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Predictor effect of the Rapid Survey (LIRAa) and priority areas for Dengue surveillance in Maranhão, Brazil

Efeito preditor do Levantamento Rápido (LIRAa) e áreas prioritárias para vigilância da Dengue no Maranhão, Brasil

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ABSTRACT

Dengue fever is a serious public health problem in Brazil. However, there are still mechanisms involved in the dynamics of the disease that need to be better elucidated, especially in Maranhão. In this sense, the objective was to evaluate the predictive effect of LIRAa in relation to the incidence of dengue fever in Maranhão in 2022, and to identify priority municipalities for interventions through geospatial analysis. This is a scholastic study, carried out with data obtained from the Zoonosis Surveillance Units **-** UVZ of the municipalities, in the Notifiable Diseases Information System (SINAN). A simple linear regression with post-hoc analyses and the Local Moran Index (LISA) were performed. A positive effect of LIRAa on the incidence of dengue fever was observed (R2 = 0.0352; p = 0.0062). LISA indicated ten high-risk municipalities and six in a transition situation to high risk of dengue fever in the state. LIRAa has proven to be an efficient entomoepidemiological surveillance tool and the identification of priority areas for surveillance can help health authorities in developing specific strategies to contain future epidemics.

Keywords: Dengue; Vector control; Linear models; Spatial analysis.

RESUMO

A dengue é um grave problema de saúde pública no Brasil. No entanto, ainda existem mecanismos envolvidos na dinâmica da doença que precisam ser mais bem elucidados, principalmente no Maranhão. Nesse sentido, objetivou-se avaliar o efeito preditivo do LIRAa em relação à incidência de dengue no Maranhão em 2022, e identificar municípios prioritários para intervenções por meio de análise geoespacial. Trata-se de um estudo escolar, realizado com dados obtidos das Unidades de Vigilância de Zoonoses - UVZ dos municípios, no Sistema de Informação de Agravos de Notificação (SINAN). Foi realizada regressão linear simples com análises post-hoc e o Índice de Moran Local (LISA). Observou-se efeito positivo do LIRAa na incidência de dengue (R2 = 0,0352; p = 0,0062). O LISA indicou dez municípios de alto risco e seis em situação de transição para alto risco de dengue no estado. O LIRAa demonstrou ser uma ferramenta eficiente de vigilância entomoepidemiológica e a identificação de áreas prioritárias para vigilância pode auxiliar autoridades de saúde no desenvolvimento de estratégias específicas para conter futuras epidemias.

Palavras-chave: Dengue; Controle de vetores; Modelos lineares; Análise espacial.

INTRODUCTION

Dengue is the world's leading arboviral disease (Wong et al., 2022). Caused by four distinct but closely related serotypes of Dengue virus (DENV) (1–4), it is transmitted primarily by infected Aedes sp mosquitoes (PAHO, 2024). While often asymptomatic resulting in mild febrile illness, in some situations, hemorrhages, critical organ damage, and even death may occur (PAHO, 2024).

The incidence of the disease has grown substantially over the past two decades, with cases reported to the World Health Organization (WHO) increasing from half a million in 2000 to more than 4.2 million in 2022 (UN, 2023). In Brazil, dengue fever is experiencing critical growth and is a serious public health problem, affecting all regions of the country, with recurring epidemics (Braga; Valle, 2007). In the first half of 2024 alone, more than 6 million notifications and 4,591 deaths were recorded in the country (Brazil, 2024). It is the country with the highest number of notifications and with the circulation of the four DENV serotypes (WHO, 2024). In Maranhão, the fourth most populous state in the Northeast, 7,369 cases of dengue were reported in 2022, and 10,935 probable cases in the first half of 2024, with six deaths (Brazil/MS, 2024).

In addition to issues problems caused by DENV in Brazil for decades, the introduction of Chikungunya virus (CHIKV) in 2014 and Zika virus (ZIKV) in 2015, into Brazilian territory further increased the challenges for controlling these urban arboviruses in the country (Nunes *et al*., 2015, Zanluca *et al*., 2015). The overlapping clinical signs and symptoms presented by them, associated with the limitations faced in differential diagnosis, have been an aggravating factor in this complex epidemiological scenario, in which the search for more effective surveillance and control strategies focused mainly on the *Aedes aegypti* vector must be developed (Brazil, 2016).

