Dengue epidemic typology and risk factors for extensive epidemic in Amazonas state, Brazil, 2010–2011

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Abstract

Background: Dengue is the most prevalent arboviral disease affecting humans. The frequency and magnitude of dengue epidemic have significantly increased over recent decades. This study aimed to identify dengue epidemic types and risk factors for the extensive epidemics that occurred in 2010–2011, across the municipalities of Amazonas state, Brazil.

Methods: Using an ecological approach, secondary data were obtained from the dengue fever surveillance system. Epidemic waves were classified according to three indices: duration, intensity, and coverage. A hierarchical model of multiple logistic regression was used for the identification of risk factors, with the occurrence of extensive dengue epidemic.

Results: During the study period, dengue virus affected 49 of the 62 Amazonas municipalities. In 22 of these, the epidemics were of high intensity, wide range, and long time span, and therefore categorized as "extensive epidemics". The final multivariable model revealed a significant association between extensive dengue epidemics occurrence and the average number of days with precipitation (adjusted OR = 1.40, 95% CI: 1.01–1.94) and the number of years with infestation (adjusted OR = 1.53, 95% CI: 1.18–1.98).

Conclusions: Our results indicate that it is crucial to integrate vector control, case management, epidemiological investigation, and health education, in order to respond to the growing threat of multiple mosquito-borne diseases, such as dengue, Zika and chikungunya, which are highly prevalent in the South America region.

Keywords: Dengue epidemics classification, Socioeconomic, Environment, Climate, Amazon

Background

Dengue is a acute febrile disease, transmitted by arthropod vectors, and caused by four different virus (DENV-1, DENV-2, DENV-3, DENV-4). Dengue virus infections may be asymptomatic or lead to a range of clinical presentations, even death [1]. The clinical manifestations include acute fever, frontal headache, retroocular pain, muscle and joint pain, nausea, vomiting, and rash [2, 3]. The illness, generally, is self-limited and lasts approximately for one week. Patients may eventually develop severe disease, characterized by acute fever with minor or major bleeding, evidence of plasma leakage, and organ involvement [4].

Dengue infections occur in more than 100 countries, reaching approximately 50 million cases each year [5]. In the Americas, the occurrence of recurring dengue outbreaks every 3–5 years with an increasing number of cases over time shows the transition from an endemic-epidemic state to a highly endemic state in recent years [6]. In the state of Amazonas, Brazil, although there is a high density of mosquitoes throughout the seasons, there is usually a peak of the disease in the first half of the year [7–9]. Since 1998, when the dengue virus was
first detected in Manaus, Amazonas state capital, an increasing number of countryside municipalities have been affected by dengue epidemics. During 2010 and 2011, dengue disease affected 49 of the 62 municipalities in Amazonas [9].

Dengue fever has been shown to spread by epidemic waves, that is, the number of reported cases suddenly increases until reaching a peak and then gradually decreases until the epidemic ends [10]. However, the magnitude of dengue epidemics is variable. Epidemics appear to largely reflect susceptibility of the human population to circulating serotypes and mosquito density, however, they are also affected by climatic, environmental, meteorological, social and demographic conditions [11, 12].

Hopp and Foley [13] built a model based on climatic variables in order to predict the mosquito population size, which was related to the number of dengue cases in South Asia and Central America. Hales et al. [14] investigated the role of meteorological covariates in determining the pattern of spatial distribution of dengue cases, concluding that average vapor pressure was the main predictor of dengue distribution. According to the authors, the average vapor pressure, which is a measure of humidity, is high only where rainfall and temperatures are high, and these are conditions that are conducive to breeding and survival of vector populations, and rapid replication of the virus [14].

In addition to recognizing epidemics, it is important to be aware of epidemic magnitude, as milder epidemics have less damaging consequences for the population and their control can be achieved with less complex measures. Conversely, extensive epidemics are more difficult to control, entails a greater financial burden and cause more damage to the population, due to the increased mortality rate and the occurrence of severe cases and temporary disability which lead to significant economic losses [14].

Although much is known about climatic and environmental conditions (temperature and precipitation) and population characteristics (vulnerability to circulating subtypes) associated with epidemic occurrence [6], there is a lack of knowledge about the conditions that determine the large scale, extent and duration of epidemics, that is, the causes of “extensive dengue epidemics”.

