









Spatiotemporal analysis of the HIV epidemic in older people in a Brazilian Amazon state

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Abstract

Objective: To analyze spatiotemporally the incidence of the human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) among older people in the State of Pará, Brazil, from 2007 to 2018. **Method:** An ecological study of HIV/AIDS case notifications in older people from the Brazilian Information System on Notifiable Diseases. The HIV/AIDS incidence rate was temporally analyzed by the joinpoint method, and spatially by the Moran autocorrelation of scanning and spatial regression techniques. **Results:** 2,639 notifications of HIV/AIDS were eligible for the study, with 1,725 (65.4%) being in men and 914 (34.6%) in women. During the study period, there was an increase of 2,422.5% in the HIV incidence rate in men and 1,929.8% in women, with the opposite being observed for the AIDS incidence rate, which increased 77.6% in women and 40.7% in men. The joinpoint method showed an increasing trend for the HIV incidence rate (APC=30%, $p=0.00$) and stability for the AIDS incidence rate (APC=3.0%, $p=0.2$). The most impacted municipalities by the HIV epidemic were those in the south-eastern part of Pará, with a moderate association ($R^2=0.65$) with its population growth. The spatiotemporal scanning analysis pointed to Belém as a risk zone for HIV/AIDS (RR=3.93, $p=0.00$; 2017-2018). **Conclusion:** While the incidence of AIDS among older people from Pará remained stable from 2007 to 2018, that of HIV tended to grow. The greatest impact of the epidemic occurred in southeastern Pará municipalities, and it was associated with the population growth; Belém presented a spatiotemporal risk for HIV/AIDS.

Keywords: Spatial Analysis.
HIV. Health of the Elderly.

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INTRODUCTION

About 38 million people are living with the human immunodeficiency virus (HIV) worldwide. Although progress has been made in fighting it, 1.7 million people were diagnosed with the virus in the year 2019¹. In this scenario, people aged 50 years and over stand out as the number of newly reported cases has been increasing. Around 100,000 people in this age group are diagnosed every year with HIV in developing countries². However, this phenomenon still occurs in developed countries as well. In Canada, the ratio of new HIV diagnoses in people aged 50 years and over went from 15.1% to 22.8% of all reported cases between 2008 and 2017³. The same happened in the European Union, with the HIV notification rate (x100 thousand inhabitants) increasing in the same age group between 2004 and 2015 from 3.5 to 4.8 in men and from 1 to 1.2 in women⁴. In the United States, one in every six HIV diagnoses in 2018 was of a person aged 50 years and over⁵. In Brazil, the age group of 50 years represented 9.34% of the total number of new HIV/AIDS cases notified in 2008, rising to 12.42% in 2018⁶.

Most studies on the HIV epidemic deal with young people and adolescents. However, although the sexual activity decreases with age, many older people remain sexually active but with little knowledge on the modes of transmission and prevention of HIV and underestimating the risk of infection, which makes them more vulnerable^{7,8}. Given this situation, the worldwide phenomenon of population aging is a concern. It is estimated that in 2050 people over 65 years of age will represent 16% of the entire world population⁹.

The spatial dynamics of the HIV epidemic must be considered when fighting it, as it is directly influenced by sociopolitical and economic factors¹⁰. In this context, spatial analysis studies stand out for allowing the identification of areas of greatest epidemiological pressures and association with territorial factors. On the other hand, temporal analysis studies allow us to assess the annual impact of public policies aimed at fighting the epidemic¹¹. Only three spatial analysis studies involved people aged 50 years and over, two in China^{12,13} and one in Brazil¹⁴. China showed a higher incidence of HIV/

AIDS in people aged 50 years and over in provinces belonging to the illicit drug trafficking circuit^{12,13}. A higher incidence of HIV/AIDS was observed in the state of Paraíba, Brazil, in the municipalities with a population of over 100,000 inhabitants, with epidemic expansion in coastal municipalities and into the countryside of the state¹⁴.