There are numerous environmental, social, and cultural factors that trigger arboviral transmission and influence the spread of these diseases (Villabona-Arenas *et al*., 2014). In this context regard, it is worth highlighting the wide dispersion of *Ae. aegypti* throughout the national territory. A predominantly urban vector, it found favorable conditions for its development, especially in breeding sites found in the peridomestic areas of residences, such as water storage containers (Soares-da-Silva *et al*., 2012; Sousa *et al*., 2021). This high proliferation favors the high incidence of dengue, the increase in severe cases and deaths (Andrioli; Busato; Lutinski, 2020). In addition, it consolidates the difficulties faced in controlling this vector, as a major challenge in underdeveloped countries (Ribeiro *et al*., 2018; Cavalcante *et al*., 2020).

In Brazil, to identify the most vulnerable areas and provide rapid and timely indexes, arbovirus control programs have utilized been applying the Rapid Survey of Infestation Index by *Ae. aegypti* (LIRAa) in by municipalities since 2003 (Brazil, 2013, Brazil, 2017). This strategy consists of a sample survey of properties, in which the Building Infestation Index (IIP) obtained is used as a reference to define priority areas to receive interventions (Brazil, 2019).

Thus, the National Guidelines for the Prevention and Control of Dengue Epidemics provide for vector control based on these indices as one of the main components for the prevention of dengue and other arboviruses (Brazil, 2013, Brazil, 2017). The use of geospatial analysis is another method that has proven efficient in elucidating the dynamics of occurrence of these diseases and their vector (Paiva Júnior *et al*., 2020; Santos *et al*., 2022).

After the COVID-19 pandemic, a period in which there was possible underreporting due to the suspension of the work of endemic agents and the concentration of public health actions in combating the pandemic, Brazil experienced the highest number of arbovirus cases in the Americas in 2022, including severe dengue, with a rising trend (PAHO/WHO, 2023). In this sense, the objective was to associate the larval indices of LIRAa obtained in the municipalities of Maranhão with the incidence of dengue and climatic variables, in order to evaluate the predictive potential of LIRAa in relation to the occurrence of cases registered in the State in 2022, and to identify the priority municipalities for interventions through the geospatial analysis of the incidence of dengue cases this year.

METHODOLOGY

Study area

Maranhão covers an area of 331,983.29 km2, making it the eighth largest state in Brazil and the second in the Northeast in in terms of territorial extension (IBGE, 2018). To the North it borders the Atlantic Ocean (639.5 km), to the South and Southwest it meets the State of Tocantins (1,060 km), to the West it borders the State of Pará (798 km) and to the East and Southeast it meets the State of Piauí, with an extension of 1,365 km. The State has five Geographic Mesoregions (North, West, Center, and South Maranhão), subdivided into 21 Geographic Microregions, where its 217 municipalities are located (IBGE, 2022). In 2022, Maranhão had an estimated population of 6,776,699 inhabitants (IBGE, 2022), the fourth largest in the Northeast region, and has the lowest Human Development Index (HDI) in Brazil, equal to 0.676 (IBGE, 2021).

Study Type and Data Collection

This is an ecological study carried out data from LIRAa, the incidence of dengue fever and meteorological data from municipalities in Maranhão in 2022. The Building Infestation Indexes (IIP), reflecting the infestation status of *Ae. aegypti* larvae and pupae in properties, were obtained from LIRAa conducted by the Zoonosis Surveillance Units (UVZ) in the municipalities (Brazil/SVS, 2019). In relation to the general LIRAa of the State, based on the four surveys carried out in the municipalities, the value of an annual LIRAa was calculated.

The confirmed dengue cases in the municipalities of Maranhão in 2022 were obtained from the Notifiable Diseases Information System (SINAN) through the Information and Informatics Department of the Unified Health System (DATASUS), fed mainly by the notification and investigation of cases of diseases and diseases of compulsory notification (Consolidation Ordinance No. 4, of September 28, 2017), available at https://datasus.saude.gov.br/acesso-a-informacao/doencas-e-agravos-de-notificacao-de-2007-em-diante-sinan/.

