DOI: https://doi.org/10.36489/nursing.2020v23i265p4107-4116

Spatial analysis of confirmed cases of Zika Virus in the state of São Paulo, Brazil

ABSTRACT | Objective: to analyze the spatial distribution of confirmed Zika Virus cases. Method: Ecological, exploratory, epidemiological study, obtained from confirmed cases of Zika Virus, reported in the Notifiable Diseases Information System, which occurred in the State of São Paulo in 2016. The georeferencing technique was applied. Spatial analysis was performed using the Kernel density estimator and the scan statistics provided by SaTScan ™ version 9.6. Result: The Kernel analysis showed hot areas in the study region. Through the scanning statistics, the Relative Risks clusters of the 645 municipalities were identified. The spatial distribution of Zika Virus followed a heterogeneous pattern, as the outbreaks tended to aggregate in specific areas. The municipalities of the north and northwest regions presented an increasing Relative Risk. Conclusion: This study offers fundamental information to assist public health managers in decision-making at the municipal and state levels.
Keywords: Zika Virus; Zika Virus Infection; Spatial Analysis; Epidemiological Monitoring.

RESUMEN | Objetivo: analizar la distribución espacial de casos confirmados de Virus Zika. Método: Estudio epidemiológico, exploratorio y ecológico, obtenido de casos confirmados de Virus Zika, reportado en el Sistema de Información de Enfermedades de Notificación, que ocurrió en el Estado de São Paulo en 2016. Se aplicó la técnica de georreferenciación. El análisis espacial se realizó utilizando el estimador de densidad de Kernel y las estadísticas de escaneo proporcionadas por SaTScan ™ versión 9.6. Resultado: el análisis de Kernel mostró áreas calientes en la región de estudio. A través de las estadísticas de escaneo, se identificaron los grupos de Riesgos relativos de los 645 municipios. La distribución espacial del virus Zika siguió un patrón heterogéneo, ya que los brotes tendieron a agregarse en áreas específicas. Los municipios de las regiones norte y noroeste presentaron un riesgo relativo creciente. Conclusión: Este estudio ofrece información fundamental para ayudar a los administradores de salud pública en la toma de decisiones a nivel municipal y estatal.
Palavras claves: Virus Zika; Infección por el virus del Zika; Análisis espacial; Monitoreo epidemiológico.

RESUMO | Objetivo: analisar a distribuição espacial dos casos confirmados de Zika Vírus. Método: Estudo epidemiológico, do tipo ecológico, exploratório, obtidos a partir dos casos confirmados de Zika Vírus, notificados no Sistema de Informação de Agravos de Notificação, ocorridos no Estado de São Paulo em 2016. Foi aplicada a técnica de georreferenciamento. A análise espacial foi feita a partir do estimador de densidade Kernel e a estatística de varredura fornecida pelo SaTScan™ version 9.6. Resultado: A análise de Kernel apontou áreas quentes na região do estudo. Por meio da estatística de varredura foram identificados os aglomerados dos Riscos Relativos dos 645 municípios. A distribuição espacial de Zika Vírus seguiu padrão heterogêneo, pois, os focos tenderam-se a agregar-se em áreas específicas. Os municípios das regiões norte e noroeste apresentaram crescente Risco Relativo. Conclusão: Este estudo oferece informações fundamentais para auxiliar gestores em saúde pública nas tomadas de decisões nos níveis municipal e estadual
Palavras-chaves: Zika Vírus; Infecção por Zika Vírus; Análise Espacial; Monitoramento Epidemiológico.

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Received on: 03/31/2020
Approved on: 04/28/2020

INTRODUCTION

The Zika Virus is a viral disease, of benign evolution, characterized by the clinical picture of low fever, itchy maculopapular rash, non-pruritic and non-purulent conjunctival hyperemia, arthralgia or arthritis, muscle pain, headache and digestive manifestations[1]. However, Zika virus infection can cause microcephaly in newborns, Guilan-Barré syndrome and death[2].

In the second half of 2014, suspicions of Zika Virus were registered in some cities in the Northeast of Brazil and confirmed, in May 2015, by the Ministry of Health of Brazil with native transmission[3,4].

The Zika Virus is an emerging flavivirus, transmitted mainly by the Aedes Aegypti mosquito, which was isolated for the first time from a sentinel monkey in the Zika forest in Uganda in 1947[5].

The Aedes Aegypti mosquito is one of the main vectors of the Zika virus for humans worldwide5. This vector is spread over a large part of the Brazilian territory. It was reported by Nunes et al. that the Aedes Aegypti mosquito was present in 5172 of the 5494 municipalities in Brazil in 2013[6].

