

Identification of surveillance and control priority areas for dengue and other arboviruses transmitted by *Aedes aegypti* in Natal-RN, Brazil: experience report

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Isabelle Ribeiro Barbosa¹
Alessandre de Medeiros Tavares²
Úrsula Priscila da Silva Torres²
Carlos André do Nascimento²
Márcia Cristina Bernardo de Melo Moura²
Valderi Barbosa Vieira²
Josélio Maria Galvão de Araújo³
Renata Antonacci Gama³

¹Universidade Federal do Rio Grande do Norte, Faculdade de Ciências da Saúde do Trairi, Santa Cruz-RN, Brasil

²Secretaria Municipal de Saúde de Natal, Centro de Controle de Zoonoses, Natal-RN, Brasil

³Universidade Federal do Rio Grande do Norte, Departamento de Microbiologia e Parasitologia, Natal-RN, Brasil

Abstract

Objective: to report the *vigi@dengue* experience, held in the municipality of Natal-RN, Brazil, from October/2015 to May/2016. **Methods:** entomological indicators were obtained from the oviposition traps, epidemiological indicators from notifications on the online Information System for Notifiable Diseases (Sinan-dengue), active search for cases and viral RNA detection (RTq-PCR) in arthropods and human serum samples; risk levels have been created based on these indicators; categories of interventions for each risk level have been established. **Results:** early identification of epidemics in three areas of the municipality, with guidance for field work for the most vulnerable areas; the municipality presented ovitrap positivity index (OPI) of 40% and eggs density index (EDI) of 51 eggs/ovitrap; identification of CHIKV, DENV-1 and DENV-3 in Natal-RN. **Conclusion:** the strategy identified the early emergence of epidemics in specific locations; it was helpful in the guidance of control measures for the areas of major risk.

Keywords: Delimitation of risk areas; Vector control; Dengue; Arboviruses; *Aedes aegypti*.

Correspondence:

Isabelle Ribeiro Barbosa – Avenida das Fronteiras, No. 1.526, Bairro Panatis, Natal-RN, Brasil. CEP: 59114-275
E-mail: isabelleribeiro@oi.com.br

Introduction

The re-emergence of dengue in Brazil occurred due to a complex arrangement of environmental, social and biological variables that, based on its complexity and dynamism, established the necessary context for the occurrence of successive epidemics, resulting in a high social and economic cost for the country.¹⁻⁴

Since 1986, almost uninterrupted epidemics of dengue have been occurring in Brazil. Nowadays, the four serotypes of dengue virus (DENV) circulate in the country, where they coexist with failures in prevention which depends on many aspects that go beyond the health sector.⁵ Dengue prevention and control have become difficult tasks, due to the high morbidity of its infectious agent, the high level of vector competence of *Aedes aegypti* and the high cost of vector control actions, as well as unfavorable implications associated with the use of insecticides in environment.^{2,3}

Dengue prevention and control have become difficult tasks, due to the high morbidity of its infectious agent, the high level of vector competence of Aedes aegypti and the high cost of vector control actions.

In the municipality of Natal, capital of Rio Grande do Norte State, dengue re-emergence dates back to 1996. Since then, the municipality has reported successive epidemics and, in 2008, it had the highest incidence rate: 1,952 cases per 100,000 inhabitants. There was also co-circulation of other arboviruses, such as chikungunya and Zika virus, both with the first cases reported in 2015.⁶ For these two arboviruses, between 2015 and 2016, Natal-RN was responsible for more than 50% of the burden of morbidity recorded in Rio Grande do Norte and about 30% of confirmed cases of microcephaly associated with Zika virus infection.⁷⁻⁹

Nowadays, the analysis of the dynamics of arboviruses transmission, with the inclusion of spatial statistical models and geoprocessing techniques has been used to understand its context of production and distribution.^{10,11} Spatial distribution has become an important tool for planning control actions, since it subsidizes the application of control strategies based on the identification of risk areas and risk

periods, which can optimize the use of resources and workforce.^{3,4,12} The identification of areas of major risk is relevant to decision making and to the implementation of measures of different magnitudes, in health surveillance.