The dengue incidence coefficient was calculated by the ratio between the number of new cases in 2022 and the resident population in Maranhão in the same period, multiplied by 100,000. The population was obtained through the 2022 demographic census, available in the IBGE database (IBGE, 2022). Climate data were obtained from the Climate data database, available at: https://pt.climate-data.org/.

For spatial analysis, the geometric features of the State of Maranhão in shapefile format were obtained from the map portal of the Brazilian Institute of Geography and Statistics-IBGE, available at: http://portaldemapas.ibge.gov.br.

Data analysis

LIRAa Analysis

Data were managed using Microsoft Excel 2013 (version 2406). Based on the definitions of epidemic risk from the Ministry of Health, which classifies Brazilian municipalities, analyses were performed according to IIP values: $< 1\%$ = satisfactory situation; $\geq 1\%$ and $< 4\%$ = alert situation; $\geq 4\%$ = high epidemic risk situation (Brazil, 2009).

To test the effect of LIRAa on the incidence of dengue fever, using data from all of Maranhão, a simple linear regression was performed. To validate the model (post-hoc analyses), the following were performed: Shapiro-Wilk test to verify the normality of the residues; Outlier deviation test of the residues; Durbin-Watson test to verify the independence of the residues; and Breush-Pagan test to verify the homoscedasticity of the residues.

To test the effect of environmental variables on Dengue Incidence and LIRAa, a multiple linear regression analysis was used (one selection for each response variable). In one analysis, the predictor variables were six climate variables and the response was Dengue Incidence; and in another, the predictor variables were six climate variables and the response was LIRAa. Data from seven environmental variables were used: mean temperature, minimum temperature, maximum temperature, air humidity, sunny days and precipitation. The autocorrelation (covariance) of the predictor variables was tested and those with correlation greater than 80% were removed.

Models were selected based on the first-order Akaike Information Criterion (AIC) using the stepwise-backward algorithm. This selection was made in order to verify whether they met the assumptions of independent residuals and whether they were distributed identically.

After selecting the best model, it was subjected to the same post-hoc tests as a simple linear regression: Shapiro-Wilk test to verify the normality of the residuals; outlier deviation test of the residuals; Durbin-Watson test to verify the independence of the residuals; Breush-Pagan test to verify the homoscedasticity of the residuals. To improve the model fit, the incidence variable was log-transformed for its normalization. The software used in the analyses was R (version 4.3.2). For all analyses, the significance level adopted was 5% ($p < 0.05$).

Spatial analysis

Kernel density estimation was used to calculate the spatial distribution of gross dengue incidence. This method allows the generation of heat maps highlighting areas with the highest incidence of dengue, making it possible to identify critical areas in the state based on confirmed dengue cases in 2022 by municipality. A raster file with multiple data frames was generated for each case from the points in order to allow comparison of dengue incidence in different municipalities. The maps were created and laid out with their cartographic elements using QGIS software (version 3.22).

To analyze local autocorrelation and identify spatial clusters among municipalities in Maranhão, the global Moran Index and the Local Indicators of Spatial Association (LISA) were performed based on the dengue incidence rate smoothed by the Empirical Bayesian method. A first-order matrix was created to verify the dependence between areas. The index ranges from -1 to +1, subdivided into four quadrants: high-high, areas of higher priority; low-low, areas of lower priority; low-high and high-low, transition areas. The LISA was obtained through the GeoDa software, version 1.14.