Wen et al. [15] criticized the use of dengue annual incidence as an only measure of epidemic wave intensity and justified the adoption of different measures to characterize epidemic severity. The authors suggested three relevant indicators: (i) frequency index, defined as the number of weeks with recorded cases divided by the total number of weeks of the study period; (ii) duration index, defined as the number of weeks with recorded cases divided by the number of epidemic waves; (iii) intensity index, the incidence rate divided by the number of epidemic waves.

The recognition of factors (modifiable and uncontrol-

lable) associated with extensive epidemics is fundamental for the adoption of measures aimed at reducing modifiable causes. Furthermore, the identification of ex-
tensive epidemic-likely scenarios would enable control program intensification or the implementation of different strategies to mitigate the effects of the epidemic.

Methods

This study aimed: (i) to identify dengue epidemic types, and (ii) risk factors for extensive epidemics occurring in 2010–2011 in the municipalities of Amazonas state, Brazil.

The state of Amazonas is located in Northern Brazil and is the largest federative unit, with an area of 1,559,161 km², divided into 62 municipalities and 9 health regions (Fig. 1). It counts 3,483,985 inhabitants, of whom 79% lived in urban zones, in 2010. Approximately 52% (1,802,525 inhabitants) of the state's population resided in the capital Manaus [16]. The general population density in the state was 2.2 inhabitants / km² and 158 inhabitants / km² in the capital [16]. The predominant climate is equatorial, characterized by high temperatures and high rainfall indices [17].

We conducted an ecological study using secondary data from dengue fever surveillance system. Amazonas state municipalities and calendar months were considered as the units of analysis.

Data on dengue cases were extracted from the Notifiable Diseases Information System (called SINAN) provided by the Health Surveillance Foundation (called FVS-AM) of the Health Department of the State of Amazonas. We included all records of dengue cases in SINAN, reported between January 1 2001, and December 31 2011, defined as classical dengue, dengue with complications, dengue hemorrhagic fever or dengue shock syndrome. The classification of the cases followed the criteria established by the Ministry of Health, in accordance with the World Health Organization (WHO) recommendations [18]. Dengue cases were georeferenced by the municipality of patient residence.

The population resident in the municipalities and regions was obtained from the censuses conducted by the Brazilian Institute of Geography and Statistics (IBGE) in 2000 and 2010. From these data, population estimates for the inter-census years were calculated using a linear interpolation technique [19].

Dengue epidemic typology and extensive epidemic definition

The identification of epidemic periods was performed based on analysis of statistical process control charts
prepared for each municipality. The control charts were constructed according to the following steps: (i) calculation of the average monthly incidence rate for the period 2001 to 2010; (ii) visual inspection of the monthly epidemic curve of dengue disease in each municipality to identify putative epidemic months (PEM) with a substantial increase in incidence rates; (iii) determination of the epidemic months, defined by an epidemic onset (the PEM with a positive change in the incidence rate greater than 60% of the incidence of the preceding month) and a termination point (the PEM with a negative change in the incidence rate greater than 60% of the incidence of the preceding month; (iv) excluding periods (epidemic months) with high incidence rates; (v) calculation of the expected maximum incidence rate corresponding to the sum of the average incidence rate with 1.96 the standard deviation of this rate; (vi) identification of the epidemic months, characterized by a monthly incidence rate in
An epidemic wave was defined as a set of consecutive epidemic months (more than 1 month) when the epidemic occurred in a given municipality or the epidemic lasting 1 month with incidence greater than 10 cases / 100 thousand inhabitants. In this study, we propose a typology of epidemic that includes two measures used in the method described by Wen et al. [15] in combination with a third aspect relating to the spatial extent of the epidemic. We defined the extent of the epidemic wave based on the variation of incidence rates calculated for each month, consistently with the method reported by Parker and Holman [11]. Epidemic waves were classified according to three indices: duration, intensity, and coverage.

The duration index \( \alpha \) was calculated by the ratio of the sum of epidemic months (EM) divided by the number of epidemic waves (EW) observed in each municipality, where \( i \) indicates the index of the epidemic wave.

\[
\alpha = \frac{\sum_i EM}{nEW}
\]

The intensity index \( \beta \) was calculated by the ratio of the sum of the average monthly incidence rates (IR) of each epidemic wave and the number of epidemic waves (EW) observed in each municipality, where \( i \) indicates the epidemic wave index.

\[
\beta = \frac{\sum_i IR}{nEW}
\]

The spatial coverage index \( \Upsilon \) was calculated by the ratio of the number of municipalities with epidemic waves (MEW) in a given region and the total number of municipalities in the region (TMR).

\[
\Upsilon = \frac{nMEW}{nTMR}
\]

