















# Spatial Analysis of Notified Zika Virus Congenital Syndrome, Maranhão, 2015 to 2018

*Análise espacial da taxa de detecção de casos suspeitos de síndrome congênita pelo vírus Zika, Maranhão, 2015 a 2018*

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**ABSTRACT:** *Objective:* To identify spatial patterns in cases of changes in growth and development related to Zika virus infection and other infectious etiologies (denominated Zika virus congenital syndrome in this study) reported in Maranhão from 2015 to 2018 and their relation with socioeconomic and demographic variables. *Methods:* Ecological study of notified Zika virus congenital syndrome cases in the 217 cities of Maranhão, Brasil. Spatial autocorrelation was calculated using GeoDa 1.14 software and the local and global (I) Moran's index in univariate and bivariate analyses on Zika virus congenital syndrome incidence rate with Municipal Human Development Index (MHDI), population density, Gini coefficient and the cities' time of administrative political emancipation. Local Moran's Index was calculated to identify clusters with significant spatial autocorrelation. *Results:* Spatial autocorrelation was checked in univariate analysis of the incidence rate of Zika virus congenital syndrome ( $I=0,494$ ;  $p=0,001$ ) and positive correlation in bivariate analysis of the incidence rate with Municipal Human Development Index ( $I=0,252$ ;  $p=0,001$ ), population density ( $I=0,338$ ;  $p=0,001$ ) and the cities' time of administrative political emancipation ( $I=0,134$ ;  $p=0,001$ ). The correlation between incidence rate with Gini coefficient was not significant ( $I= -0,033$ ;  $p=0,131$ ). Five high-incidence clusters were found in distinct areas of the state. *Conclusions:* Cities with higher MHDI, higher population density and more years of administrative political emancipation had more cases of Zika virus congenital syndrome notified.

**Keywords:** Microcephaly. Zika Virus. Spatial analysis. Public health surveillance. Socioeconomic factors.

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**Conflict of interests:** nothing to declare – **Financial support:** This is a subproject of the project "Congenital Zika virus syndrome, seroprevalence and spatial and temporal analysis of Zika and Chikungunya viruses in Maranhão", financed by the Ministry of Science, Technology and Innovation (MCTIC)/National Scientific and Technological Development Fund (FNDCT), National Council for Scientific and Technological Development (CNPq)/Ministry of Education-Coordination for the Improvement of Higher Education Personnel (MEC-CAPEs)/MS-Decit 14/2016 — Prevention and Fight against Zika virus.

**RESUMO:** *Objetivo:* Identificar padrões espaciais em casos de lactentes com alterações de crescimento e desenvolvimento relacionadas à infecção pelo vírus Zika e outras etiologias infecciosas (neste trabalho denominado de síndrome congênita pelo vírus Zika), notificados no Maranhão de 2015 a 2018 e sua relação com variáveis socioeconômicas e demográficas. *Métodos:* Estudo ecológico de casos suspeitos notificados de síndrome congênita pelo vírus Zika nos 217 municípios do Maranhão, Brasil. Calculou-se a autocorrelação espacial pelos índices de Moran local e global (I) univariado e bivariado da taxa de detecção de casos suspeitos de síndrome congênita pelo vírus Zika com índice de desenvolvimento humano municipal, densidade demográfica, índice de Gini e tempo de emancipação político-administrativa dos municípios. O índice de Moran local foi calculado para localizar *clusters* com autocorrelação espacial significativa. *Resultados:* Houve autocorrelação espacial na análise univariada da taxa municipal de detecção de casos suspeitos de síndrome congênita pelo vírus Zika ( $I=0,494$ ;  $p=0,001$ ) e, na análise bivariada, correlação positiva da taxa de detecção de casos suspeitos com índice de desenvolvimento humano municipal ( $I=0,252$ ;  $p=0,001$ ), densidade demográfica ( $I=0,338$ ;  $p=0,001$ ) e tempo de emancipação dos municípios ( $I=0,134$ ;  $p=0,001$ ). Não houve correlação significativa da taxa de detecção de casos suspeitos com o índice de Gini ( $I= -0,033$ ;  $p=0,131$ ). Cinco *clusters* de alta detecção de casos suspeitos foram encontrados em áreas distintas do estado. *Conclusões:* Os municípios com maior índice de desenvolvimento humano municipal, maior densidade demográfica e mais tempo de emancipação político-administrativa tiveram mais casos suspeitos notificados de síndrome congênita pelo vírus Zika.