Although the average HIV/AIDS detection rate in Brazil decreased between 2008 and 2018, it increased by 21.8% in the Northern region of the country. In 2019, Pará was ranked as the fifth Brazilian state with the highest HIV/AIDS detection rate, and the capital Belém was the second capital among other Brazilian capitals. Belém, Marituba, and Ananindeua were respectively the second, third, and ninth places among the 100 Brazilian municipalities with more than 100,000 inhabitants and the highest HIV/AIDS detection rates¹. Besides the low coverage of the Family Health Strategy (FHS)¹⁵, there are only 32 antiretroviral (ARV) dispensing units for the 144 municipalities in Pará (<http://azt.aids.gov.br>), of which only two located in Belém providing Pre-Exposure Prophylaxis (PreP)¹.

Pará is ranked 24th in terms of the Human Development Index (HDI) among the 27 federative units of Brazil, despite its diversified fauna and mineral resources¹⁶. Besides the low investment in urban infrastructure and low FHS coverage^{15,17}, the countryside municipalities in Pará are undergoing an accelerated urbanization process due to the development of the mineral extractive industry and, attracting many migrants in search of jobs and better living conditions¹⁸, a favorable scenario for the transmission of sexually transmitted infections (STIs).

The objective of the present study was to analyze the HIV epidemic among older people in Pará, Brazil with the use of spatial and temporal analysis techniques.

METHODS

An ecological study carried out with secondary data from the Brazilian Information System on Notifiable Diseases (SINAN) provided by the Pará State Department of Public Health (SESPA).

Pará is the second Brazilian state with the largest territorial area (1,245,870,798 Km²) and a population of 8,175,156 people, and it is estimated that the age group of 50 years and over is greater than 1,231,570 inhabitants representing 15.06% of the total population¹⁹.

The records of HIV and AIDS among people aged 50 and over notified to the Brazilian Information System on Notifiable Diseases (SINAN) and provided by SESPA were consulted. According to the Joint United Nations Programme on HIV and AIDS (UNAIDS), every person living with HIV aged 50 and over is considered an older person²⁰. Only notifications with home addresses in Pará were included in the study; information in duplicate and those without municipality of residence were excluded.

Data were collected from January to February 2020. Data were collected from the following variables: age, gender, date of diagnosis, type of diagnosis (HIV or AIDS), and the municipality of residence. To calculate the annual municipal incidence of HIV/AIDS, the number of notifications was divided by the population of people aged 50 years and over, and the result was multiplied by 100,000. The population projections for each year obtained from the website of the Brazilian Institute of Geography and Statistics (IBGE) were used here. The 2018 population projection was subtracted from the 2007 projection to obtain the percentage of population growth. The result was then divided by the 2007 population projection and multiplied by 100.

Temporal analysis

Although the HIV diagnosis has become a mandatory notification only as of 2014²¹, the HIV and AIDS incidence rates were analyzed separately in the temporal analysis to verify the behavior of the incidence rate of each one of them separately. The annual incidence rates underwent a temporal regression using the Joinpoint model²² to calculate the annual percentage change (APC). The APC is calculated based on the inflection points in a historical series where lines from multiple segments are tested to see if they better explain the behavior

of the series than just a straight line. The annual trend value is calculated based on the combination of straight lines on a logarithmic scale. The trend is increasing or decreasing depending respectively on a positive or negative APC and a $p\text{-value} \leq 0.05$. Otherwise, the trend is considered stationary.

Distribution and spatial autocorrelation of the HIV/AIDS incidence rate

For the spatial analysis, the incidence of HIV/AIDS per quadrennium (2007-2010, 2011-2014, 2015-2018) was used to avoid annual fluctuations. The incidence rate was calculated based on the population mean of each municipality for each of the quadrenniums. After that, the spatial distribution of the incidence rate was analyzed and the global Moran spatial autocorrelation was used. The global Moran index (I) ranges from -1 to 1, with negative values and $p\text{-value} \leq 0.05$ indicating the inverse self-correlation, municipality with high incidence rate surrounded by municipalities with low incidence rate, or vice versa (high-low or low-high incidence grouping, respectively). When the value of I is positive and $p\text{-value} \leq 0.05$, direct autocorrelation occurs (low-low and high-high grouping incidence). Otherwise, the random distribution is considered. Both analyzes were performed using ArcGIS software (10.6.1).

Moran's global analysis points to whether or not there is spatial aggregation. However, it does not show the location of the clusters. For this, we used the local Moran analysis with the method of local indicator of spatial association (LISA), with the first-order contiguity matrix of the queen type and the $p\text{-value}$ obtained with 999 permutations.

