Rev Rene. 2022;23:e72440.
DOI: 10.15253/2175-6783.20222372440
www.periodicos.ufc.br/rene

Original Article

Spatial analysis of Zika virus microcephaly cases in a Brazilian municipality*

Análise espacial dos casos de microcefalia por vírus Zika em um município brasileiro

How to cite this article:
Santos DAS, Cardoso MVLML, Mayorga FDO, Costa FES, Rodrigues NN, Melo GM. Spatial analysis of Zika virus microcephaly cases in a Brazilian municipality. Rev Rene. 2022;23:e72440. DOI: https://doi.org/10.15253/2175-6783.20222372440

Daisyanne Augusto de Sales Santos[1]
Maria Vera Lúcia Moreira Leitão Cardoso[1]
Fernando Daniel de Oliveira Mayorga[2]
Francisco Everson da Silva Costa[3]
Natanael Nascimento Rodrigues[1]
Gleicia Martins de Melo[1]

*Extracted from the dissertation entitled "Análise Espacial da microcefalia associada ao vírus Zika", Universidade Federal do Ceará, 2019.

[1]Universidade Federal do Ceará.
Fortaleza, CE, Brazil.
[2]Universidade Federal do Ceará.
Sobral, CE, Brazil.
[3]Escola de Saúde Pública do Estado do Ceará.
Fortaleza, CE, Brazil.

Corresponding author:
Maria Vera Lúcia Moreira Leitão Cardoso
Rua Alexandre Baraúna, 1115, Rodolfo Teófilo
CEP: 60430-160. Fortaleza, CE, Brazil.
E-mail: cardoso@ufc.br

Conflict of interest: the authors have declared that there is no conflict of interest.

ABSTRACT
Objective: to analyze the spatial distribution of microcephaly cases by Zika virus in a Brazilian municipality. **Methods:** ecological study that analyzed 53 confirmed cases of microcephaly by Zika virus, reported between 2015 and 2016, extracted from the Registry of Public Health Events - Microcephaly. Incidence rates of the disease in neighborhoods of the municipality, Global and Local Moran Index and Kernel dispersion method were calculated. **Results**: common areas with high Zika microcephaly incidence rates were identified. The value of Moran's I demonstrated the presence of clusters, with p=0.001, I=0.3159 in 2015 and I=0.2158 in 2016. According to the Kernel map, there was concentration of cases in Regional Executive Secretariats IV and VI. Most of the cases are within or near precarious settlements. **Conclusion:** the cases did not occur randomly and reinforce their relationship with the living conditions of the population. **Contributions to practice:** it is expected that this study can contribute to reflect on public policies and surveillance actions to reduce Zika transmission, recognizing the territories of higher risk for the disease. In addition, to expand discussions between managers and health professionals to qualify notification, care, and monitoring of children with microcephaly by Zika.
Descriptors: Spatial Analysis; Microcephaly; Zika Virus Infection; Social Vulnerability; Child Health.

RESUMO
Objetivo: analisar a distribuição espacial dos casos de microcefalia por vírus Zika em um município brasileiro. **Métodos:** estudo ecológico que analisou 53 casos confirmados de microcefalia por vírus Zika, notificados entre 2015 e 2016, extraídos do Registro de Eventos em Saúde Pública – Microcefalia. Foram calculadas taxas de incidência da doença nos bairros do município, Índice de Moran Global e Local e método de dispersão de Kernel. **Resultados:** identificaram-se áreas comuns com altas taxas de incidência de microcefalia por Zika. O valor do I de Moran demonstrou presença de clusters, com p=0,001, I=0,3159 em 2015 e I=0,2158 em 2016. De acordo com o mapa de Kernel, houve concentração de casos nas Secretarias Executivas Regionais IV e VI. A maioria dos casos está dentro ou próximo de assentamentos precários. **Conclusão:** os casos não ocorreram de modo aleatório e reforçam sua relação com as condições de vida da população. **Contribuições para a prática:** espera-se que esse estudo possa contribuir para refletir sobre políticas públicas e ações de vigilância para redução da transmissão da Zika, reconhecendo os territórios de maiores riscos para a doença. Além disso, ampliar discussões entre gestores e profissionais da saúde para qualificar notificação, cuidado e acompanhamento das crianças com microcefalia por Zika.
Descritores: Análise Espacial; Microcefalia; Infecção por Zika Vírus; Vulnerabilidade Social; Saúde da Criança.

Received: Nov. 22nd 2021; Accepted: Apr. 11st 2022.

