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Relationship between social inequality indicators and the spatial distribution of Zika Virus cases

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Abstract *The aim of this article was to analyze the possible relationship between social inequality indicators and the spatial distribution of ZIKV cases in a state in Northeastern Brazil in 2015-16. This is an ecological study with the data of notified ZIKV cases and the sociodemographic indicators of Rio Grande do Norte state (RN), based on information from the State Public Health Department (SESAP-RN) and DATASUS. The data were analyzed in Terraview version 4.2.2, Geoda version 1.12 and IBM SPSS Statistics 21. Both the average incidence rate (AIR) of ZIKV cases in 2015-16 (Moran = 0.139; p= 0.03) and the AIR of violence (Moran= 0.295; p= 0.02), average household income (Moran= 0.344; p=0.01) and unemployment rate (Moran= 0.231; p=0.01) exhibited a geographic spatial distribution pattern. In multiple linear regression analysis, the variables AIR of violence and average household income explained 55% of the variation in the AIR of ZIKV in 2015-16 (adjusted R2 = 0.55). Municipalities with more notifications of violence and higher average income, such as the state capital, reported a higher number of ZIKV cases, possibly due to better organization, greater awareness of socioenvironmental problems and easier access to health services.*

Key words *Zika virus, Violence, Health indicators, Microcephaly, Epidemiology*

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Introduction

The Zika virus (ZIKV) is a disease caused by a group of viruses ecologically known as arboviruses[1]. In this case, from the genus *Flavivirus*, transmitted by the genus Aedes, whose main vectors are *Aedes aegypti* and *Aedes albopictus*. There is also the possibility of blood and neonatal transmission, although the real role of these transmission pathways in spreading this infection remains unknown[2].

Despite being considered an acute disorder with mild and self-limited manifestations, the ZIKV has become a worldwide problem due to its impact on health, and its association with a series of neurological disturbances, such as Guillain-Barré syndrome (GBS) and congenital malformations, in which microcephaly stands out[2].

This virus emerged in Brazil in 2015 with the autochthonous confirmation in Bahia state, followed by Rio Grande do Norte (RN)[3,4]. It was initially detected in RN in the municipality of Natal and later in São Gonçalo do Amarante[3,5], with 8,743 and 113 suspected and confirmed cases, respectively. Between January and November 2016, 5,971 and 205 suspected and confirmed cases, respectively, were reported[6].

One of the hypotheses to justify this dissemination was the involvement of environmental and socioeconomic factors in the area, under the premise that this knowledge is essential in planning and managing health strategies to address this disorder[7,8].

A number of studies suggest a correlation between the social determinants of health such as ethnicity, schooling, and income, and increased incidence of ZIKV and its consequences, such as microcephaly[9-11].

Social inequalities in health are the perceived and measurable differences related to access to prevention, cure and health rehabilitation services. They are closely linked to the individuals' social environment and are significantly influenced by social conditions and the area in which they live[12,13].

Assessment of social inequalities in the context of arbovirus epidemics is important given that both *Aedes aegypti* and *Aedes albopictus*, the primary arbovirus vectors in the country, have extended their geographic range to urban environments, especially cities in developing countries, where the accelerated urbanization process has been poorly planned, leading to sociospatial problems[14].

An example of a sociospatial problem that impacts public health is structural inequality, involving luxurious neighborhoods with adequate infrastructure and public services on one hand and precarious neighborhoods with poorly distributed income distribution, no basic services such as a sewer system, trash collection and fresh water supply, on the other, characterizing a permanent state of physical-environmental insecurity[15,16].

The health-disease process involves complex factors related to the living conditions of individuals, known as the social determinants of health (SDH). Along with health status, these socioeconomic, cultural, ethical/racial, psychological and behavioral factors make it possible to identify where and how public health interventions should be conducted in order to provide a greater impact, thereby reducing inequities[1,17,18].

However, despite the confirmed relationship between social determinants and disease, the technological and biomedical aspects are still neglected[2]. An example of this approach is the ZIKV epidemic, revealing how global health systems neglect the diversity of experiences and the multiple situations of inequality, thereby hindering full understanding of the disease[7].