Spatial scan analysis

To identify the risk areas for the HIV epidemic, spatial scanning was applied using the SaTScan software (Version 9.6.1), a method proposed by Kulldorff and Nagarwalla²³. In summary, SaTScan employs circular or elliptical windows to calculate the spatial clusters, while for spatiotemporal clusters the windows are elliptical with a circular base, the base corresponding to space, and the height to time.

The windows move in space and time to search for risk clusters, always comparing the risk inside and outside the window. For each change found, the program calculates the log-likelihood ratio (LLR) and the statistical significance value with Monte Carlo permutations. The window with the highest LLR and with $p \leq 0.05$ is considered a risk cluster. Our study used the discrete Poisson model to identify the spatial risk clusters considering circular, non-geographically overlapping clusters, with the maximum size of each cluster not exceeding 50% of the exposed population, and 999 Monte Carlo permutations. The temporal precision in year and cluster with a maximum of 50% for the twelve years of the study were used in addition to the criteria already mentioned to identify the spatiotemporal aggregates. The estimated cluster strength was expressed by calculating the relative risk (RR). Only RRs with $p \leq 0.05$ were considered, in which $RR \geq 1$ indicated risk zones, while those with $RR < 1$ were considered protection zones, that is, those with lower risk for the event to occur. Thematic maps with the RRs were generated in the ArcGIS software (10.6.1).

Spatial regression analysis

To analyze the spatial regression, the dependent variable was the incidence of HIV/AIDS for the entire period studied, and the Human Development Indexes of the municipalities were the independent variables, as well as the percentage of population growth between 2007 and 2017 in addition to the FHS coverage rate. First, Pearson's correlation analysis was applied to verify the collinearity between the independent variables in the IBM SPSS® software version 23. Then, the stepwise technique was applied in the Geoda software (version 1.14.0) to obtain the best model of ordinary least squares (OLS). The best model was found to be the one with the lowest Akaike value (Aic), the highest R^2 and R^2 adjusted, the variance inflation factor (VIF) less than 10, and the lowest p-value. Then, the global Moran analysis was applied to discard the spatial dependence of the model residues in the ArcGIS software, and only then the residues were analyzed using the geographically weighted regression (GWR) with the Kernel adaptive

radius for better adjustment to the chosen model. In the end, the spatial dependence of the residues of the final GWR model was tested again, followed by the creation of choroplethic maps to visualize the correlations.

All maps were generated in the Datum Horizontal SIRGAS-2000 geographic coordinate system, longlat projection system EPSG 4674. All results with $p \leq 0.05$ were considered statistically significant.

The present study is part of the macro-research project "Situational Diagnosis of Sexually Transmitted Infections in the Amazon Context: Geospatial Analysis, Tracking and Development of Care-Educational Technologies", and was approved by the Research Ethics Committee of the Health Sciences Institute of Universidade Federal do Pará under opinion number 3,488,663.

RESULTS

From 2007 to 2018, 2,679 cases of HIV/AIDS in people aged 50 and over in Pará were notified to SINAN, of which 40 notifications were excluded due to incompleteness in the notification forms. Among the 2,639 eligible cases, 1,725 (65.4%) were in men and 914 (34.6%) in women. During the study period there was an increase of 2,203.85% in the incidence rate of HIV (2007: 0.78, 2018: 17.97) and of 48.50% of AIDS (2007: 7.71; 2018: 11.45). The HIV incidence rate increased 2,422.5% in men and 1,929.8% in women (Men: 2007=0.89, 2018=22.45; Women: 2007=0.67, 2018= 13.6) when analyzed separately by gender. However, in the AIDS incidence rate, women showed an increase of 77.57% and men 40.69% (Men: 2007=11.63, 2018=16.29; Women: 2007=3.79, 2018=6.73).

Table 1 shows the temporal regression analysis using the joinpoint method of annual incidence rates for the entire population aged 50 and over and separated by gender - male and female. For the general population, both males and females, the AIDS incidence rate tended to remain stable throughout the study period, while the HIV incidence rate tended to grow.