Introduction

Zika virus transmission by the infected *Aedes aegypti* mosquito belongs to the *Flaviviridae* family. In 2015, an epidemic by the virus started in Puerto Rico[1]. In Latin America, especially in the Northeast of Brazil, the infection outbreak happened in the second half of 2015, alerting the world population about the relation with the increase of newborn cases with microcephaly. Epidemiological and laboratory data indicated that intrauterine infection by Zika virus caused microcephaly and severe brain abnormalities[2], considered characteristics of congenital syndrome of Zika virus.

Microcephaly is defined as a cerebral development malformation characterized by a smaller cephalic perimeter than expected for the baby's age and sex[3]. According to the World Health Organization, the Brazilian Ministry of Health has adopted as parameters for children born at term a head circumference of 31.5 cm for females and 31.9 cm for males[4].

Due to the need to register suspected cases of microcephaly related to Zika virus, the Unified Health System Informatics Department created an online form for Public Health Events Registry - Microcephaly for compulsory notification of the disease[5].

Between the years 2015 and 2020, in Brazil, 19,622 suspected cases of congenital syndrome associated with Zika virus were notified to the Ministry of Health, of which 3,577 (18.2%) were confirmed[6]. Based on the cases confirmed until 2019, 78.3% were newborns with microcephaly, 14.9% children with microcephaly and/or central nervous system alterations, 2.8% fetuses, 2% stillbirths and1.9% miscarriages (1.9%)[7].

Although the emergency period has ended, new cases continue to occur in the country. Most deaths, among live births and stillbirths, occurred in 2016 and in the Northeast region (60.8%). Congenital malformations were the most prevalent causes of death (52.6%), with microcephaly being responsible for 24.3% of all deaths and associated with another 15.9%[6].

Regarding health care, from the cases confirmed between 2015 and 2020, 63.7% of newborns and children received care in primary care and 56.4% in specialized care. It is also noteworthy that 2,890 cases are still under investigation, i.e., there may still be hundreds of children with some sequelae of Zika virus that are not being officially registered and, probably, are without assistance[6].

These children continue to deal with the severe sequelae of the syndrome, which in some cases, were aggravated due to the interruption of stimulation therapy sessions in the period of the COVID-19 pandemic. And, despite great efforts, several gaps in knowledge are still identified, such as the transmission rate of Zika virus infection from pregnant women to fetuses, the frequency of infected fetuses who will develop malformations, and the long-term outcome of infected children without detection of abnormalities at birth[8].

In Ceará, the first cases were reported as of October 2015, and Fortaleza concentrated the highest number of confirmed deaths. After the first records were made, an active search was conducted, retrospectively, in several maternity hospitals in Fortaleza, aiming to identify possible cases of newborns with the syndrome born before October 2015. Between the years 2015 and 2020, 233 babies with suspected congenital Zika virus syndrome were registered, being 98 (42.1%) in the year 2015; and 98 (42.1%) in 2016. There was a reduction to 17 (7.2%) in 2017, followed by 9 (3.8%) of the notifications in 2018, 6 (2.6%) in 2019. In the year 2020, only 5 (2.2%) cases were reported. However, of the 233 notifications, 53 cases were confirmed (26 by clinical-radiological criteria and 27 by laboratory tests), all with microcephaly, notified between the years 2015 and 2016, which justifies the sample of this study[9].

In some Northeastern states, it was identified that Zika outbreak intensified situations involving human rights, such as access to water, basic sanitation, irregular precarious settlements, inequality in access to health and restrictions to sexual and reproductive rights[10]. Therefore, there is an understanding of the social, environmental, and climatic determinants that favor the proliferation of Aedes aegypti and arboviruses in the urban environment, which makes such infection a growing public health problem due to its power of dispersion, adaptability, and possibility of causing severe neurological damage.

A study conducted with 201 high-risk pregnant women reported that the knowledge and attitudes about Zika virus are still lacking, especially regarding the prevention of virus transmission, being necessary public policies directed to the community involving collective actions of arboviruses control and that reinforce the prevention and follow-up of pregnant women with Zika, considering the consequences that result from congenital infection, highlighting microcephaly(11).

Although there are studies that address the clinical and epidemiological profile of children with microcephaly by Zika(1,10-11), few analyze the spatial dynamics of Zika cases in Brazil(8). The epidemiological bulletins of Fortaleza(9) do not perform spatial analysis of microcephaly cases associated to Zika virus, but of arboviruses or Congenital Syndrome of Zika virus.

Thus, it is evident the need to understand the spatial distribution of microcephaly by Zika virus in the city of Fortaleza, for knowledge of the socio-territorial dynamics of infection and the probable areas considered most at risk for its occurrence, supporting public management to incorporate innovative strategies and different magnitudes for surveillance and health promotion.