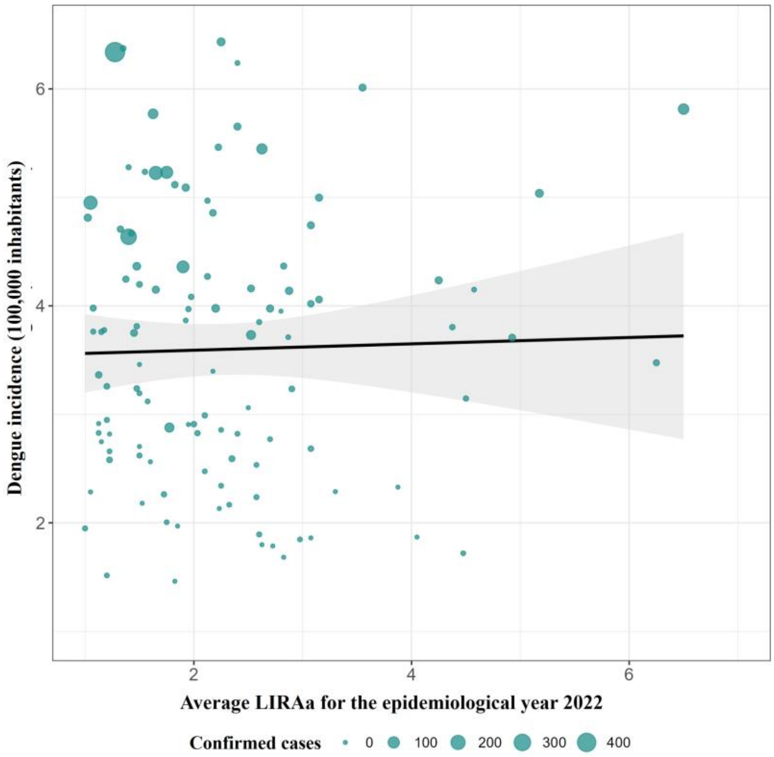
RESULTS

LIRAa Analysis on Dengue Incidence in Maranhão in 2022

The municipality of Tasso Fragoso presented the highest LIRAa index of the entire state in the year under study (11.2) and a high incidence of dengue (938.86). The second highest LIRAa index in the state was observed in Porto Franco (10.2), which presented an incidence of 334.94. São Raimundo das Mangabeiras, which in the first LIRAa exhibited an index of 7.3, presented a high incidence of dengue (1,038.8). The municipalities that presented the highest LIRAa indexes in the second, third and fourth surveys were Tutóia, Carutapera and Miranda do Norte, respectively; however, all presented low incidences of arboviruses.

The analyses showed that there is a positive effect of LIRAa on the incidence of dengue, that is, as the LIRAa index increases, the incidence of dengue also increases. In other words, there is a positive correlation between the two variables. (F = 10.41-186; R2 = 0.0352; p = 0.0062; y = 0.2019x + 3.2017) (Figure 1). All municipalities that at some point presented *Ae. aegypti* infestation rates in an alert or high-risk situation also exhibited high incidences of dengue or Chikungunya.

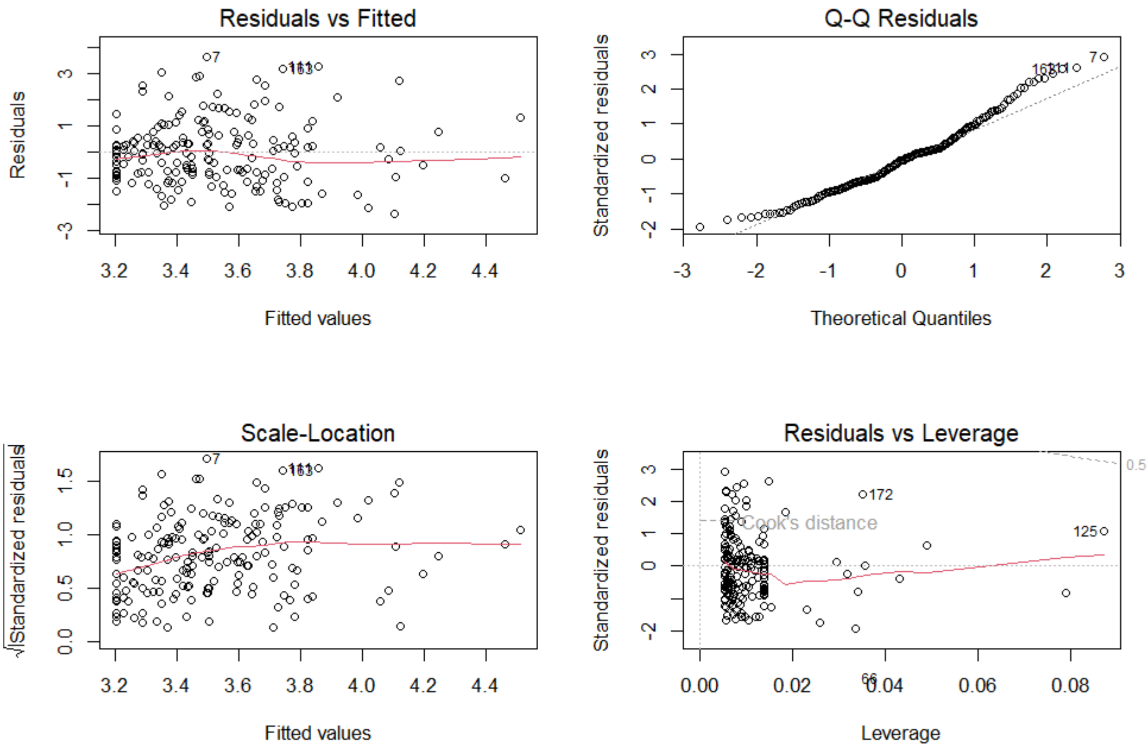
Figure 1. Simple regression analysis of LIRAa on the incidence of dengue in Maranhão in 2022.