The municipality of Natal-RN is an important tourist destination in the country, with a diverse and intense movement of people, which enables the dispersion of vectors and spread of communicable diseases.¹³ This epidemiological context, with areas of high infestation of *Aedes aegypti* and arbovirus co-circulation,^{6-8,12,15} represented an alert for the need to implement surveillance and control strategies that considered intra-urban characteristics as well as space-time aspects to identify areas of major risk of occurrence of outbreaks and epidemics.

The National Guidelines for the Prevention and Control of Dengue Epidemics,¹⁴ which aims to assess and control the vector situation, recommend the implementation of four Larval Index Rapid Assay for *Aedes aegypti* (LIRAA) per year and home visits in 100% of the households every two months. However, it is essential to add dynamicity in the collection and use of data and information to identify the most critical areas of infestation and transmission and to guide vector control actions.

This study aimed to report the *vigi@dengue* experience, held in the municipality of Natal-RN, Brazil, and defined as the process of production and analysis of epidemiological and entomological indicators, presenting a prediction of risk levels for the application of specific vector control strategies.

Methods

This is an experience report that included surveillance and control actions of dengue and other arboviruses, entitled *vigi@dengue*, held in the municipality of Natal-RN. The stages of planning, development, implementation and testing were carried out from October/2015 to May/2016. Specialists in virology, epidemiology and entomology, professors of the Federal University of Rio Grande do Norte, as well as technicians of the health management linked to municipal and state institutions and the Brazilian Ministry of Health, assessed all of the stages.

The project was based on four principles: (1) weekly collection of epidemiological and entomological

indicators; (2) development of risk categories based on epidemiological and entomological indicators; (3) weekly classification of neighborhoods of the municipality of Natal-RN in areas with different risk levels, to identify areas with higher chance of outbreaks and epidemics; and (4) organization of response stages for each risk level, considering the most appropriate interventions for each level.

Therefore, the actions were carried out in four steps:

Step 1: Weekly collection of epidemiological and entomological indicators

The number of reported cases of dengue, chikungunya and Zika virus in residents of the municipality of Natal-RN, recorded in the Information System for Notifiable Diseases (Sinan) and in FormSUS (a set of forms available in the website of the IT Department of the Brazilian National Health System [Datasus]) were used to calculate the incidences per neighborhood.

An incidence map per neighborhood (with cases in the last three weeks), a control diagram per neighborhood,¹⁵ a map of georeference cases (with cases in the last three weeks) and a Kernel density estimation map were produced with these data. The non-parametric Kernel method was used; this method counts all the points within a region of influence, weighting them by the distance of each one from the location of interest. The smoothing function chosen was quartic (biweight), with 600 meters of bandwidth and 500 x 322 regular grid cells. The public domain computer program QGIS 2.8 Wien (Oracle America, Inc. California, 2008) was used for maps' production.¹⁶

Entomological indicators were obtained from the monitoring of *Aedes aegypti* population with oviposition traps all over the municipality. On a weekly basis, 475 traps were installed at a distance of 300m between each other. The analysis of ovitraps was performed at the Entomology Laboratory of Natal Research Center for Zoonosis Control. With these data, the following entomological indicators were calculated: egg density index (EDI) per neighborhood, ovitrap positivity index (OPI) per neighborhood, and intensity of infestation at strategic points (SP).

For the identification of the arboviruses circulating in the municipality, the technique for detecting viral RNA in arthropods and in human serum samples was used.

Adult vector collection was carried out in strategic places, distributed in the whole city.

Human serum sample collection was performed by active search for febrile cases that fit the clinical and epidemiological criteria for dengue, chikungunya or Zika virus.

The samples were analyzed using the RTq-PCR¹⁷ technique (real-time quantitative PCR), in the Laboratory of Virology of the Federal University of Rio Grande do Norte.

Step 2: Development of risk categories based on epidemiological and entomological indicators of each neighborhood of the municipality of Natal-RN

A risk classification for dengue and other arboviruses was developed thanks to the *vigi@dengue* project, a pioneering project in the municipality of Natal-RN. This classification was composed of four distinct risk levels, limited according to entomological and epidemiological indicators for each neighborhood – considered as the median values of time series of the previous weeks –, as well as identification of Zika virus and chikungunya circulation, and re-introduction of dengue viral serotypes. The risk levels were defined according to the features presented in Figure 1.