Therefore, we aimed to analyze the spatial distribution of microcephaly cases by Zika virus in a Brazilian municipality.

Methods

This is an ecological study conducted in Fortaleza, capital of the state of Ceará, in the Northeast region of Brazil, with approximately 2,703,391 inhabitants. The 121 neighborhoods of the municipality were considered as the unit of analysis, organized in the seven Regional Executive Secretariats (SER), ranging from I to VI, in addition to the Regional Executive Secretariat of the Center of Fortaleza (SERCEFOR) according to the territorial division in the research period. The study was conducted in the period between March 2018 and April 2019.

The population comprised all confirmed cases in children, stillbirths or newborns with microcephaly by Zika virus, notified in the Public Health Event Registration System-Microcephaly in the period between January 1, 2015, and December 31, 2016, and residing in Fortaleza-Ceará, totaling 53 cases.

It is valid to emphasize that although the study contemplates only the years from 2015 to 2016, suspected cases of microcephaly by Zika are still being notified, however, all confirmed cases between 2015 and 2021 are concentrated in the two years of choice for data collection of the study(9). Therefore, the data that really show the frame of notification and confirmation are related to the years studied in this article.

The inclusion criteria were being a confirmed case of microcephaly by Congenital Infection associated with Zika virus, registered in the Public Health Event Registration System - Microcephaly, notified in 2015 or 2016 and being a resident in the Municipality of Fortaleza-Ceará. As exclusion criteria: duplicate cases. It is emphasized that there were no exclusions.

In the study period, there were 235 suspected cases of microcephaly due to Zika virus. Of these, 53 cases met the inclusion criteria. Thus, the sample consisted of 53 cases of microcephaly by Zika virus, of these, 27 were confirmed by laboratory tests and 26 by radiological clinical criteria, which composed the scope of analysis.

The databases came from the Epidemiological Surveillance of the Municipal Health Secretariat of Fortaleza. The cases of microcephaly were extracted from the Registry of Events in Public Health-Microcephaly; the address and neighborhood of children with microcephaly were extracted based on the registration of the place of residence of their parents in the Information System on Live Births, because the infection occurred during pregnancy. The sociodemographic information, such as data regarding the number of the population per neighborhood in the city of Fortaleza, were extracted from the Demographic Census of 2010 by the Brazilian Institute of Geography and Statistics. The cartographic base that contains the digital maps of the municipality of Fortaleza with its neighborhoods was acquired from the Institute and from the website of the Municipality of Fortaleza. Then, the banks were compiled and checked by the authors of the study.

For characterization of cases with microcephaly by Zika virus according to epidemiological variables, descriptive statistical analysis with absolute and percentage frequency distribution was used. The incidence rate of microcephaly associated with Zika virus per neighborhood was calculated, using as numerator the new cases of microcephaly by Zika virus, residents in each neighborhood, and as denominator the number of live births in the neighborhood for the years studied and multiplied by 10,000.

The process of data geo-referencing was performed in Quantum Geographic Information System (QGIS), version 3.16, with compatibility of the variable "neighborhood of residence of children with microcephaly by Zika" with the cartographic base of the 121 neighborhoods of the city of Fortaleza. The cartographic projection corresponded to the Universal Transverse Mercator system using the SIRGAS 2000 Datum 24S zone.

The determination of the existence of spatial dependence of Zika microcephaly incidence rates in Fortaleza neighborhoods was done by Moran's Global Index that provides the scatter diagram to visualize the spatial autocorrelation. This diagram provides the overall measure of linear spatial association and the patterns of local spatial association between areas and their neighboring regions, namely, High-High (HH), Low-Low (LL), High-Low (HL) and Low-High (LH)[12]. The neighborhood matrix used in the calculation of spatial dependence was the contiguity matrix, first-order queen convention, adopting a significance level of 5%.

The Local Spatial Association Indicator (LISA Map) was applied, which presents the comparison of values with a series of values obtained through interactions or permutations of the values of neighboring neighborhoods. The values are classified as non-significant and with significance of 95,99 and 99.9%[13]. Thus, it is evident where the spatial dependence was statistically significant, calculated through the Local Moran Index.

The Moran Map was used to visualize the spatial dependence. This consists of the junction of the values obtained in the Box Map with spatial statistical significance above 95%, identified by the LISA Map. The Moran Map shows the areas with significant LISA Map values ($p<0.05$), however, with the classification into four groups as presented in the Box Map of High-High, Low-Low, High-Low and Low-High. The other areas without dependence are classified as non-significant. Therefore, the units of analysis of the study, the neighborhoods, which showed statistical significance in the Moran Map as critical areas for the birth of children with microcephaly by Zika virus.