The Zika virus was introduced in Brazil between 2013 and 2015, probably imported from the Pacific, and caused an epidemiological outbreak that peaked in November 2015, spreading rapidly throughout the country[7].

In this context, research with spatial analysis methodologies is relevant to know the reality of the places where the disease has spread, if it has alien and / or autochthonous cases, as well as to assess the magnitude of the disease, being fundamental for the realization of interventions and effective actions for its control, taking into account the natural history of the disease and the social determination of the health-disease process in order to contribute to the promotion of the collective health of the population.

Spatial analysis techniques have been used by epidemiology, because they allow studies on the spatial distribution of diseases, diseases and risk situations, which makes it possible to detect vulnerable areas, to know in more detail the patterns of health conditions in a country. population, as well as evidencing disparities[8,9].

In Brazil, between 2015 and 2016, years of the Zika Virus epidemiological outbreaks, it was estimated that 65 million people lived in areas at high risk for this disease. The southeast and northeast regions of Brazil had the highest areas of high risk for Zika Virus[10].

In the State of São Paulo, research on the Zika Virus is necessary because it is an emerging disease from 2015[11]. In addition, notifications of Zika Virus cases in Brazil became mandatory in February 2016[12] and there are still few studies that performed spatial analysis of this disease in the country10 and in the State of São Paulo, no research was found on this topic.

In view of these premises, the present study sought answers to the following question: how did the spatial distribution of the Zika Virus outbreak in the State of São Paulo occur in 2016? To answer the proposed question, this research aimed to analyze the spatial distribution of confirmed cases of Zika virus in the State of São Paulo in the proposed year.

METHODOLOGY

Epidemiological, ecological, population-based study. The sample was obtained from confirmed cases of Zika Virus notified in the Notification Diseases Information System with laboratory evidence (reverse transcription polymerase chain reaction (RT-PCR) and/or epidemiological clinic, which occurred in the municipalities, distributed among the Groups of Epidemiological Surveillance of the State of São Paulo in 2016.

The State of São Paulo is made up of 645 municipalities. To coordinate the Epidemiological Surveillance Services, the State relies, at the central level, with the Epidemiological Surveillance Center - a technical directorate, composed of divisions of diseases and health problems. The Epidemiological Surveillance Center, at the regional level, is currently structured around 28 Epidemiological Surveillance Groups that make up all the municipalities in the State[13].

Variables were selected from the notification / completion form (age, sex, race / color, education, municipality of residence, street address, number, zone, final classification (confirmed), confirmation / disposal criterion, indigenous case in the municipality of residence , municipality, case evolution), which is used for Zika Virus, and for the calculation of the incidence rate, the population was obtained through the Brazilian Institute of Geography and Statistics (IBGE) 2016. In possession of the database, with confirmed notifications, duplicate cases were removed.

For data analysis, descriptive statistics were used, applying the Softwares TabWin 3.6b, Microsoft Excel 2016 and the Program R3.5.1/RStudio. In addition, the georeferencing technique of the cases was applied and, for this process, the fields "street address" and "number" were used. The automatic process was carried out using the easymapmake website and the ArcGis version 10.5 and Qgis10 GIS tools. Spatial analysis was performed using the Kernel density estimator and the scan statistics provided by SaTScan™ version 9.6 with the incidence of confirmed cases of Zika virus.

The research was approved by the Research Ethics Committee of Universidade São Judas, located in the city of São Paulo/SP, under Opinion number: 3,167,498. The use of the secondary Zika Virus 2016 database, without identifying the patients, was authorized by the responsible manager.

RESULTS

Ten thousand four hundred forty-nine cases of Zika Virus were reported in the State of São Paulo in 2016. Of these, 4,513 (43.2%) were confirmed, of which 4,323 (95.8%) were found to be autochthonous. The incidence coefficient in the State was 10.1 cases for every 100,000 inhabitants.

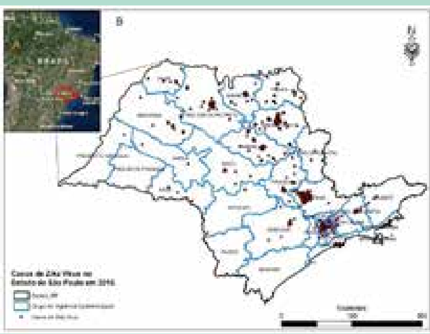
The confirmation was, for the most part, based on the clinical-epidemiological criterion (73.3%). The median age was 33 years with a standard deviation of 17. Most cases occurred in females (74.2%); non-pregnant (78.3%) and residing in an urban area (92.7%). Regarding the variables race/color and education: 44.3% and 60.6%, respectively, did not present information. The cases were confirmed in 141 municipalities in the Epidemiological Surveillance Groups (Table 1), with the largest number in the municipality of Ri-

Table 1 - Distribution of Epidemiological Surveillance Groups by number of municipalities that confirmed cases of Zika Virus. State of Sao Paulo, 2016.