As such, the aim of this study was to analyze the relationship between social inequality and spatial distribution of ZIKV cases in a state of Northeastern Brazil in 2015-2016.

Methodology

Study design, site and population

This is an ecological investigation whose study units are the municipalities of Rio Grande do Norte state (RN), located in Northeastern Brazil and bordered by the Atlantic Ocean to the East and North, Paraíba state to the South and Ceará state to the North. It is divided into 167 municipalities and covers an area of 52,811,110 Km², representing 3.42% of the Northeast region and 0.62% of the country.

According to the Brazilian Institute of Geography and Statistics (IBGE)[19], RN is divided into four geographic mesoregions, according to the following similar social and economic criteria: the Coastal Potiguar (consisting of 25 municipalities), East Potiguar (43 municipalities), Central Potiguar (37 municipalities), and West Potiguar (62 municipalities).

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Data collection and the variable studied

Based on the influence of socioenvironmental factors on the incidence of ZIVK cases, this study aimed to analyze the relationship between social inequality indicators and the spatial distribution of ZIKV cases in RN state in 2015-2016. Initially, the number of ZIKV cases in 2015-16 was obtained from the Information of Disease Notification System (SINAN), followed by adding the number of cases divided by the population during these years, obtaining a ratio per 10,000 inhabitants, denominated Average Incidence Rate (AIR) of ZIKV in 2015-2016.

The following socioenvironmental variables were tested: 1) AIR of violence in 2014: which corresponds to the incidence of violence in 2014 divided by the population of that year, obtaining a ratio per 10,000 inhabitants; 2) Average per capita household income in 2010: average household income of individuals living in a specific location, in the year under study; 3) Unemployment rate in 2010: proportion (%) of the economically active resident population aged 16 years or older unemployed during the reference period, in a specific geographic location, during the year under study; 4) Illiteracy in 2010: proportion of illiterates in the population; 5) Water supply in 2010: percent of the resident population supplied with water in 2010; 6) Sanitation facilities in 2010: percent of the resident population with sanitary facilities in 2010; 7) Gini Index in 2010: degree of inequality in the distribution of individuals according to per capita household income; 8) Gross Domestic Product (GDP) in 2013: municipal GDP. Values are presented in thousands of Brazilian reais, with no deflator or correction factor.

These socioenvironmental variables were collected from the DATASUS website under "Health Information", restricting the search to demographic and socioeconomic information during periods near 2015, the year of the ZIKV outbreak in the country.With respect to the ethical aspects of the research, this study was not submitted to the ethics committee, since there was no possibility whatsoever of physical or moral damage to the individuals, and the principles contained in resolution 466/12 were strictly adhered to.

Data analysis

The cartographic basis used was that of the IBGE, obtained on its website. First, thematic maps of the aforementioned variables were created using TerraView 4.2.2 software, a phase that included exploratory analysis of spatial data. The quantitative legend of the AIR of ZIKV in 2015-16 was divided into five ranges, using the "same steps" option. The gray scale was used for visual comparison and an image gradient to create the legend, where the municipalities with the worst situation are represented by the darkest color. Spatial dependence was analyzed using the Global Moran index, which estimates spatial autocorrelation, varying between -1 and +1, in addition to providing statistical significance (p-value). According to the spatial dependence hypothesis, the Moran values can be positive (direct correlation; similar values tend to be located near one another) or negative (inverse correlation; high values are surrounded by low values and vice versa). The presence of clusters was analyzed using the local Moran's index (LISA), which determines the dependence of data in relation to their neighbors. This indicator makes it possible to identify the spatial association that characterizes the occurrence of *clusters* between the polygons under study. These data were presented in a box map (showing the presence of clusters without considering significance), and Moran map (showing the clusters with statistical significance).GeoDa software, version 1.12 (Spatial Analysis Laboratory, University of Illinois, Urbana-Champaign, USA) was used in LISA bivariate analysis to assess the spatial correlation between the outcome variable (AIR of ZIKV in 2015-16) and the independent variables, which exhibited spatial distribution based on the Global Moran Index and met the criteria established for bivariate analysis. Thus, there is a linear association between a variable xk at location i, xk I and the spatial lag corresponding to the other variable Wyi 1 (1k1 = xk 'Wyi/n). To that end, thematic maps were created with each pair of variables and their statistical significance was determined.