In the last phase of the analysis, the Kernel dispersion method was performed. This is an exploratory interpolation technique that generates a density surface to identify "hotspots", i.e., an area of concentration of events or agglomeration of a phenomenon in a spatial distribution[12].

To identify the occurrence of microcephaly cases by Zika in urban areas of social vulnerability, the cases made available by the Epidemiological Surveillance Cell of Fortaleza that locates precarious settlements in the city of Fortaleza were georeferenced in a map. These settlements consist of areas with poor housing and mobility conditions, such as favelas, slums, irregular subdivisions, tenements, and housing developments[14]. For spatial autocorrelation calculations, significance tests, and graphical illustrations, Terraview 4.4, GeoDa version 1.18, and QGIS version 3.16 were used.

The study was approved by the Research Ethics Committee of the Federal University of Ceará under opinion no. 2,812,300/2018.

Results

Of the cases diagnosed with microcephaly by Zika, 58.5% were male and 47.2% were diagnosed in the intrauterine period. Regarding mortality, 22.6% of cases died, and 83.3% of these occurred in children under one year of age. In 2015, 19 live children were born, and one was stillborn (37.7%), and in 2016, 33 live children were born (62.3%).

Among the regions, regarding the summed raw data of 2015 and 2016 according to the SER of residence established in the Live Birth Certificate of children with microcephaly, the highest number of cases stands out in regions V (13) and VI (13), representing a total of 49% of the cases.

The following maps show the areas with the highest incidence rate of microcephaly due to Zika in 2015, ranging from 8.1 to 87.2 cases per 10,000 live births (Figure 1 - map A) and, in 2016, from 11.4 to 48.6 cases per 10,000 live births (Figure 2 - map A).

According to Moran's I value, in the analyzed years, there was positive spatial autocorrelation. Neighborhoods with high Zika microcephaly rates are neighbors of other neighborhoods with the same characteristic, showing p≤0.05 (2015, Moran's I of 0.3159 for p<0.001, and 2016, Moran's I of 0.2158 for p<0.001), that is, the null hypothesis of spatial independence for microcephaly in both 2015 and 2016 is excluded.

Box Map of Figure 1 - map B and Figure 2 - map B illustrates classified areas, according to the position of Zika microcephaly cases in Moran's Scatter Diagram, in 2015 and 2016 respectively.

It can be noticed that in 2015 there were clusters of neighborhoods with high rates of children with microcephaly by Zika and similarity with their neighbors (high-high), present in all Regional Executive Secretariats and with higher concentration in regions I, II and IV. Moreover, low rates of neighborhoods with microcephaly and neighbors with similar values (low-low) are in regions III, V and VI. There were few areas of epidemiological transition (high-low/low-high). In 2016, high-high areas stand out in Regional Executive Secretariats V and VI, and low-low areas are concentrated in regionals I, II, and III, with few and scattered areas of epidemiological transition (high-low/low-high) that year.

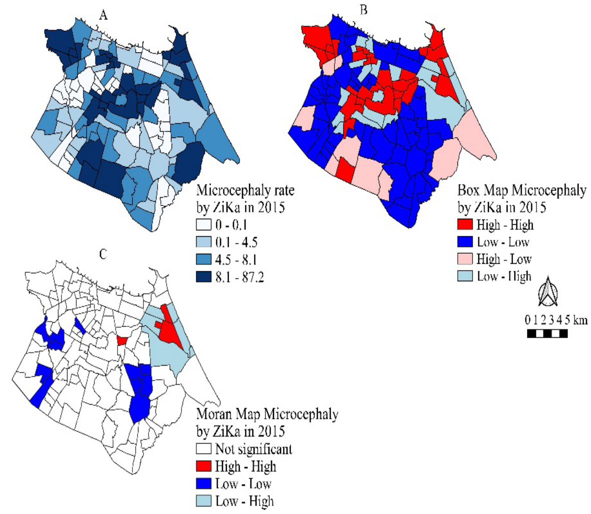

Figure 1 – Spatial analysis of Microcephaly by Zika per neighborhood, A) Incidence Rate of Microcephaly by Zika; B) Box Map; C) Moran Map. Fortaleza, CE, Brazil, 2015

The results obtained by Moran Map are presented in Figure 1 - map C and Figure 2 - map C. In these, it is identified cluster with high-risk area for microcephaly incidence by Zika due to the grouping of neighborhoods with equally high rates between them (high-high). In 2015, it stood out as high-high areas, in SER VI, the neighborhood Alto da Balança, and in SER II, the neighborhoods Cidade 2000, Manoel Dias Branco and De Lourdes, also noting other cluster areas with low rates (low-low) of SER III, V and VI. High-low areas were also identified in some neighborhoods of regional II and VI.