*Palavras-chave:* Microcefalia. Zika vírus. Análise espacial. Vigilância em saúde pública. Fatores socioeconômicos.

## INTRODUCTION

The Zika virus (ZKV) is transmitted by the bite of an infected female of *Aedes aegypti*, sexually and via the placenta. In Brazil, ZKV was first reported in the Northeast region of the country in 2014, triggering an outbreak in 2015, accompanied by the emergence of cases of Zika virus congenital syndrome (ZVCS)<sup>1</sup>. The term ZVCS refers to congenital manifestations caused by intrauterine exposure to the ZKV, which include microcephaly, seizures, muscle contractures, auditory and ocular anomalies<sup>2</sup>. From 2015 to 2018, Brazil reported 17,041 cases of changes in growth and development related to ZKV infection and other infectious etiologies<sup>3</sup>.

The Northeast region of Brazil has the lowest municipal human development indices (MHDI) and a greater income inequality (high Gini indices), at the same time having the highest detection of suspected cases of ZVCS<sup>1</sup>. Maranhão, located in this region of the country, is the penultimate in the HDI ranking among Brazilian states<sup>4</sup> and the seventh state in the region with the highest number of notifications of growth and development anomalies related to ZKV infection and other infectious etiologies until 2018<sup>3</sup>.

Spatial analysis techniques allow us to investigate the spatial distribution of health problems, diseases and risky situations, which helps to detect vulnerable areas and to learn in more detail the patterns of health conditions of a population and all disparities<sup>5</sup>. With the advancement of statistical methods and spatial analysis techniques, studies on the geographic

distribution of congenital anomalies and their etiological factors have been proven important for public health in Brazil and worldwide<sup>6</sup>.

In this study, considering that ZVCS' occurrence is greater in the poorest areas of the country, the hypothesis that, in Maranhão, there were more records of ZVCS cases in municipalities with lower MHDI and higher Gini indices was raised; as well as those with greater demographic density, leading to potential higher rates of vector infestation; in municipalities with more time of political-administrative emancipation, as they have a better epidemiological surveillance structure. The aim of this study was to identify spatial patterns of suspected cases of ZVCS reported in Maranhão from 2015 to 2018 and their relation with the aforementioned socioeconomic and demographic variables.

## METHODS

Ecological study with spatial analysis of reported suspected cases of growth and development anomalies related to ZKV infection and other infectious etiologies (in this work called ZVCS) in the municipalities of Maranhão, from January 2015 to November 2018.

The study area comprised the state of Maranhão, which has 217 municipalities and is located in the Northeast region of Brazil. In 2018, its demographic density was 22.54 inhabitants/km<sup>2</sup> and its population was 7,035,055 inhabitants<sup>3</sup>.

Suspected cases of ZVCS were notified, at birth or later, in a specific system called Public Health Event Registry (RESP, in the Brazilian acronym). RESP data collection was carried out from April to November 2018. The RESP is an online notification system developed by the Ministry of Health whose purpose is to record public health emergencies. For the immediate notification of suspected cases of microcephaly, an online form in was created RESP by the Information Technology Department of the Unified Health System (DATASUS), called RESP-Microcephaly and used to notify suspected cases of microcephaly and/or central nervous system (CNS) changes possibly associated with congenital infections.

In this study, the outcome of interest was the detection rate of suspected cases of ZVCS by municipality, calculated based on the ratio between the number of suspected cases reported and the number of live births in January 2015 to November 2018 multiplied by 10,000 inhabitants. For the state of Maranhão, the monthly detection rate of suspected cases was calculated. The number of live births for each municipality was obtained from the database of the Information System on Live Births (SINASC).

The following demographic and socioeconomic variables used were: date and city of birth, obtained from the RESP; MHDI and Gini index, taken from the 2010 census; demographic density, with the estimated population of 2018, and the year of political-administrative emancipation of municipalities taken from the website of the Brazilian Institute of Geography and Statistics (IBGE)<sup>4</sup>. To calculate the time of emancipation, the year 2015 was used as a reference.

The MHDI consists of three indicators: income, longevity and education, ranging from zero to one. The municipality's demographic density is defined by the number of inhabitants per square kilometer. The Gini index measures social inequality based on per capita income and varies from zero to one—the closer to one, the greater the social inequality<sup>4</sup>.