Spatial dependence can be direct or reverse according to the Moran value obtained. There are two types of relationships between neighbors in the clusters, as follows: High-High (high AIR of ZIKV in 2015-2016 and high rates of the independent variable), Low-Low (low AIR of ZIKV in 2015-2016 and low rates of the independent variable), High-Low (high AIR of ZIKV in 2015-2016 and low rates of the independent variable), Low-High (low AIR of ZIKV in 2015-2016 and high rates of the independent variable).

The independent variables of this study that exhibited autocorrelation in spatial analysis were tested using the multivariate spatial regression model in the GeoDa version 1.12 program and the model that best represented the relationship of the variables was the classic linear regression model. The IBM SPSS Statistics 21 program was used in regression analysis. The independent variables that best predicted the average incidence rate of the ZIKV in 2105-2016 remained in the final model.

Results

In regard to the existence of spatial autocorrelation for the AIR of ZIKV, Moran's Global Coefficient was 0.172 and significant for 2015 (p = 0.04), and 0.075 and non-significant for 2016 (p = 0.07). However, the AIR of 2015-16 showed autocorrelation in the distribution of these cases, with a Global Moran Coefficient of 0.139 and *p-value* = 0.03 (Figure 1).

With respect to analysis of spatial dependence, no spatial autocorrelation was found for the variables water supply (Moran = 0.001, p = 0.46), illiteracy (Moran = 0.039, p = 0.18), Gini index (Moran = 0.049, p = 0.22), sanitary facilities (Moran = 0.001, p = 0.46) and gross domestic product (GDP) (Moran = 0.007, p= 0.42). These indicators did not meet the criteria established for bivariate analysis and were therefore not included in subsequent analyses. In this respect, the AIR of violence, average household income and unemployment rate will be considered.

The map of RN shows that the largest number of municipalities with a high average incidence rate of ZIKV are in the Coastal Potiguar mesoregion, where the state capital is located (Figure 1c).

In relation to the box map, which shows the autocorrelation of the variables, the Coastal Potiguar mesoregion exhibited the largest number of high-high clusters in the AIR of ZIKV in 2015-2016 (Figure 2a) and AIR of violence (Figure 2b). The latter rate also displayed high-high clusters in part of the East Potiguar mesoregion (Figure 2b). This type of cluster was found in the Central Potiguar mesoregion for average household income (Figure 2c). For unemployment rate, the high-high cluster was observed in part of the Central and West Potiguar regions (Figure 2d).

The Moran Map shows all the polygons with a significant spatial autocorrelation index, where this study demonstrates that the municipalities of the East Potiguar mesoregion, such as Natal, and others belonging to the metropolitan region of the capital, including Extremoz and Parnamirim, displayed significant high-high clusters in the AIR of ZIKV in 2015-16 and the AIR of violence and average household income, but not the unemployment rate (Figure 3). For average household income, a high-high cluster was observed for municipalities in the Central Potiguar mesoregion, specifically the East Serido microregion (Figure 3c).

With respect to spatial bivariate analysis (LISA), the municipalities of Extremoz, Natal and São Gonçalo exhibited clusters with high AIR of ZIKV in 2015-16 and high AIR of violence (Figure 4a). Extremoz and Natal also obtained a high AIR of ZIKV in 2015-16 and high average household income. The last finding was also recorded for the municipality of Parnamirim (Figure 4b).

Moreover, clusters of high AIR of ZIKV were found in 2015-16 and a low unemployment rate in the municipalities of Serrinha, Caicó and Timbaúba dos Batistas (Figure 4c).