Table 1: Scores according to criteria categories for epidemics classification

| Criterion | Feature | Definition | Score |
|-----------|---------|------------|-------|
| Duration (based on index \( \alpha \)) | Low | Up to 3 epidemic months | 1 |
| | Middle | With 4 to 6 epidemic months | 2 |
| | High | Greater than 6 epidemic months | 3 |
| Intensity (based on the \( \beta \) index) | Low | Incidence rates in epidemic months less than 10 cases / 100 thousand inhabitants | 1 |
| | Middle | Incidence rates in epidemic months between \( 10^4 \) and 100 cases / 100 thousand inhabitants | 2 |
| | High | Incidence rates in epidemic months above \( 10^5 \) cases / 100 thousand inhabitants | 3 |
| Coverage (based on index \( \Upsilon \)) | Limited | Up to 1/3 of the municipalities in the region presented epidemic months | 1 |
| | Moderated | From 1/3 and 2/3 of the municipalities in the region presented epidemic months | 2 |
| | Wide | Greater than 2/3 of the municipalities in the region had epidemic months | 3 |

*1st quartile of distribution of dengue incidence rates; 2*3rd quartile of distribution of dengue incidence rates
epidemics were studied. See detailed information on obtaining these indicators in Additional file 1: Table S2.

Vector control actions were measured by Stegomyia indices widely used in the scientific literature [20], which are: average annual proportion of home visit targets achieved; number of years with an achieved target of 5 home visits; number of years with infestation; appropriate ratio of number of agents per building; appropriate ratio of number of supervisors by health agent; adequate ratio of supervisors and agents per building; household infestation mean index for the period; and number of years with household infestation mean index greater than 1%. These indicators refer to annual averages recorded between 2010 and 2011. The vector control activities data were obtained from the FVSs Department of Environmental Surveillance and Disease Control. See detailed information on obtaining these indicators in Additional file 1: Table S3.

Statistical analysis
We performed an analysis of completeness and inconsistencies in the dengue database. Records with similarities regarding patient name, date of birth, and mother’s name, and those with a period of less than 60 days between reporting dates were identified as duplicate records, and were excluded.

Summary measures (mean, standard deviation, minimum and maximum values) were used to describe the distribution of study variables. A hierarchical model of multiple logistic regression was used for the identification of risk factors, with the occurrence of extensive dengue epidemic, defined above, as the as the outcome variable. Associations between socioeconomic, meteorological, and performance characteristics of dengue surveillance services in the municipalities of Amazonas and the outcome (EDE) were initially analyzed separately for each group (hierarchical level). Subsequently, for the construction of the final model, we selected the explanatory variables showing an association with the outcome for a level of significance of 0.20 by stepwise technique backward mode. Variables associated with the outcome at a significance level of 0.05 remained in the final model. The multicollinearity between the explanatory variables selected for the final model was analyzed using the variance inflation factor test, and those variables with VIF greater than 10 were considered collinear and excluded of the model. Crude and adjusted odds ratios of the association between the outcome and the explanatory variables were calculated. Statistical package STATA

![Fig. 2 Spatial distribution of classification dimensions of dengue epidemics and extensive epidemic by Amazonas Municipalities in 2011.](image-url)

a Intensity. b Duration. c Coverage. d Extensive dengue epidemics
v.13 (StataCorp, 2013, College Station, Texas, USA) was used to perform these analyzes.

Results
Between 2001 and 2011, 85,216 cases of dengue fever were recorded in the Amazonas state. However, between 2010 and 2011, the largest epidemic occurred, resulting in 58,296 reported cases involving 49 (80%) municipalities in the state.

During this epidemic, most of the municipalities recorded at least one monthly dengue incidence rate greater than 100 cases per 100,000 inhabitants (Fig. 2a) over at least one month. With the exception of the Alto Solimões and Médio Amazonas regions, in all regions 2/3 or more of the municipalities were affected by the dengue epidemic (Fig. 2a-c). Extensive epidemics were observed in 35% (22/62) of municipalities, mostly located in Entorno de Manaus and Rio Negro region (55% [11/20]) (Fig. 2d).