Source: Authors themselves.

In Figure 2, the graphs show the dependence of dengue incidence on the influence of LIRAa. The analysis of the residuals of the models was displayed in a standardized and independent manner. In general, based on the aforementioned analyses, the model was considered to have a good fit.

Figure 2. Residue validation analyses.



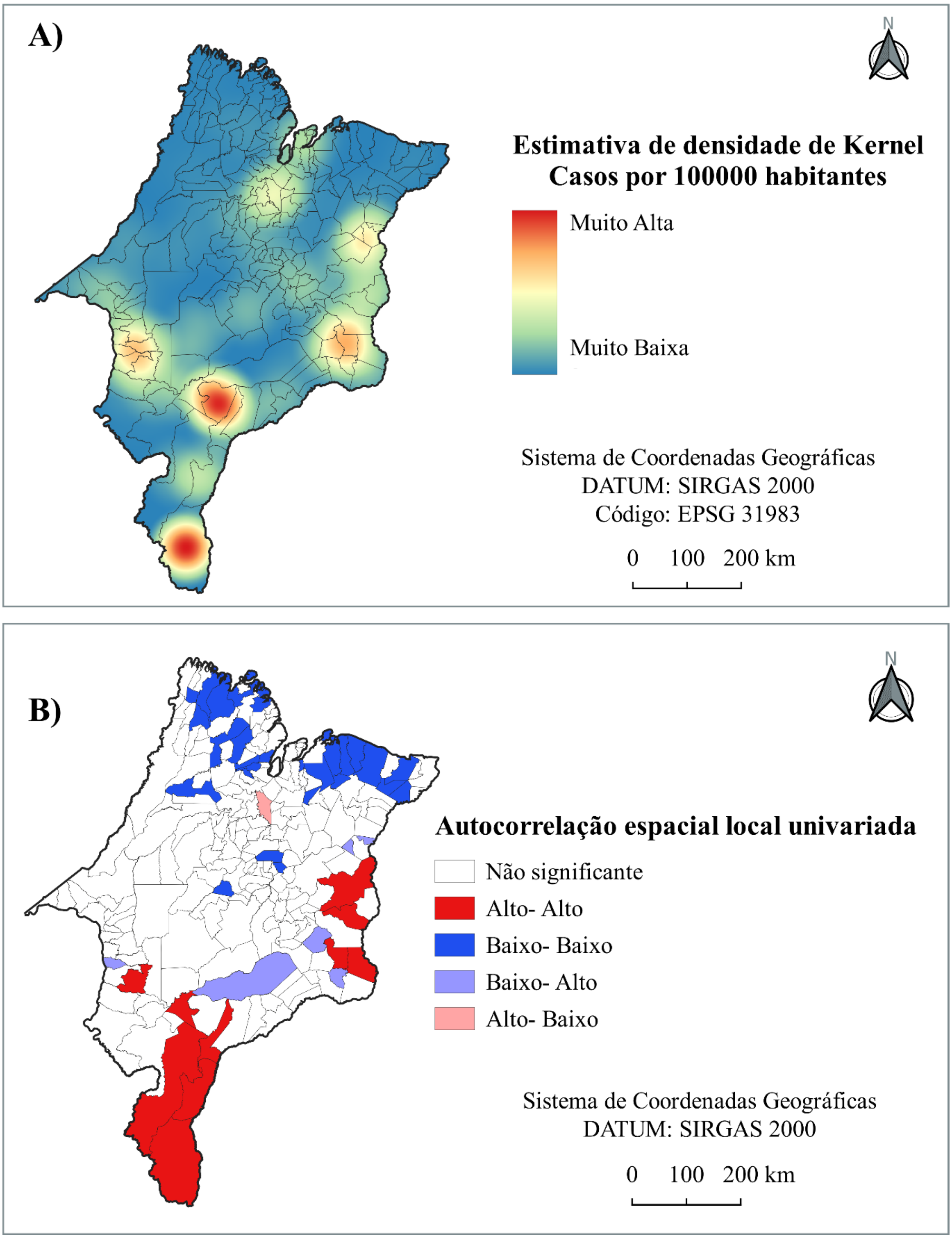
Source: Authors themselves.