In multiple linear regression, to determine whether the AIR of violence, average household income and unemployment rate would be able to predict the AIR of ZIKV, the AIR of violence and average household income explained 55% of the variation in the AIR of ZIKV (adjusted $R^2 = 0.55$). This analysis resulted in a statistically significant model [F (1.164) = 102,37; p = 0.001; adjusted R^2 = 0.550], demonstrating that the AIR of violence (β = 0.609, t = 9.402, p= 0.001) and average household income (β = 0.200, t = 3.093, p = 0.002) are predictors of the AIR of ZIKV (Table 1).

Discussion

The present study showed that the AIR of ZIKV in 2015-2016 exhibited spatial distribution in RN, with the formation of high-high clusters for AIR of violence and household income, primarily in the metropolitan region of Natal. The formation of unemployment rate clusters was diffuse in the state, which was confirmed once again in multiple regression analysis, where the variable was not a predictor for AIR of ZIKV.

These findings corroborate the importance of social inequality indicators in understanding the health-disease process of a population[7,9,20,21]. Studies have shown a correlation between the social determinants of health, such as ethnicity, schooling, income and ZIKV, and their consequences, including microcephaly[9-11].

It is important to underscore that less than one year after its introduction in Brazil, ZIKV is unequally distributed in all regions, with a high-

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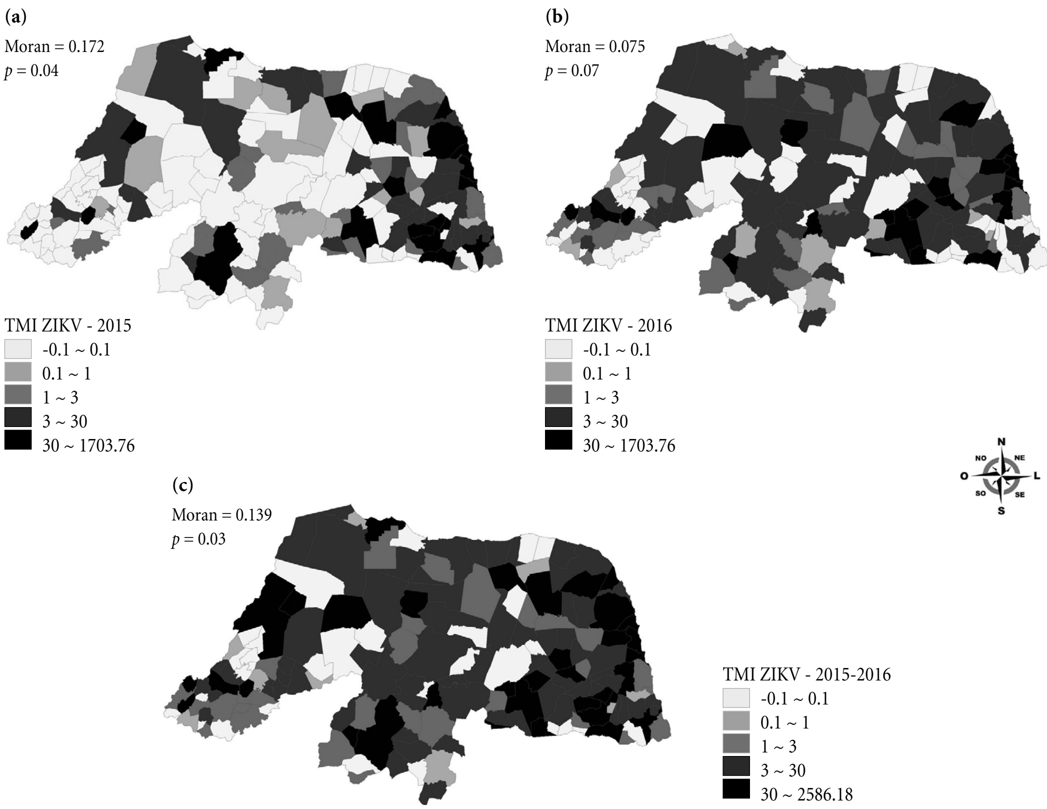

Figure 1. (a) Thematic map of the AIR of ZIKV in 2015, (b) Thematic map of the AIR of ZIKV in 2016, (c) Thematic map of the AIR of ZIKV in 2015-16 with the respective Global Moran value and its statistical significance. Rio Grande do Norte state, Brazil. Santa Cruz, 2019.

er number of cases in the Northeast and Southeast, and subsequent continuous transmission throughout most of the country[9,11,20,22].