The socioeconomic and demographic profile of Amazonas municipalities shows a high average illiteracy rate (21%), high percentage of poor population (53%), and low human development index (0.56). The most populated municipalities are Manaus, with 1.8 million inhabitants, and Parintins, with 101 thousand inhabitants. The other municipalities have less than 90

Table 2

| Feature                                      | N  | Mean | SD  | Max  | Min  |
|----------------------------------------------|----|------|-----|------|------|
| Socioeconomic profile                        |    |      |     |      |      |
| Illiteracy rate                              | 62 | 20.9 | 9.7 | 40.7 | 4.0  |
| Income Gini Index                            | 62 | 0.6  | 0.1 | 0.8  | 0.5  |
| Proportion of poor                           | 62 | 53.0 | 12.0| 74.2 | 12.9 |
| Per capita income                            | 62 | 251.3| 98.3| 790.3| 122.2|
| Unemployment rate                            | 62 | 7.6  | 3.3 | 18.9 | 1.6  |
| Prop. of pop. in households with bathroom and piped water | 62 | 36.2 | 16.0| 83.6 | 9.5  |
| Prop. of pop. in households with garbage collection | 62 | 80.3 | 19.8| 100.0| 0.1  |
| Human Development Index (HDI)                | 62 | 0.56 | 0.1 | 0.7  | 0.4  |
| Proportion of urban population               | 62 | 54.9 | 14.3| 99.5 | 4.2  |
| Meteorological and river quota               |    |      |     |      |      |
| Average wind speed                           | 62 | 0.9  | 0.4 | 1.8  | 0.1  |
| Annual average heat stroke                   | 62 | 156.0| 19.8| 193.5| 121.9|
| Average days with precipitation              | 62 | 15.8 | 1.7 | 18.9 | 1.26 |
| Annual average rainfall                      | 62 | 215.3| 23.5| 253.5| 167.9|
| Average minimum temperature                  | 62 | 23.2 | 0.9 | 25.0 | 21.4 |
| Average maximum temperature                  | 62 | 32.8 | 0.4 | 33.8 | 32.1 |
| Average relative humidity                    | 62 | 84.5 | 2.1 | 87.3 | 79.8 |
| Average temperature compensated              | 62 | 27.0 | 0.5 | 28.0 | 26.1 |
| Average of the maximum quota                 | 62 | 1181.0| 470.0| 2653.0| 425.2|
| Average of the minimum quota                 | 62 | 960.7| 469.8| 2482.5| 316.2|
| Average of the middle quota                  | 62 | 1068.9| 469.3| 2553.2| 382.6|

Vector Control

| Feature                                      | N  | Mean | SD  | Max  | Min  |
|----------------------------------------------|----|------|-----|------|------|
| Proportion of goals reached from home visits | 62 | 26.1 | 29.3| 88.1 | 0    |
| Number of years with a target of 5 home visits reached a | 62 | 0.4  | 0.8 | 3    | 0    |
| Number of years with infestation a           | 62 | 2.2  | 2.4 | 5    | 0    |
| Appropriate ratio of the number of agents per property | 62 | 0.3  | 0.5 | 1    | 0    |
| Appropriate ratio of the number of supervisors to health agent | 62 | 0.6  | 0.5 | 1    | 0    |
| Adequacy of the number of supervisors and agents for amount of building | 62 | 1.1  | 1.4 | 3    | 0    |
| Household infestation mean index for the period | 62 | 0.5  | 0.9 | 3.6  | 0    |
| Number of years with household infestation mean index higher than 1% | 62 | 0.6  | 1.1 | 4    | 0    |

aRecorded between 2006 and 2010
thousand inhabitants. Manaus has the highest population concentration in urban areas, with 99% of the urban population. In Parintins, the urban population corresponds to 68% of the total population. The meteorological feature results indicated a low wind speed (0.9 km/h) and high precipitation rate (215.3 mm). The river quota recorded in the municipalities presented a considerable variation, ranging from a minimum average quota of 316 cm to a maximum average quota of 2653 cm. The municipalities of Amazonas are characterized by a high household vector infestation and an insufficient number of health agents and supervisors. Generally, the less populous municipalities present a recent history of *Aedes* infestation and lower average rates of infestation (Table 2).

The proportion of poor, per capita income, and proportion of the population in households with bathroom/piped water were associated with the extensive dengue epidemics. When considering this level alone, an increase of one unit in per capita income increased the risk of severe epidemic occurrence by 1% (adjusted OR = 1.1, 95% CI: 1.0–1.1), after controlling for the other variables of this level (Table 3).

No meteorological and hydrology hierarchical level factors were significantly associated with EDE occurrence. However, the average number of days with precipitation, when adjusted for other conditions, increased the risk of EDE (adjusted OR = 1.4, 95% CI: 1.1–1.9), (Table 4).