Step 3: Weekly classification of neighborhoods of the municipality of Natal-RN in areas with different risk levels, to identify areas with higher chance of outbreaks and epidemics

The variables considered in the evaluation were: (i) identification of chikungunya virus circulation; (ii) identification of Zika virus circulation; (iii) identification of the circulating DENV serotype; (iv) average and maximum limits presented by the control diagram of each neighborhood; (v) average of egg density per ovitrap in each neighborhood; and (vi) average ovitrap positivity per neighborhood.

All the information was organized weekly, in spreadsheets, so the indicators were evaluated and the neighborhoods classified according to the risk level for the occurrence of outbreaks and epidemics.

Step 4: Organization of response stages for each risk level, considering the most appropriate interventions for each level

The intervention methodology for vector control is chosen according to the risk level in which the area is

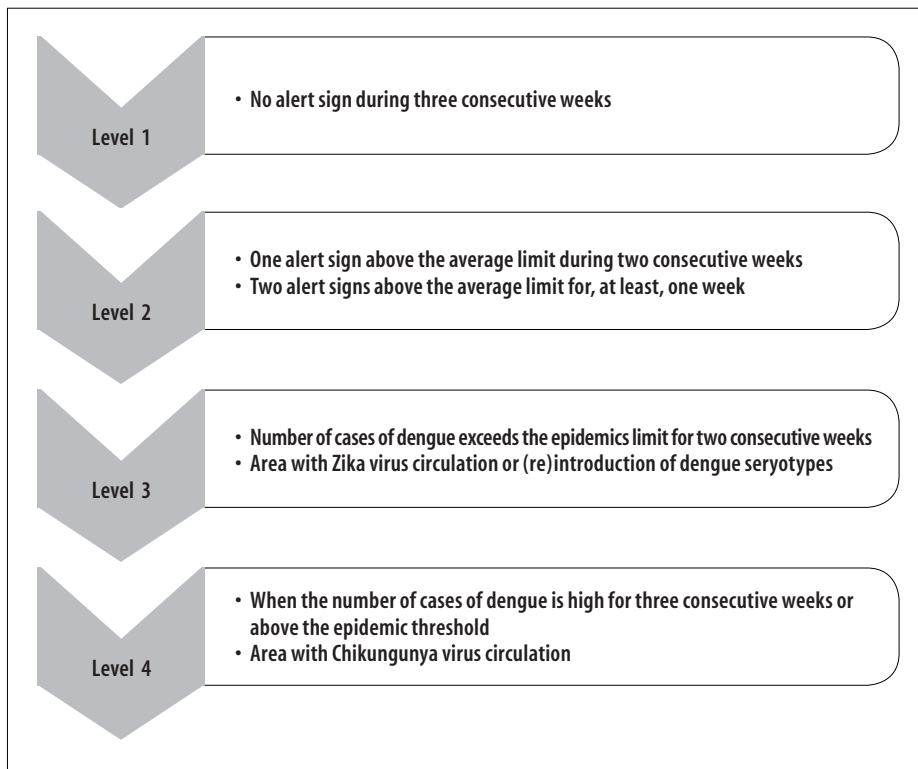


Figure 1 - Entomological and epidemiological criteria for the classification of areas at risk levels in the *vigi@* dengue project, Natal-RN, Brazil, 2016

classified, as presented in Figure 2. The responses were classified as follows: initial response; timely response; and late response. This classification considers the epidemiological characteristic that the disease assumes at the moment: initial response consists of actions in areas where the disease has endemic behavior and there is no (re)introduction of viral serotypes; timely response consists of actions in areas where the indicators show a probable epidemic or the occurrence of an outbreak; and late response consists of actions to control ongoing epidemics.^{14,18}

In order to perform active search for febrile cases and blood collection, the project was submitted to the Ethics Research Committee of the Federal University of Rio Grande do Norte, under the report No. 51057015.5.00005537, and approved on March 8th, 2016. For entomological and case-reporting information, secondary data were used, so, in this case, this project did not need to be subject to assessment by the Ethics Research Committee, in accordance with the Resolution No. 466 of the National Health Council (CNS), dated December 12th, 2012.

