two groups: those under 15 years of age and those of 15 years of age or older.

The time to notification was used as a proxy for the time to seek medical care and represents the number of days between symptom onset and the date of notification. The division of the health regions was used to evaluate the territorial distribution.

The cases were defined according to their final classification as DF, DHF or DWC, following the criteria for classification devised by the Brazil Ministry of Health[1]. DF was defined as an acute febrile illness lasting up to seven days and accompanied by at least two of the following signs or symptoms: headache, retro-orbital pain, myalgia, arthralgia, malaise or rash, with or without hemorrhage. DHF was defined as a laboratory-confirmed case meeting all of the following criteria: fever or recent history of fever for at least seven days, thrombocytopenia, hemorrhage confirmed with one or more signs and plasma leakage. DWC was defined as a case of dengue with any of the following manifestations: severe manifestations of the nervous system, cardiac dysfunction, hepatic failure, thrombocytopenia equal to or less than 50,000/mm^3, gastrointestinal bleeding, effusions, total leukocyte count equal to or less than 1,000/mm^3 or death.

The analysis was performed using SPSS version 17.0 (SPSS Inc., Chicago, Illinois, USA). The Mann-Whitney nonparametric test was used to compare the time to notification with sex and age. The chi-square test was used to determine the relationship between age or sex and disease classification. The Kruskal-Wallis nonparametric test and multiple comparison tests were used to evaluate the associations between age and health regions or disease classification. Differences with a p-value less than 0.05 were considered significant.

The study was approved by the Committee on Ethics for Research of the Center of Health Sciences at the Espírito Santo Federal University, process number 155/10.

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In 2011, 5,524 cases of DF and 371 cases of severe dengue occurred in Vitória. Of the severe cases, 78.7% were DWC. Most of the dengue cases occurred in women and in individuals 15 years of age or older. Two deaths were recorded; both were cases of DWC in women over 40 years old. Most of the cases of DWC were confirmed with laboratory tests, and DF cases were usually confirmed with epidemiological criteria (**Table 1**).

The health regions with the most cases of severe dengue were Maruípe and São Pedro, which together contributed more than half of the reported cases in the city. These regions also had the highest number of DF cases, and each of these two regions had more than 1,000 reported cases. They had the highest incidence of severe dengue, followed by the *Santo Antônio* region. In these three regions, the proportion of dengue cases that evolved to severe was greater than 6.3%, the overall value for Vitória in 2011 (**Table 2**).

Figure 1 shows the distribution of the severe dengue cases in the health territories of Vitória. Severe cases were most common in the territories of *São Pedro* (*Santo André* and *Ilha das Caieiras*) and *Maruípe* (*Maruípe, Santa Martha* and *Andorinhas*). With the exception of *Maruípe,* these territories and *Ilha do Príncipe* had an incidence of severe dengue greater than 300 cases per 100,000 persons.

There was a significant association between age, which was treated as either a continuous (p = 0.002) or categorical variable (p < 0.001), and disease severity. Individuals with DF (median age = 26) and DWC (median age = 26) were older than those with DHF (median age = 15). Dengue hemorrhagic fever was most frequent in patients younger than 15 years old. There was no association between sex and disease classification.

There was a significant association between DHF and the time to seek treatment (p < 0.001), with patients suffering from this severe form of the disease (median = 5 days) seeking health care later than those who had DF (median = 2 days) or DWC (median = 4 days).

There was a significant association between age and the time to seek treatment (p < 0.001), with a longer delay among those younger than 15 years (median = 3 days) compared to those 15 years old or older (median = 2 days). No association was found between sex and the time to seek care (median = 3 days; p = 0.773).

In Vitória, the most severe forms of dengue occurred in people 15 years of age or older, despite the changing age distribution pattern of dengue cases in Brazil[2]. Younger people, especially those less than 15 years old, were more likely to be affected by DHF. Young age is considered a risk factor for DHF, and 90% of the cases of DHF occur in patients under the age of 15 years[3].

The increased microvascular permeability secondary to the characteristics and density of capillaries and the decreased ability of the body to compensate for plasma leakage make younger people more prone to developing DHF and hypovolemic shock[4] over a shorter period of time than adults.

Similar to other countries in the Americas, Brazil is affected predominantly by DF, and fatal cases are more common in adults, with a recent increase in the number of juvenile cases. This change in the pattern of DHF and the permanence of intense viral circulation create the potential for a change in the epidemiological profile[5].

In Vitória, there was an increase in the number of dengue cases in children younger than 15 years old, indicating an increase in both the endemic level of the disease and the number of DHF cases[6]. This new pattern of dengue serves as a warning to health services, which must organize, train and empower professionals to diagnose the disease in children.