The operational level model showed the number of years with infestation, adequate ratio of number of agents per property, adequate ratio of supervisors and agents per building, household infestation mean index for the period, and number of years with household infestation mean index greater than 1% as predictors of EDE. Controlling for confounders, the risk of EDE increased by 54% with each increase by one unit in the number of years with infestation (adjusted OR = 1.5, 95% CI: 1.2–2.0), (Table 5).

The final multivariable model revealed a significant association between EDE occurrence and the average

| Table 3 | Socioeconomic factors associated with extensive dengue epidemics using bivariate and multivariable hierarchical level analysis |
|---------|----------------------------------------------------------------------------------------------------------------------------------|
| Illiteracy rate | 0.9 (0.9–1.0) | 0.151 | 0.9 (0.8–1.1) | 0.202 |
| Gini Index | 0.5 (0.3848.1) | 0.868 | – | – |
| Proportion of poor | 0.9 (0.9–1.0) | 0.023 | 1.0 (0.9–1.2) | 0.771 |
| Per capita income | 1.0 (1.0–1.1) | 0.011 | 1.0 (1.0–1.1) | 0.011 |
| Unemployment rate | 1.1 (0.9–1.3) | 0.211 | – | – |
| Proportion of population in households with bathroom and piped water | 1.0 (1.0–1.1) | 0.022 | 1.0 (0.9–1.1) | 0.610 |
| Proportion of population in households with garbage collection | 1.0 (0.9–1.1) | 0.106 | 1.0 (0.9–1.1) | 0.440 |
| HDI | 1.0 (0.3–3.5) | 0.831 | 1.0 (0.1–8.5) | 0.065 |
| Proportion of urban population | 0.9 (0.9–1.0) | 0.174 | 0.9 (0.9–1.1) | 0.380 |

*HDI*: Human Development Index, *OR*: Odds ratio

| Table 4 | Meteorological and hydrological factors associated with extensive dengue epidemic using bivariate and multivariable hierarchical level analysis |
|---------|----------------------------------------------------------------------------------------------------------------------------------|
| Average wind speed | 2.9 (0.8–10.2) | 0.092 | 31.7 (0.15–6521.4) | 0.002 |
| Annual average heat stroke | 1.0 (1.0–1.1) | 0.052 | 0.9 (0.8–1.1) | 0.486 |
| Average days with precipitation | 1.4 (0.9–2.0) | 0.057 | 1.4 (1.1–1.9) | 0.018 |
| Annual average rainfall | 1.0 (0.9–1.0) | 0.993 | – | – |
| Average minimum temperature | 1.6 (0.8–2.9) | 0.137 | 0.1 (0.1–3.7) | 0.159 |
| Average maximum temperature | 0.9 (0.2–3.5) | 0.875 | – | – |
| Average relative humidity | 0.9 (0.7–1.2) | 0.640 | – | – |
| Average compensated temperature | 2.2 (0.8–6.1) | 0.133 | 5477.3 (0.5–5555.6) | 0.064 |
| Average of the maximum quota | 1.0 (1.0–1.1) | 0.052 | 1.5 (0.2–15.8) | 0.741 |
| Average of the minimum quota | 1.0 (1.0–1.1) | 0.052 | 1.1 (1.0–1.2) | 0.144 |
| Average of the middle quota | 1.0 (1.0–1.1) | 0.052 | 6.85 (0.75–62.98) | 0.089 |
number of days with precipitation and the number of years with infestation. The risk of EDE increased by 40% as the average number of days with precipitation increased by one unit (adjusted OR = 1.4, 95% CI: 1.1–1.9). Moreover, the risk increased by 53% as the number of years with infestation increased by one unit (adjusted OR = 1.5, 95% CI: 1.2–2.0) when controlling for the average number of days with precipitation (Table 6).

**Discussion**

In areas where dengue is considered endemic, it is likely that larger epidemics may play a relevant role in the spread of disease and health status of these populations. Here, three features of the epidemics were evaluated in order to classify them according to epidemic dimensions. Only the larger epidemics, classified as extensive epidemics, were evaluated in this study to examine epidemic distribution and associated factors. Several authors use epidemic metrics to characterize dengue outbreaks [11, 12, 15, 21]. According to Galli and Chiaravalli Neto [22], the use of these epidemic indices as an alternative to the use of the incidence rate allows the identification of areas and periods of greatest risk.