Results

In the period prior to this study, entomological data available in the municipality of Natal-RN was based on the Larval Index Rapid Assay for *Aedes aegypti* (LIRAA), performed, on average, every three months. Incidence was the indicator used for risk assessment, calculated for the municipality of Natal-RN and its neighborhoods. A control diagram was used to identify and monitor epidemics in the municipality of Natal-RN.

Weekly monitoring of *Aedes aegypti* population allowed the identification of the North district as the one with the highest ovitrap positive index (OPI), the West district as the one with the highest egg density index (EDI), and the seasonality of the vector with the highest OPI and EDI in the first few weeks of the year. Figure 3 shows the results of the entomological indicators obtained for the municipality.

The highest values of ovitrap positivity were located in the neighborhoods of Potengi, Nossa Senhora da Apresentação, Redinha and Pajuçara (OPI from 16 to 25%), and the neighborhood of Bom Pastor (OPI

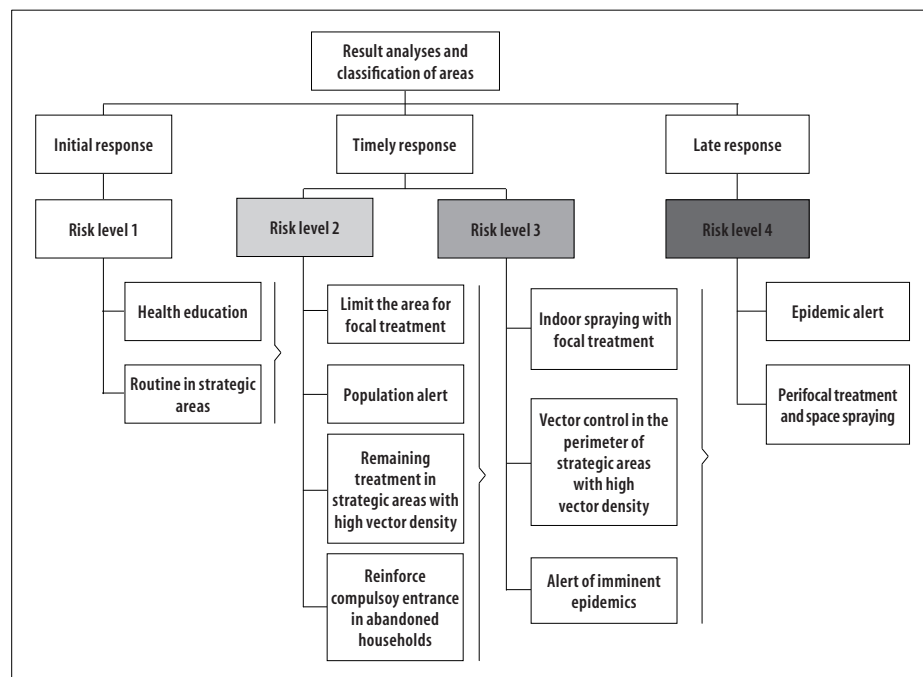


Figure 2 – Intervention methods for vector control based on the classification of risk levels and the type of response for the municipality of Natal-RN, Brazil, 2016

= 27%) in the West district (Figure 3A). In the same period, the West district had the highest vector density (EDI = 84 eggs per trap) (Figure 3B). In the analysis by epidemiological week, the OPI average was 40.3% and the EDI was of 50.8 eggs per trap (Figure 3C).

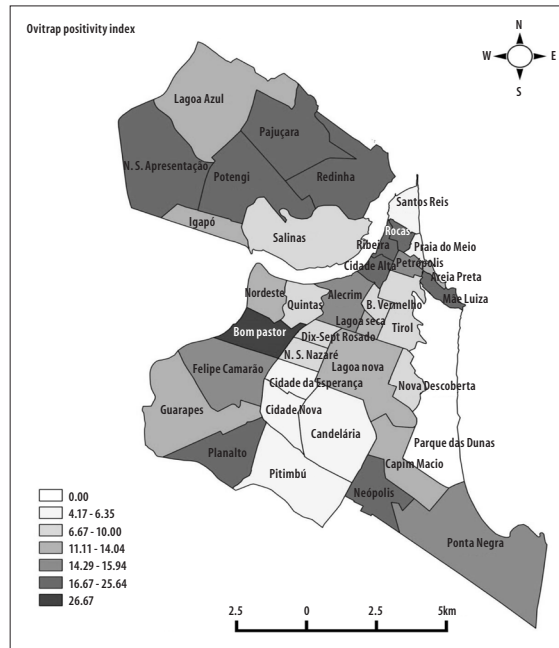
For each neighborhood of Natal-RN, an epidemics curve or control diagram was developed, which proved to be useful to early recognize the beginning of outbreaks and epidemics. After the implementation of *vigi@dengue*, the first neighborhood identified in epidemics situation, in the second half of 2015, was Nossa Senhora da Apresentação, located in the North district of the city. Comparing Figures 4A and 4B, which show the control diagrams of Natal-RN and the neighborhood of Nossa Senhora da Apresentação, respectively, we can notice that the epidemics in this neighborhood began in the epidemiological week 42, and the control diagram of the municipality of Natal-RN did not yet indicate the occurrence of epidemics.