In 2016, high-high areas are represented by SER VI, in the Sapiranga, José de Alencar neighborhoods; SER III, in Bela Vista; and SER IV in Pan Americano; low-low, predominate in SER I. In this year, no high-low and low-high areas were identified.

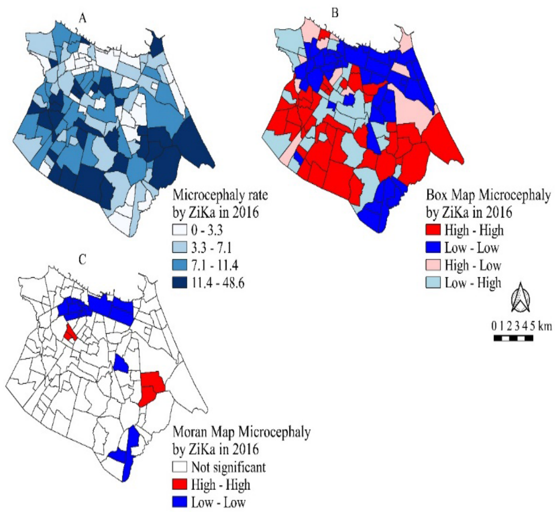

Figure 2 – Spatial analysis of Microcephaly by Zika per neighborhood, A) Incidence Rate of Microcephaly by Zika; B) BoxMap; C) MoranMap. Fortaleza, CE, Brazil, 2016

Figure 3 shows the Kernel density map with a high concentration of microcephaly cases by Zika virus in the Regional Executive Secretariats IV and VI, considering the accumulation of cases between the years 2015 and 2016, and a radius of influence of 2,000 meters.

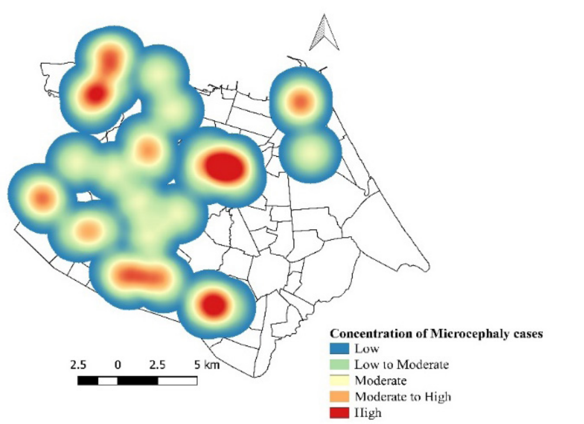

Figure 3 – Kernel density map. Fortaleza, CE, Brazil, 2015-2016

The cases of microcephaly due to Zika were georeferenced in the map of precarious settlements in the city of Fortaleza to identify if they were inserted in urban areas of greater social vulnerability. These represented 12% of the territorial area of the capital and are named as: favelas; mutirões; irregular subdivisions; tenements; and housing developments.

Most cases (73.5%), considering a radius of up to 200 meters from the territories with precarious settlements, were located within risk areas (37.7%) or very close to these areas (35.8%).

In Figure 4, the neighborhoods of the regionals with cases of microcephaly by Zika within precarious settlements are highlighted: Regional I - Barra do Ceará (4), Regional II - Cais do Porto (2) and Vicente Pinzon (1), Regional III - Olavo Oliveira (2) and Quintino Cunha (1), Regional IV - Itaperi (2) and Parangaba (2), Regional V - Planalto Ayrton Senna (2), Regional VI - Conjunto Palmeiras (3) and Jangurussu (1).

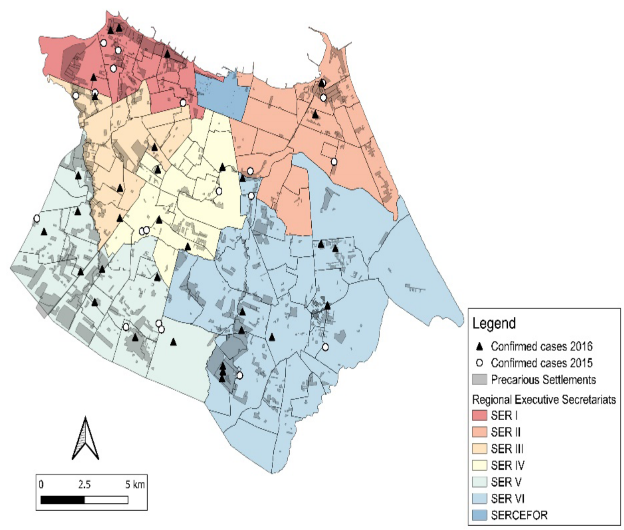

Figure 4 – Zika microcephaly cases and areas of precarious settlements. Fortaleza, CE, Brazil, 2015-2016

Discussion

The spatial autocorrelation, found in this study, allows us to analyze the most vulnerable neighborhoods for the occurrence of microcephaly cases and to understand the organization and influence of neighboring neighborhoods.