The cases of ZVCS notified were grouped by municipality, using the municipal digital grid of the state of Maranhão. All municipalities were included in the spatial analysis, regardless of case notification. The detection rate of suspected cases was smoothed by the local Bayesian estimation method.

To verify whether neighboring cities exhibited similar trends in the detection rate of suspected ZVCS cases, the univariate global Moran index (I) was calculated as a measure of spatial autocorrelation. To assess the spatial dependence between the detection rate of suspected ZVCS cases and demographic density, MDHI, Gini index and time of political-administrative emancipation, the bivariate global Moran index was applied. The global Moran index provides a general measure of spatial association existing in the dataset<sup>7</sup>. It ranges from -1 to +1, and values close to zero indicate no spatial autocorrelation; positive values indicate positive spatial autocorrelation and negative values indicate negative spatial autocorrelation. For those with a spatial pattern, the values are positive, close to 1, that is, neighboring areas have a similar behavior. On the other hand, values close to -1 indicate negative spatial autocorrelation, that is, the attribute's value in neighboring regions are contrasting<sup>8</sup>.

To identify clusters of municipalities with autocorrelation and significant spatial correlation of detection rate of suspected ZVCS cases, the local Moran index was used and demonstrated in the Lisa Cluster Map. The local Moran index provides a specific value for each area, allowing for identification of clusters with significant patterns of spatial association. This index classified the municipalities according to the significance level of their local indexes' values as: high/high (municipality with high value, surrounded by neighbors with high value) and low/low, indicating points of positive spatial association, or similar to neighbors; and high/low and low/high, indicating points of negative spatial association, that is, the location has neighbors with different values<sup>8</sup>.

The GeoDa software version 1.14 was used for spatial analysis, and the significance level for spatial autocorrelation was set at  $p < 0.05$ .

The project was approved by the Research Ethics Committee of the University Hospital of Universidade Federal do Maranhão (HUUFMA), under opinion n° 2.111.125.

## RESULTS

In RESP, 426 cases of ZVCS were registered during the study period. Of these, four were duplicates, so 422 were analyzed. The detection rate of suspected ZVCS cases per 10,000 live births in the state was 15.99 in 2015; 13.84 in 2016; 5.75 in 2017 and 1.49 in 2018. Suspected ZVCS cases were reported in 111 municipalities, with the highest detection rate of suspected cases in Alcântara — 62.97/10,000 live births (data not shown in tables). The children began

to be born in January 2015, although the ZVCS outbreak was only noticed in October of the same year. The peak of reported suspected cases occurred in December 2015 and there was a decrease after the first quarter of 2016, more accentuated after February 2018 (Figure 1).

The univariate global Moran index showed significant positive spatial autocorrelation for the estimated suspected case detection rate from 2015 to 2018. The bivariate global Moran index showed a positive correlation of suspected ZVCS case detection rate with population density, MHDI and time of emancipation of the municipalities from 2015 to 2018. No statistically significant spatial correlation was detected with the Gini index (Table 1).

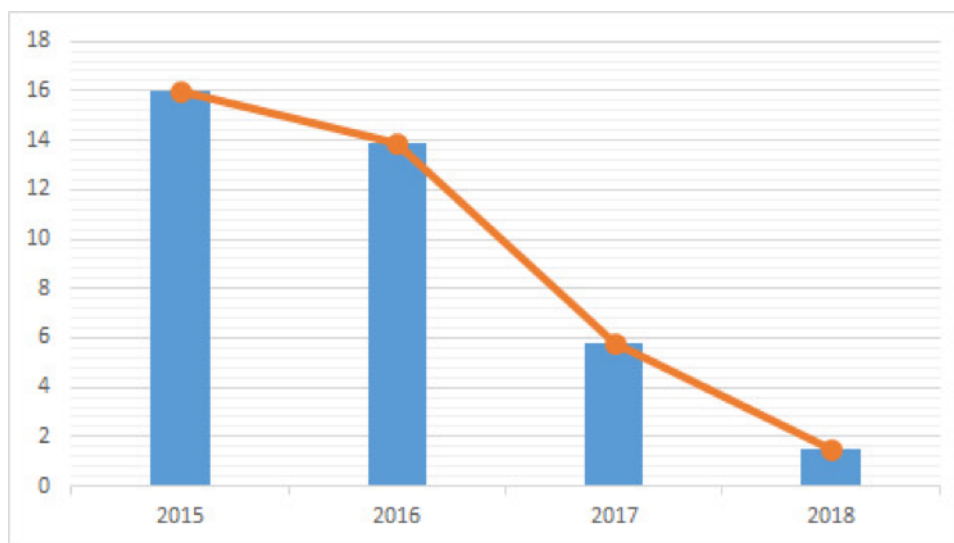


Figure 1. Annual detection rate of suspected cases of Zika virus congenital syndrome per 10,000 live births in Maranhão, from 2015 to 2018.