Table 1. Time regression analysis of incidence rates by gender for HIV and AIDS in people aged 50 years and over in Pará in the period from 2007 to 2018. Pará, 2020.

| Period | HIV | | | Aids | | |
|-------------|------|-------------|-----------------|------|------------|-----------------|
| | APC | (95%CI) | <i>p</i> -valor | APC | (95%CI) | <i>p</i> -valor |
| Male/Female | | | | | | |
| 2007-2018 | 30 | (22.4-38.1) | <i>p</i> <0.001 | 3 | (-2.1-8.4) | 0.2 |
| Male | | | | | | |
| 2007-2018 | 31.8 | (21.7-42.8) | 0.04 | 3.2 | (-2.3-9.1) | 0.2 |
| Female | | | | | | |
| 2007-2018 | 24.7 | (18.6-31) | <i>p</i> <0.001 | 2.7 | (-2.8-8.4) | 0.3 |

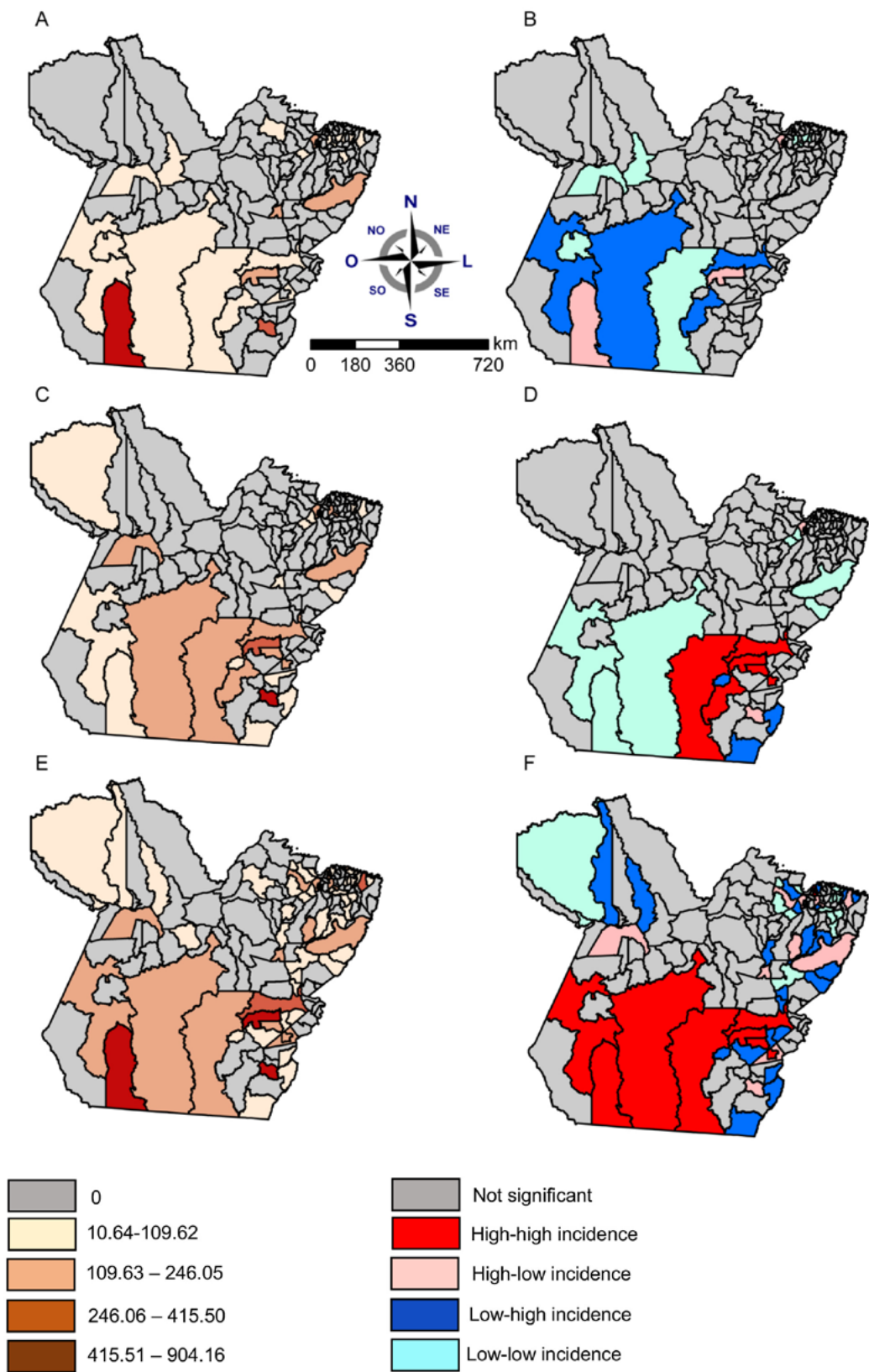
Figure 1 shows the maps of the spatial distribution of HIV/AIDS incidence, in which the municipalities of southern and southwestern meridional Pará have the highest rates. Although the global Moran's analysis did not present statistical significance in any of the four-year years evaluated (2007-2010: $I=-0.18$, $p=0.80$; 2011-2014: $I=-0.11$, $p=0.67$; 2015-2018: $I=0.05$, $p=0.27$), the local Moran analysis indicated a low-low incidence cluster in the southwest meridional (Altamira, Itaituba and Novo Progresso) and another high-high incidence cluster in the southeast (São Félix do Xingu, Canaã dos Carajás, Parauapebas, Marabá and Ourilândia do Norte) in the quadriennium 2011-2014. In the quadriennium 2015-2018 there was only one high-high incidence cluster formed by the municipalities of Altamira, Itaituba, Novo Progresso, São Félix do Xingu, Canaã dos Carajás, Parauapebas and Marabá.