Zika microcephaly cases were not randomly distributed in Fortaleza territory, there was positive spatial autocorrelation in both years of the study. Indeed, some neighborhoods of Fortaleza showed high incidence rates of the disease, with higher number of neighborhoods, with statistical significance level for microcephaly by Zika as in 2015 ($p<0.05$) and in 2016 ($p<0.01$), while others showed insignificant values. In addition, the formation of clusters and areas in epidemiological transition phase were identified.

Epidemics spread by mosquitoes can expand rapidly, which highlights the need for effective vector control. The Zika epidemic disproportionately affected the country[15] as well as vulnerable groups, creating unequal social and health services, and contributing to the increase of inequalities in the region, being these one of the reasons why the Northeast was the epicenter of the epidemic[16].

Thus, vector control, expansion of coverage of selective collection of solid waste, conditions that favor access to water and sanitation, and intensification of maternal guidance for prevention of infection by the vector or sexually, especially in the first and second trimesters of pregnancy are fundamental to reduce Zika virus transmission and microcephaly cases[17].

Georeferencing the cases of microcephaly by Zika on the map of 121 neighborhoods in Fortaleza, most of them (73.5%) are in risk areas (37.7%) or very close to these areas (35.8%). These territories present great social vulnerability and low Human Development Index, especially in Conjunto Palmeiras (0.119), Planalto Ayrton Senna (0.168) and Jangurussu (0.172), which are among the ten worst neighborhoods in the city regarding development[18].

The socioeconomic condition is the factor that most contributes to family breakdown, acting directly in the most vulnerable of this group: the children who are threatened and with their fundamental rights violated, such as the right to quality housing. Of the 69 families of children victims of congenital syndrome by Zika virus in Ceará, 32 lived with one minimum wage per month, followed by those with monthly income lower than one minimum wage. Most parents were young, with complete high school education. An important number of mothers gave up their jobs to take care of their children, characterizing families with unfavorable economic situation[19].

The consequences arising from the situation that is experienced by the family include many problems experienced by caregivers of children with congenital syndrome by Zika, such as job abandonment, excessive workload with the child and, several times, absence of family support. These result in a great concern, interfering in their daily functioning, favoring the emergence of somatic symptoms that reflect negatively in the health of these mothers[20].

Thus, main factors for Zika virus infection and, consequently, for microcephaly are related to socioeconomic scenario. Issues such as housing, urbanization and basic sanitation must be considered. These socioeconomic and demographic indicators can confirm that the outbreak had different impacts according to social class, reflecting social inequality in Brazil[21].

To mitigate the impacts, government measures were implemented to address issues related to poverty and inequality of access, such as actions to provide repellent to pregnant women accompanied in the public service, monthly payment of cash benefit for children diagnosed with congenital syndrome by Zika virus, standardization and improvement of microcephaly surveillance, new diagnostic tests, intensification of vector control measures, development of vaccines against the virus, therapies and diagnostics, preparation of health services for follow-up of neurological syndromes, sharing of information relevant to public health and general restrictions on travel or trade with countries or regions with Zika virus transmission[6,22].

Although high rates of the disease do not currently occur, new cases of microcephaly by Zika continue to be reported in the country. With the pandemic by COVID-19, children victims of congenital syndrome by Zika virus, cited as a vulnerable group, experience a second potentially fatal viral outbreak[6,23]. For many children, therapies and consultations have been replaced by extended home stays, telecare, and socioeconomic crises.

Thus, since the current treatment of arboviruses is still merely symptomatic and primary prevention measures are of vital importance to prevent the occurrence of fetal infection and congenital anomalies, the mapping of diseases becomes essential to describe their spatial behavior, allowing the correlation of several factors that are present in the territory, such as infrastructure, living conditions and inequalities. Such conjuncture is necessary to reinforce the actions of public policies in child health, preventing adverse fetal outcomes and new epidemiological emergencies by Zika virus.

Study limitations

The limitations of the study involve the underreporting of cases and unsatisfactory records of information, which collaborates to the difficulty regarding the treatment and depuration of the databases collected involving many cases that are still under investigation, consolidation, and organization of microcephaly cases in the official neighborhoods of the city of Fortaleza.

Contributions to practice

The data can contribute to local planning for restructuring basic sanitation conditions and health surveillance actions, enabling reflection on public policies and health education for reducing mosquito infestation and, consequently, reducing the Zika virus transmission rate to the population.