Table 1. Univariate analysis of the municipal detection rate of suspected cases of Zika virus congenital syndrome from 2015 to 2018 and bivariate analysis of the detection rate of suspected cases with municipality emancipation time, demographic density, Gini index and municipal human development index in the 217 municipalities of Maranhão.

Univariate analysis		
	Global Moran Index	p-value
Detection rate of suspected cases from 2015 to 2018	0.494	0.001
Bivariate analysis with the detection rate of suspected cases between 2015 and 2018		
	Global Moran Index	p-value
Municipality emancipation time	0.134	0.001
Demographic density	0.338	0.001
Gini Index	-0.033	0.131
Municipal Human Development Index	0.252	0.001

The local Moran index identified clusters formed by 18 municipalities with a high detection rate of suspected ZVCS cases in the north (where the state capital is located), west, southwest and south regions; clusters formed by 12 municipalities with high detection rates of suspected ZVCS cases and with longer political-administrative emancipation time, as well as clusters (nine municipalities) with high demographic density were identified in the north; clusters (21 municipalities) with high detection rate of suspected ZVCS cases and high MHDI values were also found in the north, west and southwest of the state (Figure 2) (Table 2).

## DISCUSSION

A significant spatial pattern of the distribution of reported suspected cases in the state was identified, with clusters of high detection of suspected cases especially around the state capital. A similar pattern was verified in Maranhão by Costa et al.<sup>9</sup> in relation to the incidence rate of Zika. Zika clusters can become ZVCS clusters approximately three months after the outbreak in a given region<sup>10</sup>.

In a study carried out in the northeastern state of Rio Grande do Norte, Cunha et al.<sup>11</sup> found higher notification of ZKV cases in municipalities with higher average income,

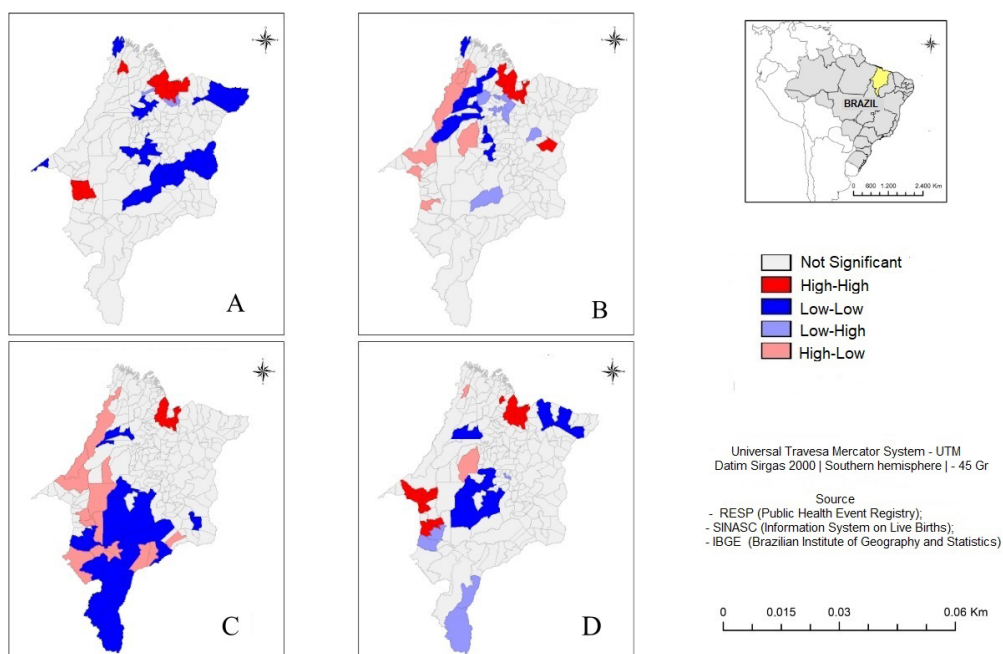


Figure 2. Lisa Cluster Map of the detection rate of suspected cases of Zika virus congenital syndrome (A) and spatial correlations between detection rate of suspected cases of Zika virus congenital syndrome and emancipation time of municipalities (B), demographic density (C) and municipal human development index (D). Maranhão, 2015–2018.

probably with better infrastructure and greater access to health services, such as the capital Natal. Such discrepancy was attributed to a better capacity to recognize and notify cases.