Spatial distribution of dengue incidence in the state of Maranhão

When analyzing the spatial distribution of dengue, the Kernel tool identified critical for the diseaseareas in the southern region of Maranhão, in the municipalities of Alto do Parnaíba, São Raimundo das Mangabeiras, Tasso Fragoso; a point in the eastern region with high density, represented by the municipality of Lagoa do Mato, and two point with intermediate incidence identified in the municipalities of Caxias and Matões (Figure 3A).

According to the univariate local spatial autocorrelation, ten municipalities were considered to be at high risk of dengue fever in Maranhão: Alto Parnaíba, Balsas, Caxias, Fortaleza dos Nogueiras, Lagoa do Mato, Matões, Sambaíba, São Francisco do Maranhão, São João do Paraíso, and Tasso Fragoso. In addition to these, six municipalities are in transition to high-risk conglomerates: Afonso Cunha, Buriti Bravo, Campestre do Maranhão, Duque Bacelar, Mirador, and Sucupira do Riachão (Figure 3B).

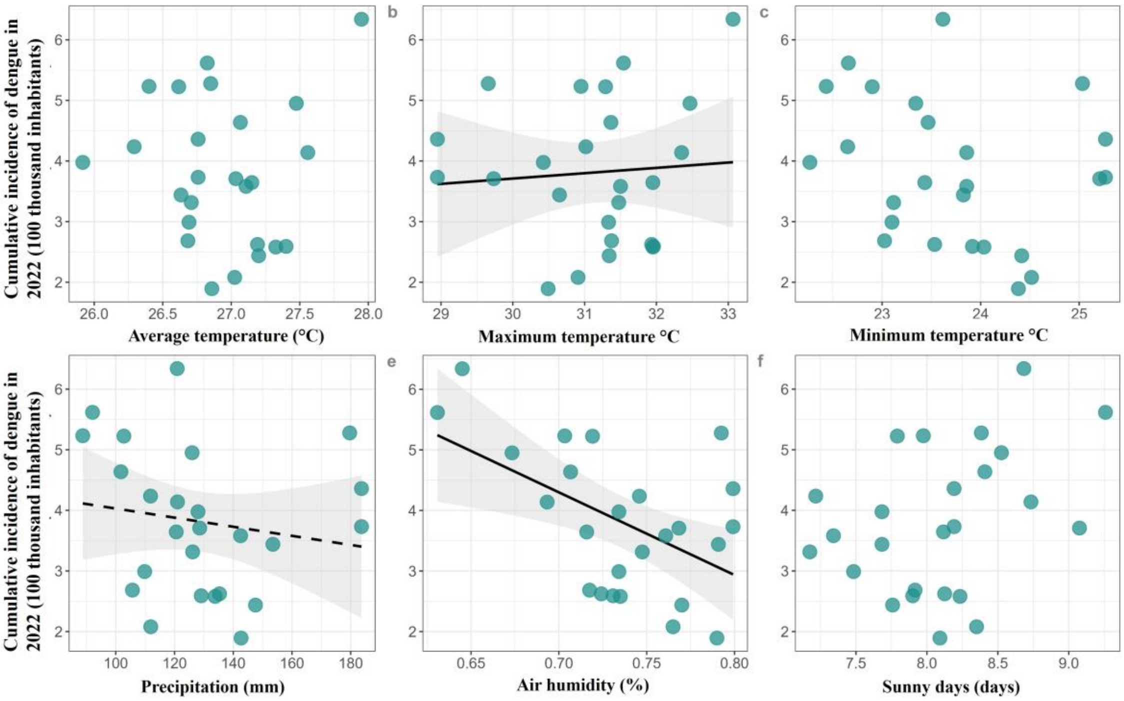
Figure 3. Spatial distribution of dengue incidence in the state of Maranhão, 2022. **A)** Map of the Kernel density estimate of the crude incidence. **B)** Map of local indicators of spatial association for the incidence smoothed by the Empirical Bayesian method.