Grupo de Vigilância Epidemiológica (GVE)	n	%
ARAÇATUBA	7	4,96
ARARAQUARA	12	8,51
ASSIS	3	2,13
BARRETOS	7	4,96
BAURU	4	2,84
BOTUCATU	3	2,13
CAMPINAS	9	6,38
CAPITAL	1	0,71
CARAGUATATUBA	4	2,84
FRANCA	10	7,09
FRANCO DA ROCHA	1	0,71
JALES	7	4,96
MARÍLIA	2	1,42
MOGI DAS CRUZES	4	2,84
OSASCO	3	2,13
PIRACICABA	6	4,26
PRESIDENTE VENCESLAU	1	0,71
RIBEIRÃO PRETO	16	11,35
SANTO ANDRÉ	3	2,13
SANTOS	5	3,55
SÃO JOÃO DA BOA VISTA	6	4,26
SÃO JOSÉ DO RIO PRETO	16	11,35
SÃO JOSÉ DOS CAMPOS	2	1,42
SOROCABA	5	3,55
TAUBATÉ	4	2,84
TOTAL	141	100,00

Source: SINAN-NET 2016

Figure 1 – Distribution of confirmed Zika Virus cases, by municipality of residence / Epidemiological Surveillance Group. State of Sao Paulo, 2016.



Source: SINAN-NET 2016

beirão Preto (1023)/Ribeirão Preto Epidemiological Surveillance Group; Barretos (760)/Barretos e Jardinópolis Epidemiological Surveillance Group (505)/Ribeirão Preto Epidemiological Surveillance Group (Figure 1) and deaths were not confirmed.

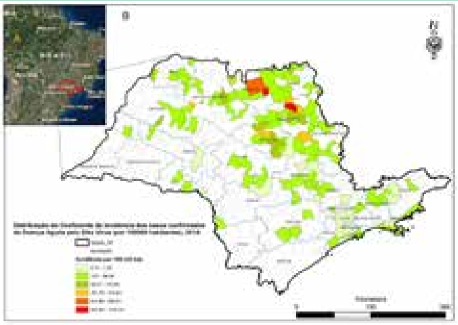
The municipalities of Jardinópolis/Ribeirão Preto Epidemiological Surveillance Group; Jaborandi and Barretos/Epidemiological Surveillance Group Barretos had a higher risk of the disease (incidence of 1,192.22; 1,115.94 and 633.61, respectively, per 100,000 inhabitants) (Figure 2).

The Kernel analysis showed hot areas (case densities) in the study region (Figure 3). In addition, through scanning statistics, provided by the SaTScan™ tool, the clusters of the high Relative Risks of the 645 municipalities distributed among the 28 Epidemiological Surveillance Groups of the State were identified. The centroides of the 13 clusters with a statistically significant "p" value ($p \leq 0.05$) were more intense in the municipalities of Barretos/Barretos Epidemiological Surveillance Group; Ribeirão Preto/Ribeirão Preto Epidemiological Surveillance Group; São José do Rio Preto/São José do Rio Preto Epidemiological Surveillance Group; Pereira Barreto/Epidemiological Surveillance Group Araçatuba; Alto Alegre and Penápolis/Araçatuba Epidemiological Surveillance Group; Cravinhos/Ribeirão Preto Epidemiological Surveillance Group; Gavião Peixoto/Araraquara Epidemiological Surveillance Group; Jaci/São José do Rio Preto Epidemiological Surveillance Group; Porto Ferreira/Araraquara Epidemiological Surveillance Group; Piracicaba/Piracicaba Epidemiological Surveillance Group; Sumaré and Campinas/Campinas Epidemiological Surveillance Group with relative risk variation between ≥ 2.22 and ≤ 67.24 (Figure 4).

DISCUSSION

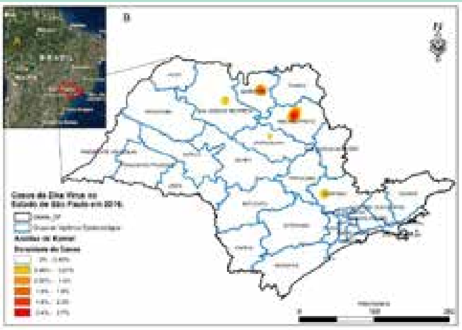
There were many confirmed cases, as well as a high incidence of Zika Vi-

Figure 2 – Distribution of the Incidence Rate of confirmed Zika Virus cases (per 100,000 inhabitants), by municipality of residence / Epidemiological Surveillance Group. State of Sao Paulo, 2016.