The epidemics dynamics in the neighborhood of Nossa Senhora da Apresentação was monitored by georeferencing of suspected and/or confirmed cases of dengue, chikungunya and Zika virus. Georeferencing of cases and Kernel density analysis indicated the pattern of cases agglomeration in an area of the neighborhood,

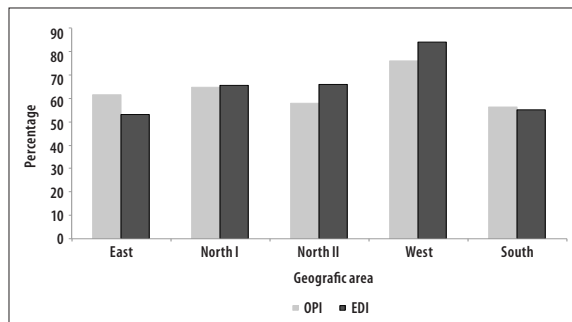
showing that the spread occurred in adjacent areas of bordering neighborhoods, as we can see in Figure 4E. The proximity between the incidence of cases and ovitraps that had the highest EDI in the neighborhood was also observed (Figure 4D).

The active search for febrile cases was a relevant instrument to detect the first confirmed cases of chikungunya in the municipality of Natal-RN. Active search for febrile cases that fit clinical and epidemiological criteria for dengue, chikungunya or Zika virus resulted in the collection of 83 blood samples. Chikungunya virus RNA was detected in 31 of those samples. The first cases in residents detected were of Lagoa Azul and Potengi. Other samples belonged to individuals living in the neighborhoods of Igapó, Cidade da Esperança, Cidade Alta, Santos Reis, Nossa Senhora da Nação, Pajuçara, Mãe Luiza, Ribeira and Salinas, showing the geographical spread of the virus in most neighborhoods of the city.

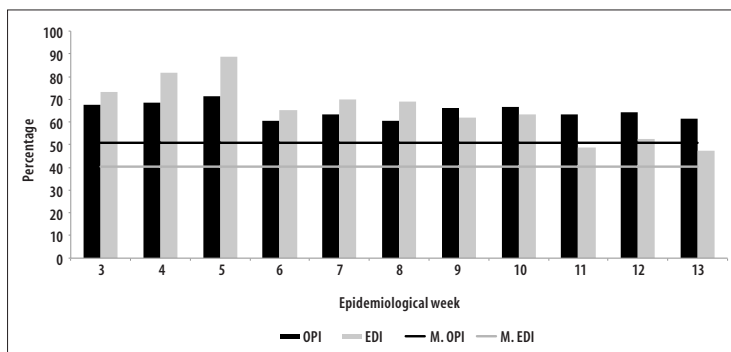
Virological monitoring in arthropods detected the circulation of DENV-1 and DENV-3, in Natal-RN, in 2015. The circulation of DENV-1 was identified in the neighborhoods of Lagoa Azul, Nossa Senhora da Apresentação, Nova Descoberta and Pitimbu. In the



3A – Spatial distribution of ovitrap positivity index – OPI – in the epidemiological weeks 41 to 43, according to neighborhood, 2015