It is also expected that this study will broaden the discussions between managers and health professionals, especially nursing to qualify the health team in the process of notification, care and monitoring of children with microcephaly and strengthening of family support networks.

Further investigations in regions with high incidence rates are necessary, requiring continuous monitoring of cases to ensure that measures are effectively implemented.

Conclusion

It is concluded that the cases of microcephaly by Zika were not randomly distributed in the territory of Fortaleza, there was positive spatial autocorrelation in the two years of the study. In addition, most affected individuals resided within or near territories with socioeconomic vulnerability, a fact that afflicts society and highlights the structure of inequality in the city studied, in the state and in the country itself.

Authors' contribution

Design, analysis, and interpretation of data, writing and approval of the final version to be published: Santos DAS.
Design and interpretation of data, writing and approval of the final version to be published: Cardoso MVLML.
Data design, interpretation, and statistics: Mayorga FDO.
Data collection and interpretation, and article writing: Costa FES and Rodrigues NN: Costa FES and Rodrigues NN.
Critical revision of the intellectual content and approval of the final version to be published: Melo GM.
Agreement to be responsible for all aspects of the manuscript related to the accuracy or completeness of any parts of the work to be investigated and properly resolved: Santos DAS, Cardoso MVLML, Mayorga FDO, Costa FES, Rodrigues NN, Melo GM.

References

1. Read JS, Velasquez BT, Lorenzi O, Sanchez AR, Torres ST, Rivera LV, et al. Symptomatic Zika Virus infection in infants, children, and adolescents living in Puerto Rico. JAMA Pediatr. 2018;172(7):686-93. doi: https://dx.doi.org/10.1001/jamapediatrics.2018.0870
2. Rasmussen SA, Jamieson DJ, Honein MA, Petersen LR. Zika virus and birth defects: reviewing the evidence for causality. N Engl J

Med. 2016;374(20):1981-7. doi: https://dx.doi.org/10.1056/nejmsr1604338

3. World Health Organization (WHO). Birth defects surveillance: a manual for programme managers [Internet]. 2018 [cited Jan 5, 2022]. Available from: http://www.who.int/iris/handle/10665/110223

4. Ministério da Saúde (BR). Secretaria de Vigilância em Saúde. Protocolo de atenção à saúde e resposta à ocorrência de microcefalia relacionada à infecção pelo vírus Zika [Internet]. 2016 [cited Jan 5, 2022]. Available from: https://www20.anvisa.gov.br/segurancadopaciente/index.php/publicacoes/item/protocolo-de-atencao-a-saude-e-resposta-a-ocorrencia-de-microcefalia-relacionada-a-infeccao-pelo-virus-zika

5. Ministério da Saúde (BR). Secretaria de Vigilância em Saúde. Departamento de Vigilância das Doenças Transmissíveis. Protocolo de vigilância e resposta à ocorrência de microcefalia e/ou alterações do sistema nervoso central (SNC) [Internet]. 2015 [cited Jan 5, 2022]. Available from: https://saude.rs.gov.br/upload/arquivos/201702/22112109-protocolo-de-vigilancia-e-resposta-a-ocorrencia-de-microcefalia-relacionada-a-infeccao-pelo-virus-zika.pdf

6. Ministério da Saúde (BR). Secretaria de Vigilância em Saúde. Situação epidemiológica da síndrome congênita associada à infecção pelo vírus Zika, 2015 a 2020. Bol Epidemiol [Internet]. 2020 [cited Jan 5, 2022]. Available from: https://www.gov.br/saude/pt-br/media/pdf/2021/fevereiro/11/boletim_epidemiologico_svs_4.pdf

7. Ministério da Saúde (BR). Secretaria de Vigilância em Saúde. Síndrome congênita associada à infecção pelo vírus Zika: situação epidemiológica, ações desenvolvidas e desafios, 2015 a 2019. Bol Epidemiol [Internet]. 2019 [cited Jan 5, 2022]. Available from: http://plataforma.saude.gov.br/anomalias-congenitas/boletim-epidemiologico-SVS-especial-2019.pdf

8. Lowe R, Barcellos C, Brasil P, Cruz OG, Honório NA, Kuper H, et al. The Zika virus epidemic in Brazil: from discovery to future implications. Int J Environ Res Public Health. 2018;15:E96. doi: https://dx.doi.org/10.3390/ijerph15010096