The scanning analysis showed two regions of spatial risk for HIV/AIDS, with the highest ($RR=2.73$, $p=0.00$) being observed in the southwestern meridional municipalities (São Félix do Xingu, Tucumã, Canaã dos Carajás, Parauapebas, Marabá, Ourilândia do Norte, Xinguara, Rio Maria, Redenção, Pau D'Arco, Bannach and Água Azul

do Norte) and the other in the municipality of Belém ($RR=2.69$, $p=0.00$). The spatiotemporal scan indicated only Belém as the municipality at risk in the period from 2017 to 2018 ($RR=3.93$, $p=0.00$) (Figure 2).

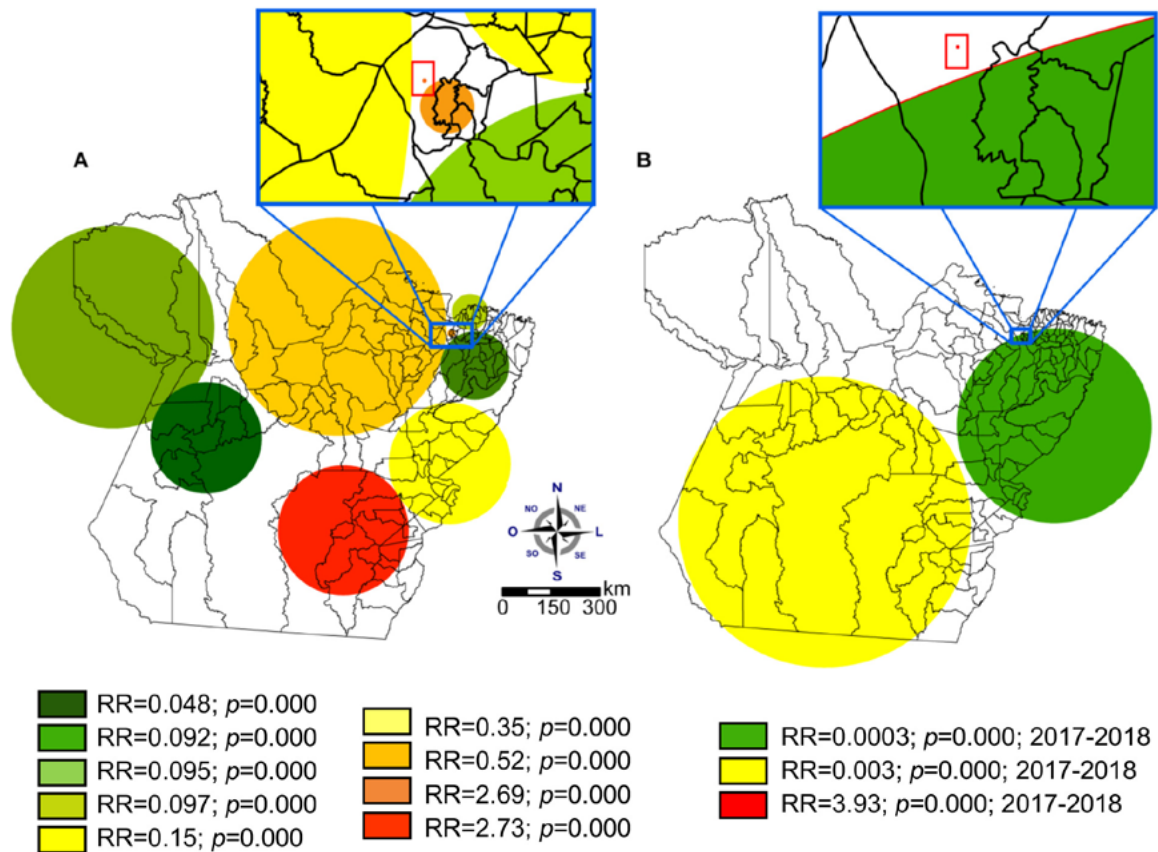
For spatial regression, Pearson's correlation showed statistical significance between the dependent variable (incidence of HIV/AIDS) with the variables of percentage population growth ($r=0.028$, $p=0.00$) and with the HDI-m ($r=0.41$, $p=0.00$). However, in the construction of the OLS model, the explanatory model of percentage population growth was chosen as it presents VIF less than 10 ($VIF=1.40$) (Table 2).