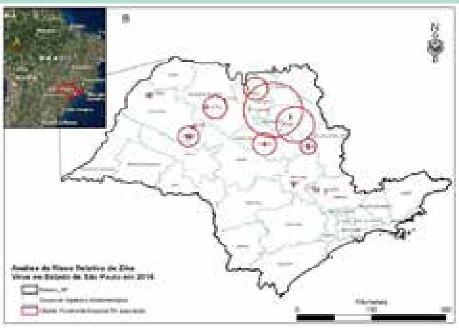
Source: SINAN-NET 2016

Figure 3 – Kernel analysis of confirmed Zika Virus cases, by municipality of residence / Epidemiological Surveillance Group. State of Sao Paulo, 2016.



Source: SINAN-NET 2016

Figure 4 – Relative Risk Analysis of confirmed Zika Virus cases, by municipality of residence / Epidemiological Surveillance Group. State of Sao Paulo, 2016.



Source: SINAN-NET 2016

rus in the State of São Paulo in 2016, compared to 2015 (82 confirmed cases - Epidemiological Surveillance Center: unpublished data). However, there were no deaths. In the same year, the Brazilian Ministry of Health registered 216,207 probable cases of Zika Virus and confirmed eight laboratory deaths, four in Rio de Janeiro, two in Espírito Santo, one in Maranhão and one in Paraíba[14].

The descriptive analysis found that all individuals in the State of São Paulo were vulnerable to the Zika Virus. It is important to note that the Zika Virus affects all age groups and both sexes and that all States and the Federal District of Brazil were at risk for the Zika Virus[15].

Regarding sex, the prevalence of most confirmed cases was observed in women of economically active age. This is a pattern already reported in several surveys, that is, they claim that this group is the most affected16-18. This result is suggestive that, in general, women who remain in contact with the domestic environment for a longer time are more susceptible to the Zika Virus.

The analysis of the spatial distribution of the Zika Virus made it possible to determine the pattern of the situation of this health problem in the State of São Paulo, showing spatial disparities that led to the delimitation of the risk area.

It was found that the spatial distribution of the Zika Virus in the State of São Paulo followed a heterogeneous pattern, as the outbreaks tended to aggregate in specific areas. In addition, the municipalities of the north and northwest regions presented an increasing relative risk.

Despite this result, Costa et al.19 conducted a study on spatial analysis of probable cases of dengue, chikungunya and Zika Virus in the State of Maranhão in Brazil and found that in the years 2015 and 2016 the distribution of Zika Virus cases was homogeneous. In addition, it showed a significant spatial pattern of Zika virus in the western and northern regions of the state.

Regarding the possible explanatory factors for the distribution of Zika Virus, the population density was relevant in the spatial analysis. According to Lima-Camara20, population density is considered a fundamental factor for the high incidence rates of arboviruses, since more populous environments favor the proliferation of the vector due to the ideal conditions for its reproduction, as well as the greater number of individuals susceptible to new infections.

Aedes Aegypti mosquitoes generally do not live at altitudes above 2000 meters (6500 feet) due to environmental conditions. However, most Brazilian territories are low. Thus, these factors can contribute concomitantly to the wide distribution of this mosquito and disease in most of the State of São Paulo and Brazil[21].

In Colombia, in 2016, most reported cases occurred mainly in low-lying areas, and persistent hot spots were observed. Higher infection rates have been reported in the northeastern part of the study area[22].

Finally, this work had limitations due to the use of secondary data, which may be inconsistent in terms of quantity, quality, and information processing. And as a strong point, when analyzing the spatiality of the incidence of the Zika Virus in the State of São Paulo, it was evidenced its close relationship with the areas of greatest presence of the vector.

CONCLUSION

The potential for epidemics in certain Municipalities in the State of São Paulo is of concern, given the large number of people potentially susceptible to the Zika Virus.

The results of this study provide fundamental information to assist public health managers in making time-sensitive decisions at the municipal and state levels.

Knowledge of areas of potential concern interferes with prior planning and has gathered sufficient resources that are essential for the formulation of successful public health programs.

Preventive actions must be taken to eliminate the mosquito and reduce the transmission and cases of Zika virus, as well as other arboviruses, such as dengue, chikungunya, and yellow fever, especially in the areas indicated by the study.

The use of risk maps can help guide decisions for the prevention and control of the Zika Virus.

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