TABLE 1 - Characterization of dengue cases in Vitória, State of Espírito Santo, Brazil, 2011.

Variables	DWC (n = 292)	DHF (n = 79)	DF (n = 5,524)	Total (n = 5,895)	P value
Sex (%)					
male	49.7	46.8	46.3	46.5	0.548*
female	50.3	53.2	53.6	53.4	
unknown	0.0	0.0	0.1	0.1	
Age group years (%)					
< 15	28.8	48.1	24.8	25.3	0.000*
≥ 15	71.2	51.9	75.2	74.7	
Criteria (%)					
laboratory	61.3	100.0	40.5	42.3	-
epidemiological	38.7	0.0	59.5	57.7	
Outcome (%)					
cure	99.3	100.0	90.3	90.9	
death	0.7	0.0	0.0	0.0	-
unknown	0.0	0.0	9.7	9.1	

DWC: dengue with complications; DHF: dengue hemorrhagic fever; DF: dengue fever. *Chi-square test, (-) Value was not calculated.

TABLE 2 - Incidence and proportion of severe dengue in the health regions of Vitória, State of Espírito Santo, Brazil, 2011.

Health regions	Confirmed	Severe	Population	Incidence*	Proportion**
São Pedro	1,368	101	33,746	299.29	7.38
Maruípe	1,627	108	57,270	188.58	6.64
Centro	543	36	25,618	140.53	6.63
Santo Antônio	572	44	29,254	150.41	7.69
Forte São João	734	34	65,509	51.90	4.63
Continental	1,025	48	107,634	44.60	4.68

*Incidence per 100,000 people. ** Percentage of confirmed dengue cases that evolved to severe dengue.
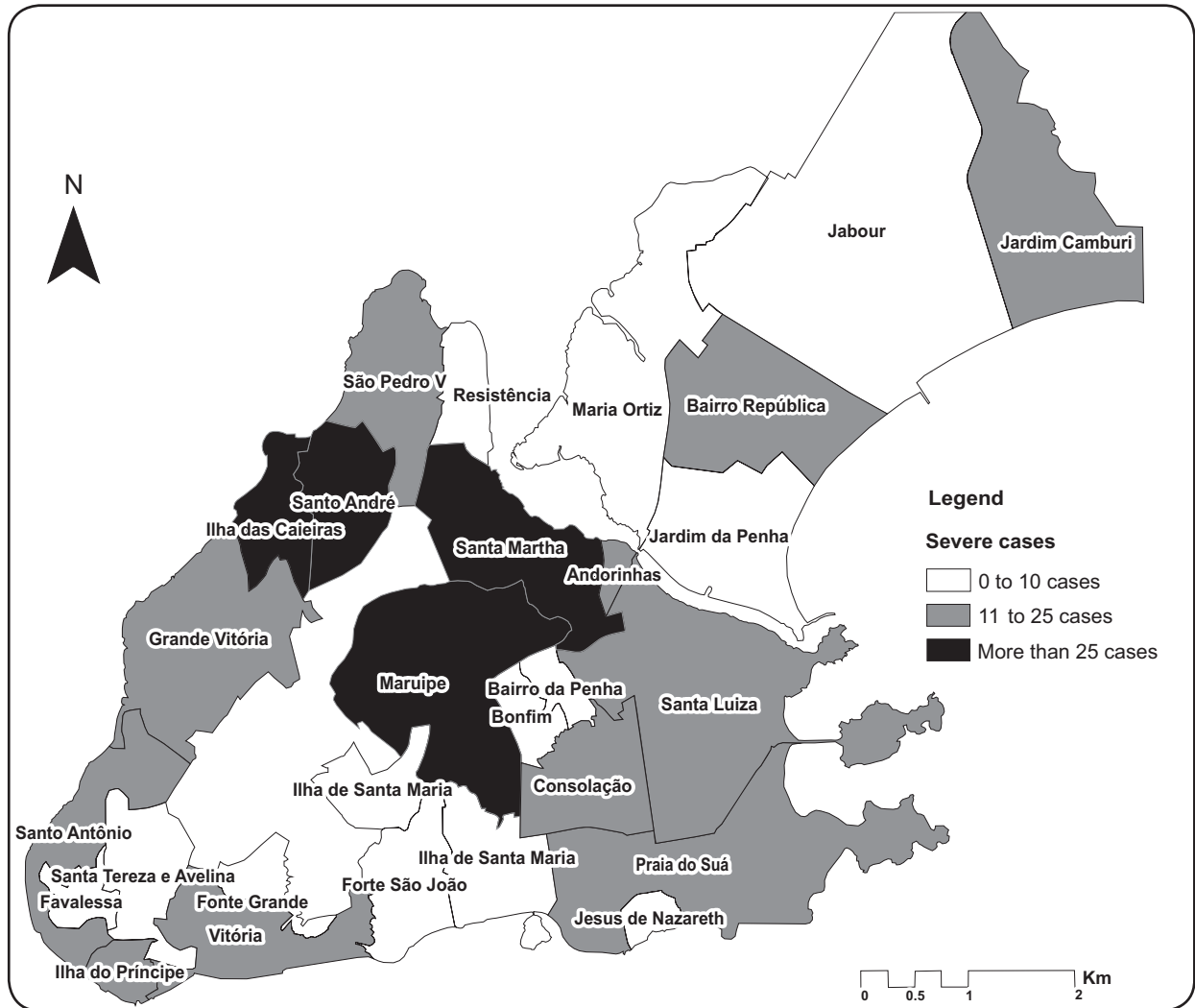