The GWR analysis proved to be the best explanatory model for model 2 than for OLS, which explains 65% of the model chosen ($R^2=0.65$, R^2 adjusted=0.51, and $AIC=1845.73$), with the residues generated not showing spatial autocorrelation ($I=0.04$, $p=0.46$). Figure 3C shows the direct correlation between the GWR coefficients and the highest rates observed in the southern meridional municipalities in Pará Cumaru do Norte, Santa Maria das Barreiras, Santana do Araguaia, Bannach, Redenção, Concórdia do Pará, Santana do Araguaia, Rio Maria).



A, C, E: Spatial distribution of the HIV/AIDS incidence rate; B, D, F: MAPAS LISA; A,B: 2007-2010; C, D: 2011-2014; E,F: 2015-2018.

Figure 1. Spatial distribution of the HIV/AIDS incidence rate. Pará, 2020.

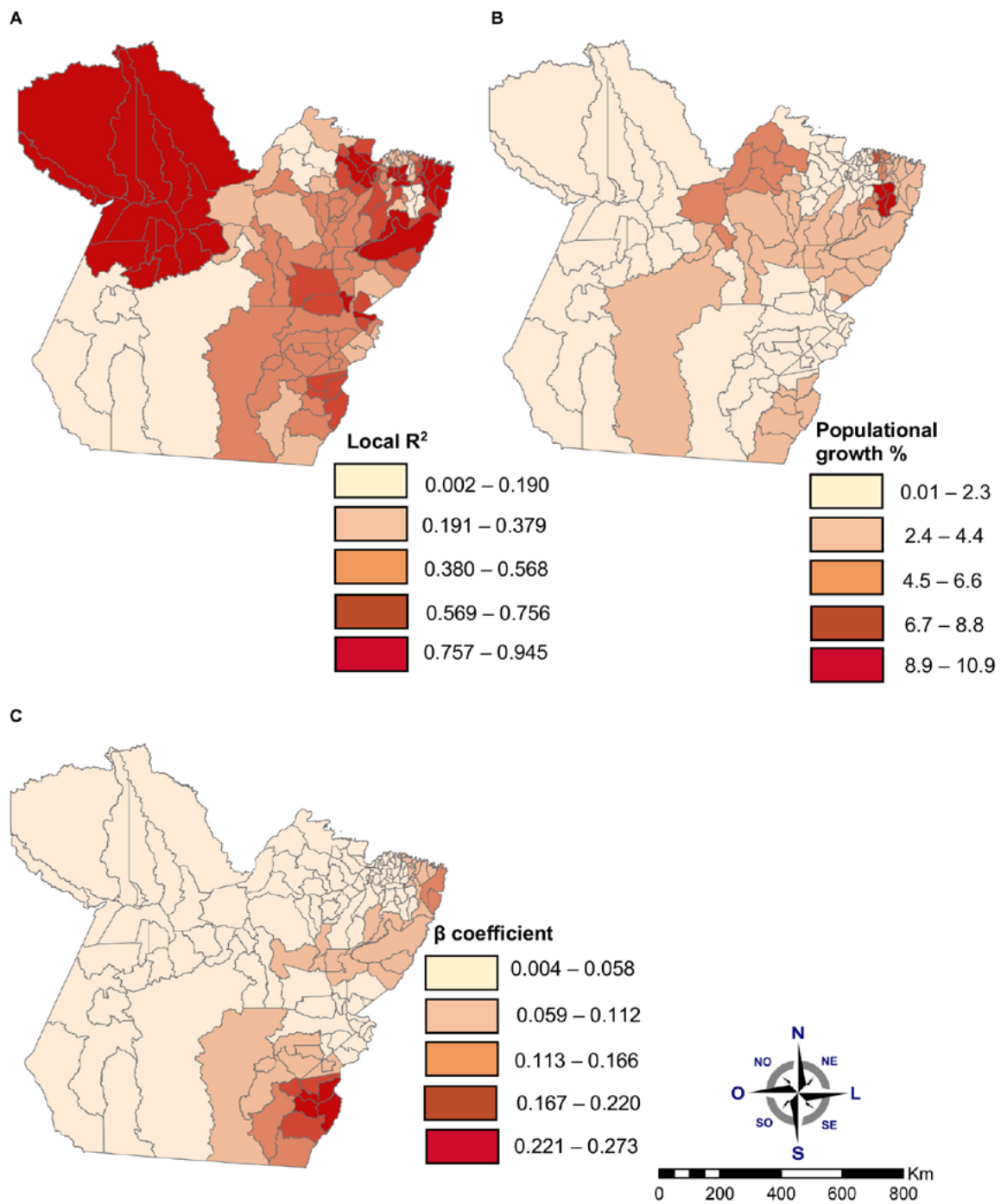


(A) Space risk; (B) Spatiotemporal risk for HIV/AIDS; The red rectangle delimits the circle indicating Belém as a region of spatial and spatiotemporal risk for HIV/AIDS.

Figure 2. Spatial scan analysis for HIV/AIDS. Pará, 2020.

Tabela 2. Multiple linear regression (OLS) of the percentage of municipal population growth and HDI-m with the HIV/AIDS incidence rates. Pará. 2020.

| Variables | Estimate | Standard Error | p-value |
|---|----------|----------------|-------------|
| Model 1 | | | |
| Constant | -551.15 | 160.15 | $p < 0.001$ |
| Percent population growth | 1067.25 | 277.77 | $p < 0.001$ |
| HDI-m | 0 | 0 | 0.08 |