Among the determinants of ZIKV evolution, Garcia[20] includes the difficulties in vector control, poor family planning measures, the lack of maternal-infant care, in addition to significant inequalities that characterize the country. These aspects contribute to the Zika virus and its most devastating consequence, namely, microcephaly in babies, becoming endemics that affect primarily low-income families living in underdeveloped regions.

The relationship between average household income and the AIR of ZIKV in 2015-2016 has been reported in studies that found poor socioeconomic conditions associated with an increase in ZIKV incidence and its comorbidities, such as microcephaly. These studies highlight the fact that poor socioeconomic conditions may compromise fetal development, due to lack of access to health services and social vulnerability in addition to mothers' difficulties understanding the real needs of their baby[10,21,23].

Studies underscore the importance of not disregarding the influence of social, economic and environmental factors related to the ZIKV, given that knowing the profile and cause of diseases in an area is essential to help plan public health policies and strengthen the National Health System (SUS), which could reduce the incidence of disease in the region under study[7,24,25].

One of the factors that has contributed to the correlation between a high AIR of ZIKV in 2015-16 and a high average household income is the fact that these municipalities with better incomes (capitals and metropolitan regions) also have better case notification. Ishitani et. al.[26] also observed this characteristic, which justifies this relationship with better technical-operational

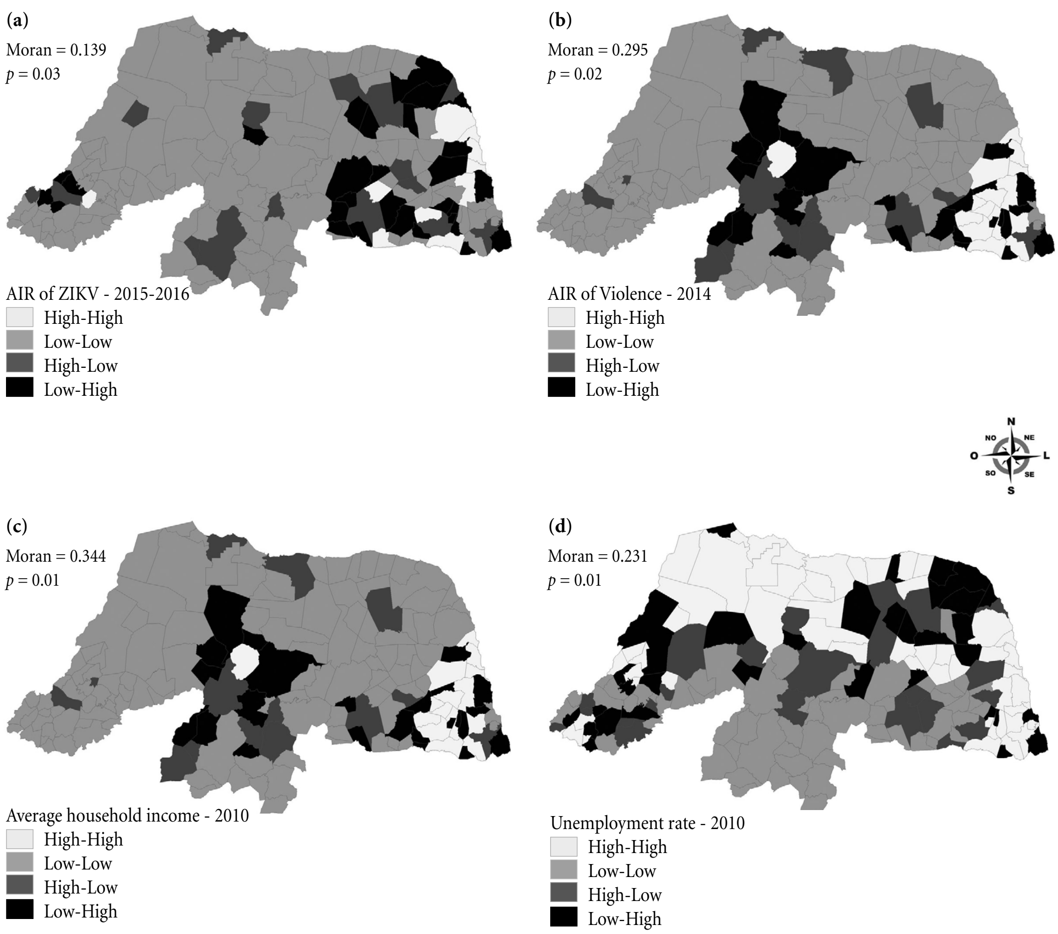

Figure 2. (a) Spatial autocorrelation map (box map) of the AIR of ZIKV in 2015-16, (b) Spatial autocorrelation map (box map) of the AIR of violence in 2014, (c) Spatial autocorrelation map (box map) of average household income in 2010, (d) Spatial autocorrelation map (box map) of the unemployment rate in 2010. Rio Grande do Norte state, Brazil. Santa Cruz, 2019.

conditions in the epidemiological surveillance system to detect, notify and investigate cases[27,28].

These technical-operational conditions may explain another finding of the present study, namely the high rates of violence with a high AIR of ZIKV in the East Potiguar mesoregion that encompasses metropolitan Natal, the state capital, with health services better able to detect and notify cases.

Studies suggest that violence is associated with socioenvironmental factors such as high population density, unequal resource distribution, low family income, among other situations, and that these factors result in social inequities in terms of access to essential consumer goods such as health services[29-32].

According to Ferri et al.[33], violence is linked to disturbances over the course of life that result in negative neonatal outcomes when they occur during pregnancy. The incidence of violence is a public health problem with repercussions for individual and collective health, requiring the creation of specific practices and services. This becomes even more evident given the incidence of violence in RN, with the highest homicide rate in Northeastern Brazil (53.4 murders per 100,000 inhabitants in 2016). This reinforces the importance of investing in governance tools that allow