9. Secretaria Municipal de Saúde do Estado de Ceará. Coordenadoria de Vigilância em Saúde - Célula de Vigilância Epidemiológica. Informe Semanal Dengue, Chikungunya, Zika. Cenário epidemiológico no Município de Fortaleza 2021 [Internet]. 2021 [cited Jan 18, 2022]. Available from: https://www.cmfor.ce.gov.br/wp-content/uploads/2021/10/Informe-semanal-ARBOVIROSES-39%C2%AA_2021-SMS-Fortaleza-CE.pdf

10. Human Rights Watch. Neglected and unprotected: the impact of the Zika outbreak on women and girls in Northeastern Brazil [Internet]. 2017 [cited Jan 18, 2022]. Available from: https://www.hrw.org/report/2017/07/13/neglected-and-unprotected/impact-zika-outbreak-women-and-girls-northeastern

11. Garbin CAS, Teruel GP, Saliba TA, Moimaz SAS, Garbin AJI. Knowledge and attitude of women with high-risk pregnancy about the Zika virus transmission. Ciênc Saúde Coletiva. 2021;26(1):233-40.doi:http://dx.doi.org/10.1590/1413-81232020261.25752018

12. Almeida E. Econometria espacial aplicada. São Paulo: Editora Alínea; 2012.

13. Anselin L. Local Indicators of Spatial Association – LISA. Geogr Anal. 1995;27(2):93-115. doi: https://doi.org/10.1111/j.1538-4632.1995.tb00338.x

14. Prefeitura de Fortaleza. Fortaleza em mapas. Mapas georreferenciados Fortaleza em bairros [Internet]. 2019 [cited Jan 5, 2022]. Available from: https://mapas.fortaleza.ce.gov.br/

15. Brady OJ, Osgood-Zimmerman A, Kassebaum NJ, Ray SE, de Araújo VEM, et al. The association between Zika virus infection and microcephaly in Brazil 2015–2017: an observational analysis of over 4 million births. PLoS Med. 2019; 16(3):e1002755. doi: https://doi.org/10.1371/journal.pmed.1002755

16. Dias FM, Berger SMD, Lovisi GM. Strong women and special mothers? Reflections on gender, care and motherhood in the context of post-zika epidemic in Brazil. Physis. 2020;30(4):e300408. doi: https://doi.org/10.1590/S0103-73312020300408

17. Duarte G, Miranda AE, Bermúdez XPD, Saraceni V, Espinosa FEM. Brazilian protocol for sexually transmitted infections 2020: Zika virus infection. Epidemiol Serv Saúde. 2021;30(spe1):e2020609. doi:https://dx.doi.org/10.1590/S1679-4974202100017.esp1

18. Secretaria Municipal de Desenvolvimento Econômico de Fortaleza. Desenvolvimento humano, por bairro, em Fortaleza [Internet]. 2014 [cited Dec 1, 2021]. Available from: http://salasituacional.fortaleza.ce.gov.br:8081/acervo/documentById?id=22ef6ea5-8cd2-4f96-ad3c-8e0fd2c39c98

19. Batista LL, Andrade NM, Lessa AP, Souza LE, Costa NM, Pessoa AL, et al. Condições de vida e acesso às políticas sociais das famílias de crianças com Síndrome Congênita pelo vírus Zika atendidas em Fortaleza, Ceará, em dezembro de 2016. Rev Med UFC. 2020;60(2):5-10. doi: https://dx.doi.org/10.20513/2447-6595.2020v60n2p5-10

20. Bulhões CSG, Silva JB, Moraes MN, Reichert APS, Dias MD, Almeida AM. Psychic repercussions in mothers of children with congenital Zika virus syndrome. Esc Anna Nery. 2020;24(2):e20190230. doi:https://dx.doi.org/10.1590/2177-9465-ean-2019-0230

21. Mocelin HJS, Catão RC, Freitas PSS, Prado TN, Bertolde AI, Castro MC, et al. Analysis of the spatial distribution of cases of Zika vírus infection and congenital Zika virus syndrome in a state in the southeastern region of Brazil: sociodemographic factors and implications for public health. Int J Gynecol Obstet 2020;148(Suppl. 2):61-9. doi: https://doi.org/10.1002/ijgo.13049

22. World Health Organization (WHO). Screening, assessment and management of neonates and infants with complications associated with Zika virus exposure in utero [Internet]. 2016 [cited Jan 5, 2022]. Available from: http://apps.who.int/iris/bitstream/10665/204475/1/WHO_ZIKV_MOC_16.3_eng.pdf?ua=1

23. Gama GL, Silva BM, Silva MB, Ferreira RVB, Tavares JS, Melo A. Mental health and burden in mothers of children with congenital Zika syndrome during COVID-19 pandemic. Rev Bras Saúde Mater Infant. 2021;21(Supl. 2):481-90. doi: https://doi.org/10.1590/1806-9304202100S200009