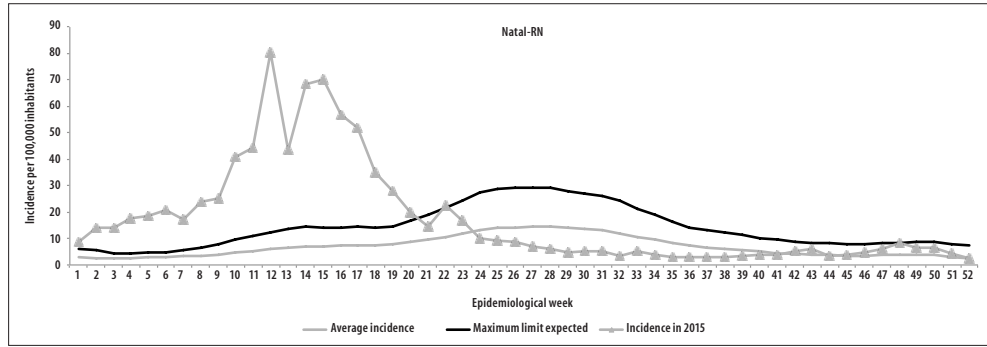


3B – Ovitrap positivity index – OPI – and egg density index – EDI –, according to sanitary district in the epidemiological week 43, 2015

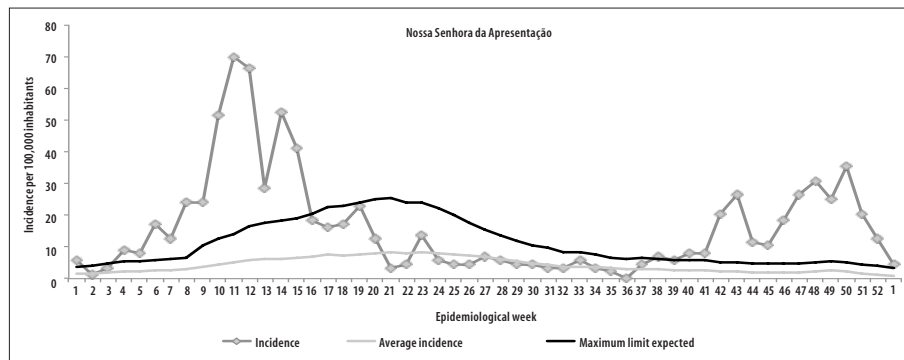


3C – Ovitrap positivity index – OPI – and egg density index – EDI – according to epidemiological week, 2016

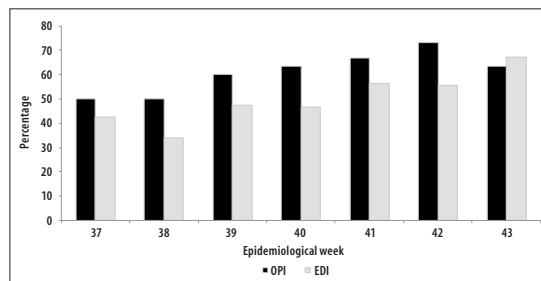
Figure 3 – Entomological indicators based on results of oviposition traps in the municipality of Natal-RN, 2015-2016



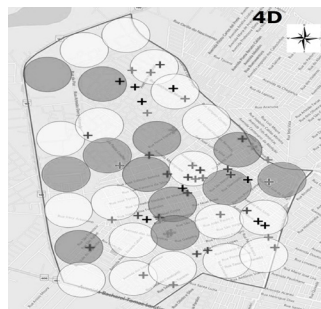
4A – Epidemic curve in the municipality of Natal-RN



4B – Epidemic curve for the neighborhood of Nossa Senhora da Apresentação



4C – Ovitrap positivity index – OPI – and egg density index – EDI –, per epidemiological week, in the neighborhood of Nossa Senhora da Apresentação



4D – Intensity of oviposition in each ovitrap (radius of 300 meters) and georeferenced cases of dengue in the epidemiological week 48, in the neighborhood of Nossa Senhora da Apresentação



4E – Kernel density map for the occurrence of dengue in epidemiological week 48, in the neighborhood of Nossa Senhora da Apresentação

Figure 4 – Entomological and epidemiological indicators for the neighborhood of Nossa Senhora da Apresentação (NSA), in the municipality of Natal-RN, 2015

neighborhood of Felipe Camarão, the circulation of DENV-1 and DENV-3 was verified. In the neighborhood of Lagoa Azul, in addition to the circulation of DENV-1, chikungunya virus circulation was detected in arthropods, confirming the findings of real-time PCR, performed in human samples.