Source: IBGE, 2022.
Prepared by: Medical Entomology Laboratory – UEMA.
Analysis of dengue, climate variables and LIRAa

The analyses showed that there is an effect of environmental variables on the incidence of dengue (F = 9.8743-21; R2 = 0.5259; y = -0.8334x + 0.0180x -35.4534x + 53.5194). (Figure 4). The influence of maximum temperature (p = 0.0033) and relative humidity (p = 0.0000) were significant. However, there was no effect of environmental variables on LIRAa. (F = 2.3912-23; R2 = 0.0548; p = 0.1257) (Table 3).

Figure 4. Reported cases of dengue, climate variables and LIRAa in municipalities of Maranhão in 2022.



Source: Authors themselves.

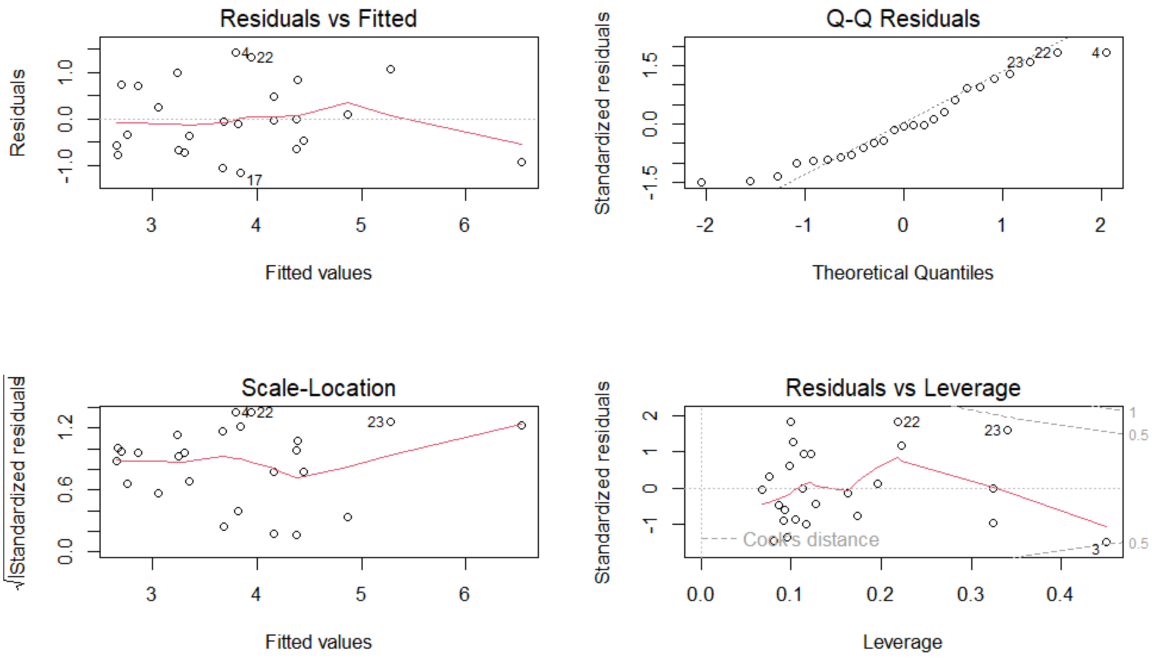
Table 1. Relationship between incidence and environmental predictors.