Among the 49 municipalities that recorded dengue cases in the study period, we identified 22 municipalities that met the criteria for extensive dengue epidemics, that is, this municipalities presented epidemics with high intensity, extent, and duration. These municipalities surround the Capital and the main economical centers of the State, including Coari, Tefé, and Parintins. Extensive dengue epidemics occurrence in these municipalities is likely to support the widespread dispersal of dengue cases in the region, revealing the potential for dissemination of other arboviruses, such as Zika and Chikungunya, as well as the complexity of controlling these diseases in the region. In areas with widespread disease distribution, it is important to differentiate the severity levels of the areas affected by the disease. This approach allows investigate with greater precision the etiological factors of large epidemics, and also it is an important tool for public managers and decision makers, since they generate alerts with different risk levels.

Multivariable analysis results indicate that climatic and environmental conditions, as well as vector control activities, has independent effects on occurrence of extensive dengue epidemics in the Amazonas municipalities.

The urbanization process triggered by economic development may favor the establishment and spread of the *Aedes* mosquito, due to its ability to adapt to urban environments [21]. Furthermore, population mobility facilitates viral circulation and the climate changes generated in this space enhance disease transmission cycle [23]. Our results corroborate this hypothesis as the risk of extensive dengue epidemics is higher in the municipalities with higher economic development, characterized by higher average per capita income, a larger proportion of the population living in households with toilets and water supply, and lower proportion of poor population. Even when controlling for other socioeconomic conditions, average per capita income was associated with the occurrence of extensive epidemics.

Seasonal climatic forecasts are important tools for dengue epidemics prediction [24, 25]. The findings of this study show that an increase in insolation time, number of days with precipitation, and river quota, increased the risk of extensive dengue epidemics occurrence, presenting borderline *p*-value in the single regression model. Cazelles et al., studied synchronous dengue epidemics in 2005 and found a positive correlation between the incidence of dengue hemorrhagic fever and temperature and precipitation increase [26].

### Table 5 Vector control activities associated with extensive dengue epidemic using bivariate and multiple logistic regression analysis

|                          | Crude Odds Ratio (95% CI) | p-value | Adjusted Odds Ratio (95% CI) | p-value |
|--------------------------|----------------------------|---------|-------------------------------|---------|
| Average proportion of goals reached from home visits | 1.0 (1.0–1.1) | 0.121 | 0.9 (0.9–1.0) | 0.100 |
| Number of years with an achieved target of 5 home visits | 1.8 (0.9–3.5) | 0.075 | 3.5 (0.8–15.7) | 0.107 |
| Number of years with infestation | 1.5 (1.2–2.0) | 0.001 | 1.5 (1.2–2.0) | 0.001 |
| Appropriate ratio of the number of agents per property | 4.8 (1.5–15.1) | 0.007 | 495.8 (0.1–1260.0) | 0.410 |
| Appropriate ratio of the number of supervisors to health agent | 2.7 (0.9–8.2) | 0.087 | 0.3 (0.1–5.9) | 0.352 |
| Adequate ration of supervisors and agents per building | 1.8 (1.2–2.7) | 0.004 | 0.1 (0.1–63.9) | 0.520 |
| Household infestation mean index for the period | 2.3 (1.2–4.5) | 0.013 | 1.6 (0.3–7.2) | 0.567 |
| Number of years with household infestation mean index greater than 1% | 1.8 (1.1–3.1) | 0.020 | 1.8 (0.5–5.9) | 0.355 |

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### Table 6 Extensive dengue epidemic predictors based on hierarchical multiple logistic regression analysis

|                          | Adjusted Odds Ratio (95% CI) | p-value |
|--------------------------|-------------------------------|---------|
| Average number of days with precipitation | 1.4 (1.1–1.9) | 0.041 |
| Number of years with infestation | 1.5 (1.2–2.0) | 0.009 |
studies also showed a positive association between these climate variables and river height with dengue [25, 27], demonstrating the consistency of our findings.

The National Dengue Control Programme in Brazil [18] advocates home visits to 100% of the properties every two months and, during epidemic periods, intensification of vector control actions in locations previously determined by the LIRAa (vector infestation rate surveys). Our results showed that municipalities with dengue epidemics had insufficient number of agents and supervisors and a high household infestation index. These findings support the hypothesis that structural problems in public health services, such as insufficient numbers of health agents, can lead to the non-execution of or failure to achieve target home visits, and, consequently, the increase of vector infestation rates in a given locality. As quoted by Gubler [28], most mosquito control actions focused on eliminating adult vectors, with an unsuitable method and, without changing people’s lifestyles, they continue to provide habitats larvae in their homes. This may result in the vector’s geographical expansion and increased mosquito population density, increased viral circulation and occurrence of cases and severe epidemics.