In addition to classifying neighborhoods according to their respective risk levels and conducting corresponding control actions, the characterization of these indicators and the application of these georeferencing techniques gave the necessary support to the organization of multisectoral actions to minimize determinants of disease.

Following the example of the neighborhood of Nossa Senhora da Apresentação, which, based on epidemiological and entomological indicators, was classified as level 4 and became the target of late response actions, social mobilization and health education actions were also carried out, as well as clean street campaigns, compulsory opening of closed or abandoned households for inspection, and allocation of 80% of the endemic disease control agents of the municipality of Natal-RN for control actions in these areas.

Discussion

The definition of areas of higher incidence proved to be useful for surveillance and for epidemiological investigations according to the proposed methodology. The experiment carried out in the municipality of Natal-RN enabled the identification of arbovirus patterns, dispersion and vector density of *Aedes aegypti*, and detection of circulating viral serotypes that supported planning and development of more effective interventions thanks to a risk classification based on epidemiological and entomological indicators. A direct result of this experiment was the minimization of the impact of an epidemic occurred in 2015 in Natal-RN, whose number of cases was lower than in previous epidemics, a fact attributed to the coordinated and articulated responses of the *vigi@dengue*. Since the methodology is simple, using easy-to-obtain data, at a low cost and with comprehensive coverage, this strategy has proved to be easily adaptable and possible to be applied in any small and medium-sized municipality.

Spatial stratification, according to the level of risk of the areas, was an important tool to support the planning of arboviruses control actions.¹¹ Nowadays,

the municipality of Natal-RN has weekly information to prioritize actions and guide the work of agents of endemic disease control in the most critical areas of infestation and transmission. By determining priority areas, the analyses indicate where the control actions should be performed, becoming an important tool for the surveillance of these diseases and conditions.¹⁹

The georeferencing of cases identified the highest transmission areas within each neighborhood. These data assigned priority areas for guiding control actions, especially when the data was crossed with vector population indicators. Hence, it enabled the development of educational/social mobilization and vector control actions to the most vulnerable areas through focal treatment, perifocal treatment and space spraying – the latter when necessary.

In the last ten years, several studies have been conducted in Brazil aiming at stratifying the risk of dengue epidemics, whether considering environmental factors, such as rainfall and temperature,^{11,12} or social and economic determinants,²⁰⁻²² or, individually, the record of cases, to design a space-time model.³ This project not only used epidemiological indicators that can be produced from the number of reported cases, but also emphasized active surveillance in search for febrile cases, entomological indicators based on oviposition traps, and virological surveillance. The use of these indicators provided more agility for analyzing a highly complex and dynamic epidemiological structure.

An important aspect of this project refers to taking into consideration the intersectionality among several sectors with commitment of the Municipal Health Department of Natal, in order to adding forces, potentialities and resources to solve a common problem.

The proposal of incorporating active case search minimized the limitation of the use of data based only on reported cases, since they reflect only part of the reality. It is a well-known fact that many infection cases do not end up being recorded in official statistics.^{14,18}

Another limitation of this study is the difficulty of comparing results of the analyzed proposal and the working methodology for every two months of household visits (previously used in Natal-RN) recommended by the National Guidelines for the Prevention and Control of Dengue Epidemics.¹⁴ Despite the positive results achieved with this new strategy, incidence of arboviruses may have been influenced by other variables, such as the circulating viral serotypes, disease transmission dynamics, population dynamics, rainfall regime, and

factors such as planning of surveillance and control services and organization of social space.²³⁻²⁶

The identification of areas with different risk levels for the occurrence of these arboviruses, the stratification and the prioritization of specific areas for vector control can be carried out based on the data collected. As we can see from the data presented, areas with different epidemiological and entomological situations could have special treatment, in the planning of control actions.

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Authors' contributions

IBarbosa IR, Tavares AM, Torres UPS, Nascimento CA, Moura MCBM, Vieira VB, Araújo JMG and RGama RA contributed to the conception and design of this study, data collection, analysis and interpretation of data, manuscript's drafting and review of its intellectual content. All the authors approved the final version of the manuscript and declared to be responsible for all aspect of the study, ensuring its accuracy and integrity.

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