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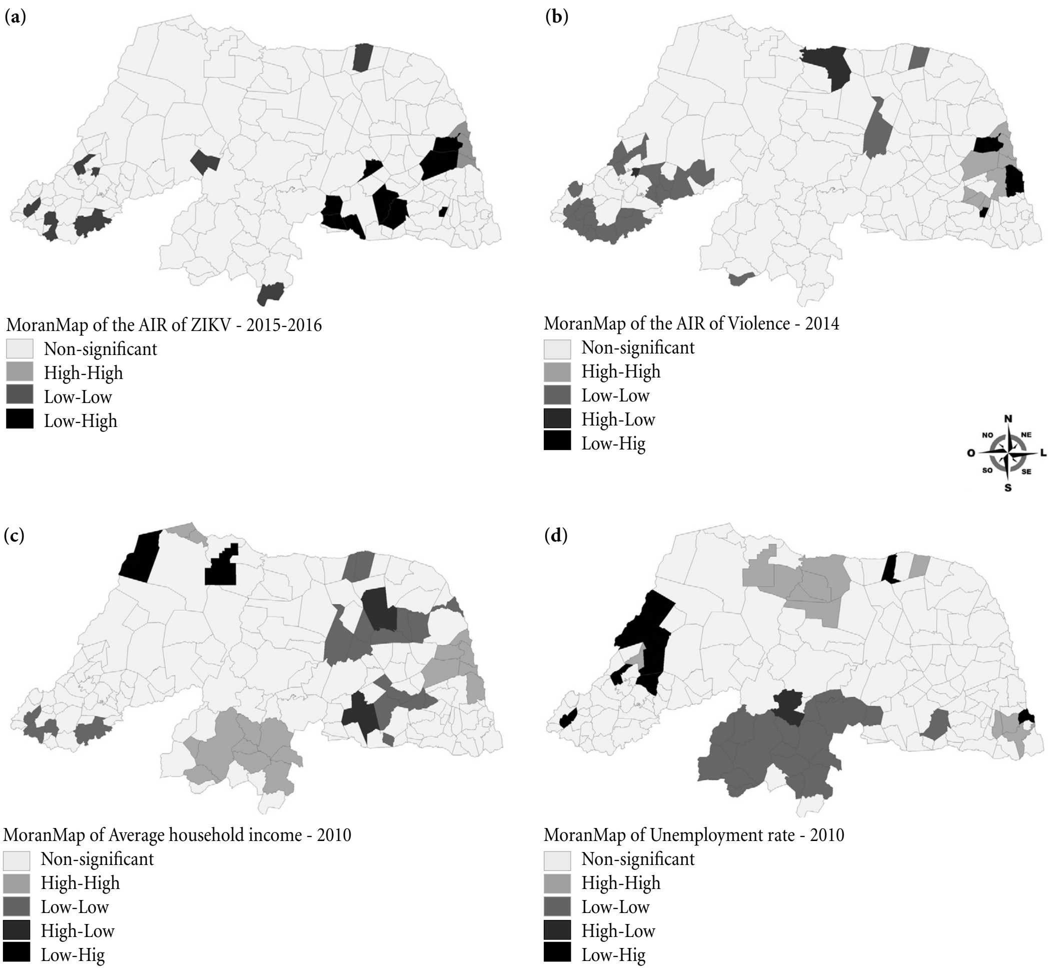

Figure 3. (a) Spatial autocorrelation map (MoranMap) of the AIR of ZIKV in 2015-16, (b) Spatial autocorrelation map (MoranMap) of the AIR of violence in 2014, (c) Spatial autocorrelation map (MoranMap) of average household income in 2010, (d) Spatial autocorrelation map (MoranMap) of the unemployment rate in 2010. Rio Grande do Norte state, Brazil. Santa Cruz, 2019.

the states to implement pacification policies[34-36].

However, one of the limitations of this study was to not georeference information using more detailed geographic levels (studies with data points, neighborhoods and census blocks) that could determine the existence of vulnerable areas in these municipalities due to the effects of scale and area aggregation. Furthermore, the coefficients of correlation may be different from those at the individual level, causing the so-called "ecological fallacy"[37].

Another limitation is the disadvantage of working with a secondary database, namely the collection date. For the independent variables, updated data for the same period as the ZIKV outbreak were not available in the DATASUS and IBGE databases. However, data closest to the analysis period of the present study (ZIKV incidence) were collected. According to Freitas et. al.[38], this limitation occurs because these variables are obtained from demographic censuses, which causes data discontinuity, since they are only collected every ten years.

Moreover, despite exhibiting ecological correlations, the present study will help create public policies aimed at preventive measures that can be