Precipitation and non-effective control measures were the best predictors of extensive epidemic risk, when considering proximal and distal levels. In our model, socioeconomic conditions may be understood as distal variables, influencing outcome to a lesser extent than the proximal ones, explaining why they were not included in the final model. This corroborates the results of other studies identifying an association between dengue epidemics and rainfall and household vector infestation [29–32]. Furthermore, socioeconomic factors (per capita income), other environmental factors (river water level) and other vector control measures adopted (adequacy of human resources for vector control level of building infestation) can also identify municipalities with a high propensity to extensive epidemics.

Secondary data obtained from the SINAN database were used in this study. There are generally issues with the underreporting, completeness and quality of this type of data. However, in this study only variables with at least 70% of completeness were considered. Searches for duplicates records were performed and dates were reviewed to identify any mistakes.

Conclusions

The findings presented here showed influences of local and regional climate variability on the occurrence of extensive dengue epidemics. These results can provide basic knowledge for the development of an early warning system in the future and support for decision makers implementing dengue prevention strategies under different environmental conditions. Furthermore, there is a strong need to integrate vector control, case management, epidemiological investigation, and health education, in order to respond to the growing threat of multiple mosquito-borne diseases, such as dengue, Zika, and chikungunya, highly prevalent in South American.

Additional file

| Additional file 1: Structure of epidemic indicators, Epidemic indicators definition, units and scale. (DOCX 21 kb) |

Abbreviations

CI: Confidence interval; EDE: Extensive dengue epidemic; EM: Epidemic months; EW: Epidemic wave; FVS-AM: Health Surveillance Foundation; HDI: Human development index; IR: Incidence rate; Max: Maximum value; MEW: Municipalities with epidemic waves; Min: Minimum value; N: Sample size; OR: Odds ratio; PEM: Putative epidemic months; SD: Standard deviation; SINAN: Notifiable Diseases Information System; TMR: Total number of municipalities in the region; WHO: World Health Organization

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Availability of data and materials

The datasets supporting the conclusions of this article are available by request in the “Sistema Eletrônico do Serviço de Informação ao Cidadão” repository, [http://esic.cgu.gov.br/sistema/site/indexhtml] and the socioeconomics datasets analyzed during the current study are available in the “Departamento de Informática do SUS” repository, [http://datus.saude.gov.br/] and Human Development Atlas repository, [http://www.atlasbrasil.org.br/2013/pt/consulta/].

Authors’ contributions

DBC, VSS, BCA, RCP, MS, RAP, CFC, and JUB contributed to the conceptualization, resources, supervision, project administration, and funding acquisition; RCP, MS, RAP, and CFC made substantial contributions to acquisition of data and interpretation of data; DBC, VSS, and JUB contributed to the validation, formal analysis, investigation, and visualization; DBC, VSS, and JUB contributed to the design of methodology; DBC, VSS, BCA, RCP, MS, RAP, CFC, and JUB contributed to writing and editing original draft, and revise the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of the Adriano Jorge Foundation Hospital, under protocol number 1162956, on July 7 2015. The institutional review board waived the need for written informed consent from participants as the study involved only secondary data and the confidentiality of the patients’ identities was protected.

Consent for publication

Not applicable.
Competing interests
The authors declare that they have no competing interests.