The positive spatial correlation between the municipal rates of detection of ZVCS suspected cases and MHDI is probably explained by the better structure for registering cases in the municipalities with the best HDI. However, two studies carried out in Recife/PE found a higher risk of ZVCS in districts with a low HDI<sup>12</sup> and in places with poor housing conditions<sup>13</sup>. An analysis of the relationship between socioeconomic factors and suspected ZVCS cases in Brazil did not find an association between the detection rate of suspected cases and MHDI, but it attested to a strong correlation between the distribution of cases

Table 2. Characteristics of the clusters of the municipal detection rate of suspected cases of Zika virus congenital syndrome. Maranhão, Brazil, 2015–2018.

<i>Clusters</i>	Number of municipalities in <i>clusters</i>
<b>Detection rate of suspected cases</b>	
High-high	18
Low-low	39
Low-high	3
High-low	0
<b>Detection rate of suspected cases x Time of political-administrative emancipation</b>	
High-high	12
Low-low	7
Low-high	8
High-low	9
<b>Detection rate of suspected cases x Demographic density</b>	
High-high	9
Low-low	21
Low-high	0
High-low	16
<b>Detection rate of suspected cases x MHDI</b>	
High-high	21
Low-low	15
Low-high	5
High-low	2

MHDI: municipal human development index.



with higher poverty rate. The same study infers that socioeconomic factors influenced the development of the ZVCS outbreak that started in the Northeast<sup>14</sup>.

A positive correlation was found between the detection rate of suspected ZVCS cases and population density. Amaral et al.<sup>15</sup> found a higher incidence rate of microcephaly in Brazilian cities with larger populations, higher mobility rate and coverage by primary care, which can be explained by the greater ease of transmission of congenital infections and the greater ease of diagnosis (in this case coverage of primary care).

Corroborating our findings, an analysis of the spatial distribution of congenital anomalies in the state of Paraná resulted in a significant association with the degree of urbanization, highlighting the greater capacity for health surveillance in urbanized areas<sup>16</sup>, while Mocelin et al. found a lower number of ZVCS notifications in rural municipalities of Espírito Santo<sup>17</sup>.

There was no statistically significant spatial correlation between the detection rate of suspected cases and the Gini index. In Brazil, Ali et al.<sup>18</sup> demonstrated a strong correlation between ZVCS and lower gross domestic product (GDP) per capita in the federative units and postulated that the proximity of socioeconomically distinct areas can facilitate the transmission of ZKV, overcoming social barriers. In the Americas, Gardner et al.<sup>19</sup> also found a positive correlation with population density, and a negative association between GDP per capita and ZKV transmission.

The finding of more ZVCS records in municipalities with higher MHDI, greater demographic density and longer time of political emancipation suggests that municipalities with these characteristics have a better structure of health services, including health surveillance. While the simple fact of emancipating a municipality does not guarantee its development<sup>20</sup>, it is assumed that although ZVCS is a disease related to poverty, municipalities with lower HDI, lower demographic density and less time of emancipation have not been able to structure epidemiological surveillance and thus guarantee the notification of cases.

Another aspect to be considered is the fact that the most populous environments, characterized by disorderly urban growth, poor housing conditions and ineffective basic sanitation services such as inadequate solid waste disposal can favor the risks of infections transmitted by multiplying vectors in these vulnerable areas and contribute to the increase in cases<sup>21</sup>.

Among the limitations of the study, it is noteworthy that multivariate spatial analysis was not performed to rule out the collinearity between population density and MHDI. All notifications were included, which represents a limitation related to the specificity of the outcome. Another limitation is the use of data (Gini, MHDI) from the 2010 census, given the unavailability of more recent socioeconomic indicators. It is noteworthy that the use of the spatial analysis unit was not punctual according to the address of residence of suspected case, that is, there was a certain degree of imprecision in analysis. Additionally, the spatial analysis unit at the municipal level does not allow the identification of intra-municipal disparities. The low frequency of cases contributes to imprecise estimates and the low magnitude of the spatial correlation found is evidence in favor of this interpretation. Furthermore, among the limitations of ecological studies, there is the possibility of an ecological fallacy.