| R ² : 0.17; Adjusted R ² : 0.16; AIC: 1889.71; Multicollinearity: 23.91 | | | |
| Model 2 | | | |
| Constant | 61.51 | 15.63 | $p < 0.001$ |
| Percent population growth | 0.01 | 0 | $p < 0.001$ |
| R ² : 0.08; Adjusted R ² : 0.07; AIC: 1,902.05; Multicollinearity: 1.40 | | | |
| Model 3 | | | |
| Constant | -658.88 | 148.85 | $p < 0.001$ |
| HDI-m | 0.01 | 0 | $p < 0.001$ |
| Multiple R ² : 0.15; Adjusted R ² : 0.14; AIC: 1,890.79; Multicollinearity: 20.89 | | | |



A: % of municipal population growth; B: R² location adjusted; C: Coefficient β of the percentage of municipal population growth with the HIV/AIDS incidence rate.

Figure 3. Geographically Weighted Regression mapping of percentage municipal population growth with the HIV/AIDS incidence rate. Pará, 2020.

DISCUSSION

The results of the present study showed that while the incidence of HIV tends to grow in the population aged 50 years and over in Pará, the incidence of AIDS tends to stabilize. The spatial analysis showed that the municipalities in southeastern and southwestern Pará have the highest incidences of HIV/AIDS, with the highest spatial risk zones formed by municipalities in southeastern Pará and Belém, while the spatiotemporal analysis showed that Belém was the highest risk region in the years 2017-2018. Spatial regression showed that the high incidence of the HIV epidemic in southeastern Pará was strongly associated with the population growth in these municipalities.