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References
1. Rigau-Pérez JG, Clark GG, Gubler DJ, Reiter P, Sanders EJ, Vorndam AV. Dengue and dengue hemorrhagic fever. Lancet. 1998;352:971–7.
2. Kalayanarooj S, Vaughn DW, Nimmannitya S, Green S, Suntayakom S, Kunentrasi N, et al. Early clinical and laboratory indicators of acute dengue illness. J Infect Dis. 1997;176:313–21.
3. Cobra C, Rigau-Pérez JG, Kuno G, Vorndam V. Symptoms of dengue fever in relation to host immunologic response and virus serotype, Puerto Rico, 1990-1991. Am J Epidemiol. 1995;142(11):1204.
4. Pan American Health Organization. Dengue and dengue hemorrhagic fever in the Americas: guidelines for prevention and control. Washington, DC: Pan American Health Organization, Scientific Publication; 1994. p. 548.
5. WHO. Global strategy for dengue prevention and control 2012–2020. Geneva: World Health Organization; 2012.
6. Brathwaite Dick O, San Martín JL, Montoya RH, del Diego J, Zambrano B, Dayan GH. Temporal-spatial pattern of dengue haemorrhagic fever outbreaks in the Americas. Am J Trop Med Hyg. 2012;87:584–93.
7. Ríos-Velásquez CM, Cedeño CT, Honório NA, Sabroza PS, Moresco M, Cunha ICL, et al. Distribution of dengue vectors in neighborhoods with different urbanization types of Manaus, state of Amazonas, Brazil. Mem Inst Oswaldo Cruz. 2007;102:617–23.
8. Pinheiro VCS, Tadei WP. Frequency, diversity, and productivity study on the Aedes aegypti most preferred containers in the city of Manaus, Amazonas, Brazil. Rev Inst Med Trop São Paulo. 2002;44:245–50.
9. Mde S B, Figueiredo RM, Ramosavmy R, Ipiriema E, Gimaque JBL, Santos LO, et al. Simultaneous circulation of all four dengue serotypes in Manaus, state of Amazonas, Brazil in 2011. Rev Soc Bras Med Trop. 2012;45:393–4.
10. Cummings DAT, Iriarte RA, Huang NE, Endy TP, Nisalak A, Ungchusak K, et al. Travelling waves in the occurrence of dengue hemorrhagic fever in Thailand. Nature. 2004;427:344–7.
11. Parker D, Holman D. Event history analysis of dengue fever epidemic and inter-epidemic spells in Barbados, Brazil, and Thailand. Int J Infect Dis. 2012;16(11e):e793–8.
12. Ritchie SA, Pyke AT, Hall-mendelin S, Day A, Mores CN, Christofferson RC, et al. An explosive epidemic of DENV-3 in Cairns, Australia. PLoS One. 2013;8:e68137.
13. Res C, Hopp MJ, Foley JA. Worldwide fluctuations in dengue fever cases related to climate variability. Climatic Res. 2003;25:85–94.
14. Hales S, Hales S, de Wet N, Maindonald J, Woodward A. Potential effect of population and climate changes on global distribution of dengue fever: an empirical model. Lancet. 2002;360(9336):830–4.
15. Wen T, Lin NH, Lin C, King C, Su M. Spatial mapping of temporal risk characteristics to improve environmental health risk identification: A case study of a dengue epidemic in Taiwan. Sci Total Environ. 2006;367:631–40.
16. IBGE. Censo Demográfico 2010 - Características da população e dos domicílios - Resultados do universo. Rio de Janeiro: Instituto Brasileiro de Geografia e Estatística; 2011.
17. Alvarez CA, Stape JL, Sartelhias PC, de Moraes Gonçalves JL, Sparovek G, Köppen’s climate classification map for Brazil. Meteorol Z. 2013;22:711–28.
18. Brazilian Ministry of Health. Diretrizes Nacionais para Prevenção e controle de Epidemias de Dengue. Brasília: Ministry of Health, Department of Health Surveillance, Department of Epidemiological Surveillance; 2009. p. 160.
19. IBGE. Projeções da População. Brasil e unidades da federação. Rio de Janeiro: Instituto Brasileiro de Geografia e Estatística; 2013.
20. Bowman LR, Runge-Ranzinger S, McCall PJ. Assessing the relationship between vector indices and dengue transmission: a systematic review of the evidence. PLoS Negl Trop Dis. 2014;8:e2848.
21. Barcellos C, Lowe R. Expansion of the dengue transmission area in Brazil: the role of climate and cities. Tropical Med Int Health. 2014;19:159–68.
22. Galli B, Chiavarotti NF. Temporal-spatial risk model to identify areas at high-risk for occurrence of dengue fever. Rev Saúde Pública. 2008;42:656–63.
23. Jetten TH, Focks DA. Potential changes in the distribution of dengue transmission under climate warming. Am J Trop Med Hyg. 1997;57:285–97.
24. Cámara FP, Gomes AF, dos Santos GT, Cámara DCP. Clima e epidemias de dengue no Estado do Rio de Janeiro, Rev Soc Bras Med Trop. 2009;42:137–40.
25. Lowe R, Bailey TC, Stephenson DB, Jupp TE, Graham RJ, Barcellos C, et al. The development of an early warning system for climate-sensitive disease risk with a focus on dengue epidemics in Southeast Brazil. Stat Med. 2013;32:864–83.
26. Cazelles B, Chavez M, McMichael AJ, Hales S. Nonstationary influence of El Niño on the synchronous dengue epidemics in Thailand. PLoS Med. 2005;2:e106.