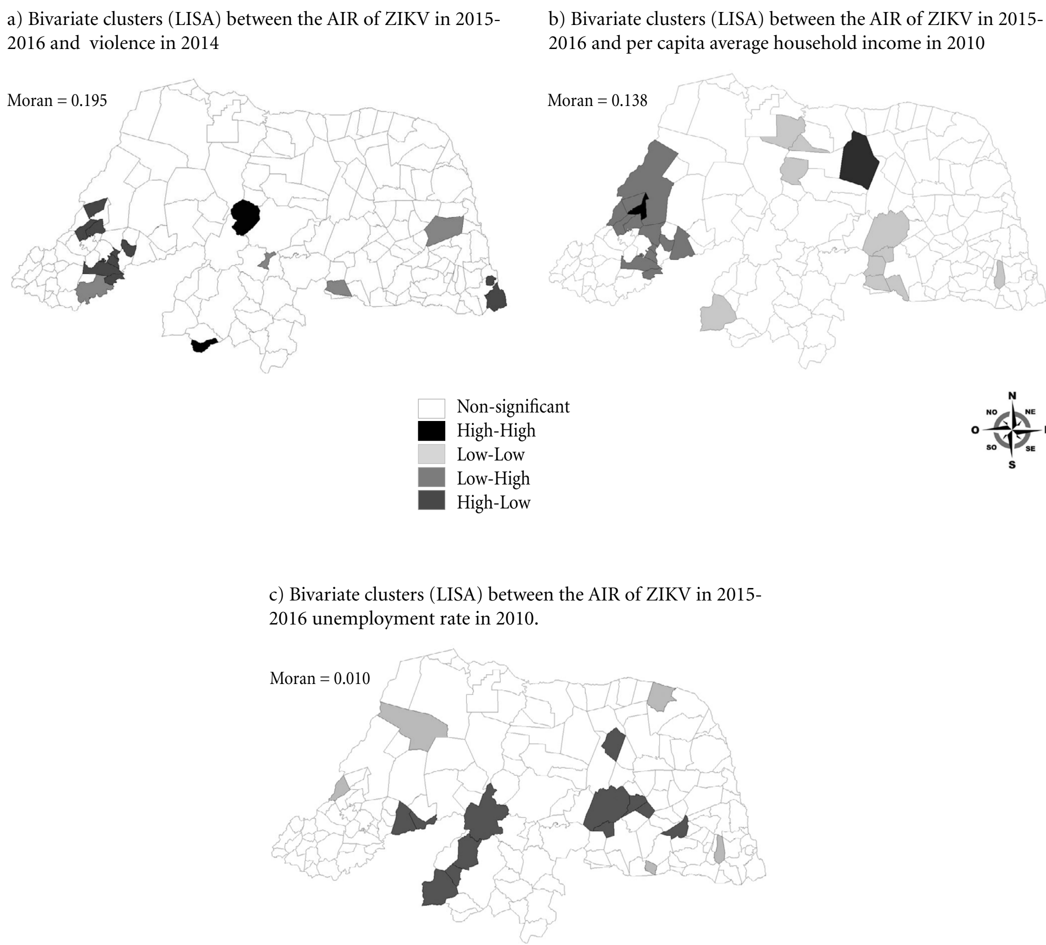

Figure 4. Spatial correlation between average incidence rate of ZIKV in 2015-16 with: incidence of violence in 2010; (b) per capita average household income in 2010 and (c) unemployment rate in 2010. Rio Grande do Norte state, Brazil, 2019.

Table 1. Multiple linear regression model with predictors of the dependent variable average incidence rate of ZIKV in 2015-2016.

	Non-standardized coefficient		Standardized coefficient	t	p
	B	Standard error	Beta		
(Constant)	-152.656	50.233		-3.039	0.003
Incidence of violence in 2014	5.644	0.600	0.609	9.402	0.000
Average household income in 2010	0.529	0.171	0.200	3.093	0.002

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used as criteria for equitable distribution of public resources, prioritizing regions with the worst social inequalities in health.

Conclusion

This study demonstrated that municipalities in the East Potiguar mesoregion, such as Natal and its metropolitan area, with more notifications of violence and favorable average income, exhibit higher AIR of ZIKV cases, possibly due to better access to health services, which improves the notification of ZIKV cases in these municipalities.

These findings may also reflect the demographic density of these municipalities, given that high population density may shed more light on socioenvironmental problems.

The findings of the present study indicate a correlation between socioenvironmental determinants and ZIKV cases in RN state. This may prompt new discussions on the issue, which is currently highlighted by the damage it causes, making essential to understand both the life cycle and transmission of the ZIKV.

In addition, the Health Information Systems for Epidemiological Surveillance are vital for analyzing social inequalities in health, under the premise that this knowledge is essential when devising health planning and management strategies to cope with this disorder and its consequences.

Collaborations

LS Cunha, WR Medeiros, FAV Lima Junior, SA Pereira actively contributed to this article, including writing and revising the text and presenting the results.

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