This study draws attention to the need to improve the quality of health surveillance in the state's municipalities. Our strengths were the contribution to understanding the determinants related to ZVCS cases and the identification of priority areas through spatial analysis, which considers inequalities in geographic spaces.

## ACKNOWLEDGMENTS

We acknowledge CNPq for the financing of the project “Congenital syndrome caused by Zika virus, seroprevalence and spatial and temporal analysis of Zika and Chikungunya viruses in Maranhão”.

## REFERENCES

1. Barbeito-Andrés J, Schuler-Faccini L, Garcez PP. Why is congenital Zika syndrome asymmetrically distributed among human populations? *PLoS Biol* 2018; 16 (8): e2006592. <https://doi.org/10.1371/journal.pbio.2006592>
2. Moore CA, Staples JE, Dobyns WB, Pessoa A, Ventura CV, Fonseca EB, et al. Characterizing the pattern of anomalies in congenital Zika syndrome for pediatric clinicians. *JAMA Pediatr* 2017; 171 (3): 288-95. <https://doi.org/10.1001/jamapediatrics.2016.3982>
3. Ministério da Saúde. Secretaria de Vigilância em Saúde. Monitoramento integrado de alterações no crescimento e desenvolvimento relacionados à infecção pelo vírus Zika e outras etiologias infecciosas, até a Semana Epidemiológica 52 de 2018. Ministério da Saúde [Internet]. 2019 [accessed on Dec 22, 2019]. Available from: <http://portalarquivos2.saude.gov.br/images/pdf/2019/marco/22/2019-001.pdf>
4. Instituto Brasileiro de Geografia e Estatística. Conheça cidades e estados do Brasil [Internet]. 2019 [accessed on Nov 10, 2019]. Available from: <https://cidades.ibge.gov.br/>
5. Almeida Filho N, Barreto ML. *Epidemiologia & Saúde: fundamentos, métodos, aplicações*. Rio de Janeiro: Guanabara Koogan; 2012.
6. Lima LMM, Melo ACO, Vianna RPT, Moraes RM. Análise espacial das anomalias congênitas do sistema nervoso. *Cad Saúde Colet* 2019; 27 (3): 257-63. <https://doi.org/10.1590/1414-462X201900030313>
7. Druck S, Carvalho MS, Câmara G, Monteiro AMV. Spatial analysis of geographic data [Internet]. Brasília: Embrapa Cerrados; 2004. [accessed on Jan 7, 2021]. Available from: <http://livimagens.sct.embrapa.br/amostras/00075490.pdf>
8. Câmara G, Carvalho MS, Cruz OG, Correa V. Análise espacial de áreas. In: Druck, S, Carvalho MS, Câmara G, Monteiro AVM, editores. *Análise espacial de dados geográficos*. Brasília: São Paulo: Instituto Nacional de Pesquisas Espaciais; 2002.
9. Costa SDSB, Branco MDRFC, Aquino Junior J, Rodrigues ZMR, Queiroz RCS, Araujo AS. Spatial analysis of probable cases of dengue fever, chikungunya fever and zika virus infections in Maranhao State, Brazil. *Rev Inst Med Trop Sao Paulo* 2018; 60: e62. <https://doi.org/10.1590/S1678-9946201860062>
10. Vissoci JRN, Rocha TAH, Silva NCD, de Sousa Queiroz RC, Thomaz EBAF, Amaral PVM, et al. Zika virus infection and microcephaly: Evidence regarding geospatial associations. *PLoS Negl Trop Dis* 2018; 12 (4): e0006392. <https://doi.org/10.1371/journal.pntd.0006392>
11. Cunha LS, Medeiros WR, Lima Junior FAV, Pereira SA. Relationship between social inequality indicators and the spatial distribution of Zika Virus cases. *Cien Saude Colet* 2020; 25 (5): 1839-50. <https://doi.org/10.1590/1413-81232020255.34642019>
12. Souza AI, Siqueira MT, Ferreira ALCG, Freitas CU, Bezerra ACV, Ribeiro AG, et al. Geography of microcephaly in the Zika Era: a study of newborn distribution and socio-environmental indicators in Recife, Brazil, 2015-2016. *Public Health Rep* 2018; 133 (4): 461-71. <https://doi.org/10.1177/0033354918777256>
13. Souza WV, Albuquerque MFPM, Vazquez E, Bezerra LCA, Mendes ADCG, Lyra TM, et al. Microcephaly epidemic related to the Zika virus and living conditions in Recife, Northeast Brazil. *BMC Public Health* 2018; 18 (1): 130. <https://doi.org/10.1186/s12889-018-5039-z>