It was also evident that while the AIDS diagnosis remained stable throughout the period the HIV diagnosis tended to grow. This fact may be related to the mandatory notification of HIV diagnosis from 2014 onwards, and the decentralization of screening tests for the virus that are performed by the ESFs²¹. However, unlike what has been observed in the African continent after the universalization of anti-HIV testing and antiretroviral treatment with a reduction in the virus transmission, Aids, and mortality from Aids in all age groups^{23,24}, the present study showed an increase in the HIV incidence rate and stability in the AIDS rate.

Besides the need to expand testing and antiretroviral treatment in Pará, it is necessary to implement public policies to raise awareness about the forms of transmission and prevention of HIV specifically for this age group studied. A study carried out in South Korea with people over 65 years of age showed that those sexually active, and especially men, had multiple sexual partners and did not use condoms. However, those who were aware of the risks of sexually transmitted infections (STIs) practiced safer sex⁶.

The gender disparity observed in our study, in which the AIDS incidence rate showed the highest percentage increase in women, was also evidenced in the previous studies^{2,12}. The incidence of HIV/AIDS in men aged 50 years and over decreased in the United States between 2014 and 2018, remaining stable among women². In China, the ratio of HIV

cases reported in women over 50 years went from 17.83% in 2010 to 38.10% in 2016¹². Gender inequality resulting from biological, social, cultural, economic, and religious factors puts women in a situation of greater vulnerability to STIs.

The spatial analysis showed that the municipalities in southeastern and southwestern Pará were the most impacted by the HIV epidemic, a phenomenon that is directly associated with population growth. The municipalities in southeastern and southwestern Pará present an intense urbanization process promoted by the expansion of the mining industry, cattle-raising activity, and the construction of hydroelectric plants. The population growth of these municipalities has been taking place in an accelerated, disorganized way and without the proportional monitoring of investment in urban infrastructure^{18,19}. In sub-Saharan Africa, the high mobility of the population in search of better living conditions has been identified as a catalyst for the HIV epidemic²⁵. Population growth and density are directly associated with the expansion of STI, being directly influenced by social, educational, and per capita income inequality²⁶.

Categorized as the second-highest spatial risk for HIV, Belém is the city in Pará with the highest demographic density¹⁶. These results are consistent with a study carried out with older people in Rio de Janeiro, in which the most populous cities in the state, Rio de Janeiro and Niterói, had the highest incidence of AIDS²⁷.

Low investment in health can also contribute to the scenario of the HIV epidemic in Pará, a state with one of the lowest FHS coverage in Brazil (54.5%), most of them located in urban areas, which makes it difficult to access inhabitants in the countryside of Pará due to the geographic characteristics of the region and the high level of poverty of the inhabitants^{15,28}. The FHS plays a leading role in the fight against HIV/AIDS with actions ranging from the promotion of sexual health, prevention of STIs, diagnosis and monitoring of patients²⁹. Testing for HIV was intensified in Belém at the end of 2016 with the decentralization of tests for FHSs³⁰. This fact is consistent with the results of the spatiotemporal scan pointing to Belém as the region of greatest risk in the period from 2017 to 2018.

As this is an ecological study, causality between HIV transmission and race or skin color, immigration, or other social phenomena cannot be inferred due to the confounding factors omitted in this type of analysis. Additionally, the study was limited by the forms with incomplete data, but they were in small numbers and did not affect the analysis.

CONCLUSION

The present study showed that while the incidence of AIDS in people aged 50 years and over remained stable from 2007 to 2018 in Pará, the incidence of HIV tended to increase among women and men. The spatial analysis revealed the greatest impact of the epidemic on this age group in the southern meridional

municipalities in Pará, with a strong association with its population growth. The spatiotemporal analysis showed that Belém is the municipality with the highest risk, which may be associated with the intensification of public policies to fight HIV as of December 2016 by the Health and Environment Secretariat of Belém.

Given the above, there is a need for greater investment in public health policies in southeastern and southwestern Pará, Brazil, to fight HIV, contemplating not only the expansion of coverage of the Family Health Strategy but also investment in infrastructure following urban development to entitle citizens with their universal right to health.

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