Model	Estimated	Standard error	t-value	p-value	Significance
Intercept	53.5194	11.3113	4.7320	0.0001	***
Maximum temperature	-0.8334	0.2511	-3.3190	0.0033	**
Precipitation	0.0181	0.0094	1.9230	0.0682	.
Air Humidity	-35.4534	6.6720	-5.3140	0.0000	***

Source: Authors themselves.

In Figure 5, the graphs show the validation analyses of the models: validation of the variance inflation factor test, normal distribution, independence and constant variance of the residuals. The graphs show that the validation analyses presented a model with excellent fit.

Figure 5. Analysis values for model validation.



Source: Authors themselves.

DISCUSSION

Arboviruses are a serious public health problem worldwide. In Brazil, in the first four weeks of 2024 alone, the country accounted for approximately 70% of the dengue cases reported in the Americas (WHO, 2024). In view of this alarming situation, the use of instruments and methods aimed at vector control, statistical tests, and spatial distribution have proven to be efficient in analyzing and interpreting data related to dengue and other neglected diseases (Rosso *et al.*, 2021; Mugabe *et al.*, 2021; Abdulsalam *et al.*, 2022).

This study reinforces the importance of reliably performing LIRAa in Brazilian municipalities and, at the same time, reaffirms that this technique can support local public policies to direct vector control and arbovirus prevention actions. The association observed between the high LIRAa rate and the increase in the number of dengue cases in Maranhão further strengthens the role of this instrument in monitoring *Ae. aegypti* and in taking measures to prevent arbovirus outbreaks, especially dengue.

Similar results were found in the study carried out by Rivas et al. (2018) in Southern Brazil, and in that of Silva et al. (2020) in neighborhoods in Recife-PE, where the authors concluded that the information obtained through LIRAa allows vector control actions to be targeted more effectively. In addition to these, Ribeiro et al. (2021) when carrying out a comparative analysis between the IIP values and the Incidence Rates of 2011, 2012, 2013, 2015 and 2016, also obtained a significant correlation.

On the other hand, other authors question the prospect of LIRAa being a reference for guiding control actions (Chiaravalloti Neto *et al.*, 1999). Some have shown that LIRAa presents a certain degree of inaccuracy, and recommend adjustments in its implementation and the use of complementary policies to increase its predictive capacity (Souza *et al*., 2018; Enslen; Lima Neto; Castro, 2020). However, the analyses carried out in this work show that the information obtained through LIRAa can be used to reliably indicate the regions with the greatest possibility of outbreaks in the territory.

The spatial distribution of dengue fever highlighted the most incident points in the southern region of Maranhão. These same municipalities, according to data from the Maranhão Health Department (SES), showed high incidences of dengue fever in 2022. Only two municipalities, Lagoa do Mato and Matões, which despite having appeared as incidents on the kernel map, according to the dengue fever data provided by SES for the year under study, showed low incidences of dengue fever and other arboviruses this year.

Univariate spatial autocorrelation indicated ten municipalities as areas of greatest risk of dengue fever in , and six that are in transition to these clusters, indicating that the incidence of dengue fever in a municipality can influence the occurrence and increase of this incidence in neighboring municipalities. In other words, the data reveal the municipalities that are priority areas for intensifying epidemiological surveillance in the state, and highlight those that are in transition to high-risk areas, and therefore need to strengthen actions aimed at preventing this disease.

Modeling of climate variables showed that relative humidity and maximum temperature positively influence the occurrence of dengue cases. Other authors have also reported that at the beginning of the year, due to the rainy season, which presents high relative humidity, there is an increase in the number of dengue cases (Costa *et al*., 2021). Temperature is a climate variable that has been shown to regulate the occurrence of dengue, with the favorable thermal threshold for the occurrence of the disease between temperatures considered high (Viana *et al*., 2018). However, the lack of a relationship between environmental variables and LIRAa may attribute greater responsibility for the increase in this index to the population.

The data reveal efficiency in the predictive effect of LIRAa in relation to the incidence of dengue in Maranhão, and the spatial modeling indicated the areas with the highest risk of dengue and priority for the intensification of entomoepidemiological surveillance in the state. This study presented important techniques that can assist health authorities in the development of specific strategies and reinforces the need for more effective prevention and control actions in order to reduce the impact of the number of cases and the severity of dengue and other arbovirus epidemics.

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