14. Campos MC, Dombrowski JG, Phelan J, Marinho CRF, Hibberd M, Clark TG, et al. Zika might not be acting alone: using an ecological study approach to investigate potential co-acting risk factors for an unusual pattern of microcephaly in Brazil. *PLoS One* 2018; 13 (8): e0201452. <https://doi.org/10.1371/journal.pone.0201452>
15. Amaral P, Carvalho LR, Rocha TAH, Silva NC, Vissoci JRN. Geospatial modeling of microcephaly and zika virus spread patterns in Brazil. *PLoS One* 2019; 14 (9): e0222668. <https://doi.org/10.1371/journal.pone.0222668>
16. Freire MHS, Barros APM, Andrade L, Nihei OK, Fontes KB. Análise geoespacial dos nascimentos com anomalias congênitas, Paraná, 2008-2015: estudo ecológico. *Rev Bras Enferm* 2020; 73 (3): e20180741. <https://doi.org/10.1590/0034-7167-2018-0741>
17. Mocelin HJS, Catão RC, Freitas PSS, Prado TN, Bertolde AI, Castro MC, et al. Analysis of the spatial distribution of cases of Zika virus infection and congenital Zika virus syndrome in a state in the southeastern region of Brazil: Sociodemographic factors and implications for public health. *Int J Gynaecol Obstet* 2020; 148 (Suppl 2): 61-9. <https://doi.org/10.1002/ijgo.13049>
18. Ali S, Gugliemini O, Harber S, Harrison A, Houle L, Ivory J, et al. Environmental and social change drive the explosive emergence of Zika virus in the Americas. *PLoS Negl Trop Dis* 2017; 11 (2): e0005135. <https://doi.org/10.1371/journal.pntd.0005135>
19. Gardner LM, Bóta A, Gangavarapu K, Kraemer MUG, Grubaugh ND. Inferring the risk factors behind the geographical spread and transmission of Zika in the Americas. *PLoS Negl Trop Dis* 2018; 12 (1): e0006194. <https://doi.org/10.1371/journal.pntd.0006194>
20. Magalhães J. Emancipação político-administrativa dos municípios no Brasil. In: Carvalho A, Albuquerque C, Mota J, Piancastelli M. Dinâmica dos municípios [Internet]. Brasília: IPEA; 2007 [accessed on Dec 22, 2019]. Available from: [http://www.ipea.gov.br/portal/images/stories/PDFs/livros/Capitulo1\\_30.pdf](http://www.ipea.gov.br/portal/images/stories/PDFs/livros/Capitulo1_30.pdf)
21. Almeida LS, Cota ALS, Rodrigues DF. Sanitation, Arboviruses, and Environmental Determinants of Disease: impacts on urban health. *Cien Saude Colet* 2020; 25 (10): 3857-68. <https://doi.org/10.1590/1413-812320202510.30712018>

Received on: 08/23/2021

Revised on: 10/08/2021

Accepted on: 11/03/2021

**Authors' contribution:** Falcão Neto, P.A.O.: Conceptualization, Formal Analysis, Writing – Revision and Editing. Branco, M.R.F.C.: Conceptualization, Formal Analysis, Project management, Writing – First Draft. Costa, S.S.B.: Conceptualization, Formal Analysis, Writing – First Draft. Câmara, A.P.B.: Conceptualization, Formal Analysis, Writing – First Draft. Marques, T.M.N.F.: Conceptualization, Data Curatorship, Writing – First Draft. Araujo, A.S.: Conceptualization, Writing - First Draft. Loureiro, F.H.F.: Conceptualization, Writing - First Draft. Dias Júnior, J.J.: Conceptualization, Writing – First Draft. Silva, M.S.: Conceptualization, Writing – First Draft. Queiroz, R.C.S.: Conceptualization, Writing - First Draft. Ribeiro, M.R.C.: Writing – Revision and Editing. Kulkarni, M.A.: Writing – Revision and Editing. Silva, A.A.M.: Obtaining Funding, Project Management, Writing – Revision and Editing. Santos, A.M.: Conceptualization, Project Management, Writing – Revision and Editing.