FIGURE 1 - Distribution of severe dengue cases in the health territories of Vitória, State of Espírito Santo, Brazil, 2011.

The clinical profile of dengue in children is similar to that of other common febrile exanthematic diseases. Surveillance should be properly planned to increase the sensitivity and specificity of the diagnosis of acute febrile diseases, which are listed as differential diagnosis of dengue[7].

Monitoring of the circulating serotypes should be prioritized because the reintroduction of an old serotype may result in the infection of individuals who were not affected in the previous epidemic, including younger people who had not been born at that time[8].

In areas in which dengue is endemic, such as Vitória, there is a greater probability that adults and older children have already been exposed to dengue infection, making these populations more susceptible to successive infections, which can cause DHF. Successive infections increase the risk of DHF and dengue shock syndrome (DSS) by 40- to 80-fold[9]. Age is indicated as a risk

factor for death in patients with successive infection, and death is 15 times more frequent in children than in adults[10].

Most of the cases of severe dengue occurred in *Maruípe* and *São Pedro*, which, together with *Santo Antônio*, showed a higher incidence of severe dengue than in the Vitória municipality as a whole. *São Pedro* stood out as the region with the highest frequency of dengue in people younger than 15 years old. In *São Pedro*, 28.1% of the residents are less than 14 years old[11]. The Urban Quality Index of *São Pedro* is one of the lowest in Vitória, and its rate of *Aedes aegypti* infestation is more than twice as high as that of the municipality as a whole.

Low education levels and socioeconomic status are associated with a higher frequency of *A. aegypti* infestation, leading to the persistence of high endemic levels and the risk of secondary infection. The persistence of these conditions favors the increase in cases of severe dengue among young people in the region, highlighting the importance of vector control and the monitoring of suspected cases.

Active surveillance is part of the Global Strategy for Dengue Control[1]. One of the goals of this program is to reduce the mortality of DHF through early diagnosis and appropriate treatment[12]. To achieve this objective, people should be encouraged to seek medical attention as soon as the first symptoms of the disease appear.

The present study showed that patients with DHF generally sought medical care later than those with DF or DWC. This behavior delays the introduction of fluid replacement therapy, which would contribute to a better prognosis for the disease. On average, people sought medical attention on approximately the fourth or fifth day after the onset of symptoms[13], which coincides with the onset of the warning signs of severe disease.

A longer delay in notification was observed among people younger than 15 years old. This factor might be related to the difficulty in diagnosing the disease in younger people. This result reinforces the importance of training professionals to identify and treat the patient upon the first contact.

This study has several limitations, which are inherently linked to its use of preexisting data and are primarily related to imprecision and a lack of information.

There may have been flaws in the surveillance process; for example, some cases may have been reported the day after the patient visited the health service for the first time. However, there is no reason to believe that this error was not random or that it compromised the results of the study.

The final classification of severe cases may have been influenced by the difficulty of applying the classification criteria of the World Health Organization due to the rigidity and low sensitivity of their definitions. Cases that were classified as DWC may not have been identified as DHF because they failed to meet the four criteria for its diagnosis.

Additional investigations using other study designs should be conducted to confirm the associations found in this study.

The analysis revealed a higher incidence of DHF among younger people, a longer time to seek treatment in cases of DHF and severe cases concentrated in younger patients in *São Pedro*. The results indicate a change in the profile of DHF, with an increasing involvement of young people. This profile highlights the importance of delay in seeking treatment, low socioeconomic status with poor urban environments and high endemicity as possible risk factors. Further research should be conducted to more clearly elucidate these relationships and to identify health policies that can effectively circumvent the presented problems.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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