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ORIGINAL ARTICLE

Spatial and Spatio-temporal Analysis of Congenital Malformations of Nervous System in the State of Paraíba from 2010 to 2016

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Abstract

Introduction: In Brazil, congenital malformation anomaly of the nervous system has been the most frequent among the anomalies. Knowledge of your geographical distribution both in space as throughout the time, can assist public managers in the decision-making process about the areas that must be prioritized for the monitoring of this disease.

Objective: Detecting spatial and spatio-temporal clusters of congenital malformations of nervous system.

Methods: An ecological study based on secondary data from the National Information System on Live Births in the period from 2010 to 2016 in the state of Paraíba. We estimated the spatial incidence ratios and applied circular and spatio-temporal Scan statistics to detect clusters with of abovementioned malformations.

Results: The spatial pattern was different throughout the years of the occurrence of these malformations, since the spatial clusters were detected on different regions of the state, except in the years 2013 and 2015, which revealed a higher concentration in the central-west and northwest regions of the state. The retrospective spatio-temporal analysis revealed three clusters that persisted during the years of 2015 and 2016.

Conclusion: The findings indicated the regions that must be prioritized for the monitoring of congenital malformations of nervous system in the state of Paraíba in time and space.

Keywords: spatial analysis, spatiotemporal analysis, cluster analysis, congenital defects.

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Authors summary

Why was this study done?
This study was performed due to a paucity of research related to spatial and spatio-temporal analysis for congenital malformation of nervous system.

What did the researchers do and find?
The researchers developed an ecological study using secondary data from National Information System on Live Births. Spatial Incidence Ratio, circular spatial Scan and spatio-temporal Scan Statistics for detecting spatial clusters were used on congenital malformation of nervous system data. The spatial patterns of the clusters were different throughout the years, except 2013 and 2015, in which was verified a higher concentration in the central-west and northwest regions of the state. Three spatial clusters persisted throughout the years 2015 and 2016.

What do these findings mean?
They suggest a methodology able to indicate areas which prioritized for their monitoring of congenital malformations of nervous system in the state of Paraíba in time and space. This methodology can support decision making process regarding this subject by public health managers.

INTRODUCTION

A congenital malformation (CM) is an internal or external structural defect in genesis, which is usually identified at birth[1]. Most happens between the third and eighth week of gestation[2]. The large anomaly is a defect that requires significant surgical or aesthetic interventions, but in the case of a small, this type of intervention may not be necessary[1].

The etiology may be due to genetic, environmental or multifactorial causes. The multifactorial causes include the gene-teratogen interactions and malformations of unknown origin and correspond to 55% of cases. The genetic causes include the chromosomal malformations and single gene mutations and represent 30% of occurrences. The environmental causes involve drugs/medication, environmental pollutants, infectious diseases and maternal diseases, they constitute 15% of cases[2]. The literature highlights that pregnancies of women younger than 20 years or older than 35 years have an increased risk for CM[3,4]. However, in addition to age, other factors may increase the likelihood of the occurrence of malformations, including: family history, acute diseases in the first quarter and exposure to physical factors[3,5].

It is a condition that has a great impact on society, especially in the family context. Since they face difficulties in understanding the diagnosis, in dealing with prejudices, in addition as well as obstacles in the search for proper care that the child will depend for years to have a better quality of life[6].

The most frequent CM in Brazil is the malformation of nervous system[7,8]. In 2016, there were 4,820 cases this type, with the Northeast region ranking second in the number of occurrences, with only the Southeastern region in front of it[9]. A study conducted in Brazil using data from the National Census of Isolated Populations on Brazilian populations with a high frequency of genetic diseases or congenital anomalies or environmental, identified CM in the Sertão Paraibano region[10].

When one takes spatial and spatio-temporal (ST) information into consideration in the decision-making process, it is important to know its geographic distribution. The spatial analysis enables the identification of characteristics related to these events in the territory in order to plan prevention and control measures[11] that can contribute to a better organization of health care management. In a study on the occurrence of congenital anomalies in space and time, their geographical distributions are used to support public managers in the care given to these children and families. No studies associating CM of nervous system and their geographical distributions in the state of Paraíba were found in the literature. Therefore the main goal of this study is detecting spatial and ST clusters of CM of nervous system in the state of Paraíba in the period from 2010 to 2016.

METHODS

This study is exploratory, quantitative and ecological in nature, using secondary data from the National Information System on Live Births (SINASC). All live births with CM of nervous system in the state of Paraíba, in the period from 2010 to 2016, were included. The state of Paraíba is composed of 223 municipalities and is situated in the Northeast of Brazil.

The Spatial Incidence Ratio (SIR) were calculated for all municipalities (geo-objects) and circular and ST Scan statistics were applied to analyze the data in order to detect spatial and ST clusters of malformations above mentioned. Understanding the concepts of geographical region and geo-object is crucial for the analysis of the SIR.

The region is a geographic area in which the events of interest occur. While the geo-object is manifested by distinct entities and detected geographically in the geographical region[12]. Formally, therefore, SIR are represented by a geographical region R composed by a set of n geo-objects represented as r_1, r_2, ..., r_n. Where $C(r_i)$, $i=1,..., n$, is a random variable representing the number of cases of an epidemiological event in a given interval of time for each geo-object ri and is expressed by c_1, c_2, ..., c_n. Where $P(r_i)$ is the population at risk for that epidemiological event in each geo-object r_i, denoted as p_1, p_2, ..., p_n[13]. The SIR in each geo-object r_i is presented in the following equation:

$$SIR(r_i) = \frac{\frac{C(r_i)}{P(r_i)}}{\frac{\sum_{i=1}^{N} C(r_i)}{\sum_{i=1}^{N} P(r_i)}}$$

The explanation of the $SIR(r_i)$ can be performed according to the following categories: if the geo-object ri under study has no epidemiological incidence, the SIR will be equal to 0; if $0<SIR(r_i)<0.5$; , then the SIR is less than half of the total incidence of the geographical region in that geo-object r_i; if $0.5\leq SIR(r_i)<1.0$ then SIR is more than half of the total incidence, but is less than the epidemiological incidence of the geographical region; $1.0\leq SIR(r_i)<1.5$ then SIR is higher than the overall incidence of the geographical region by less than 50%; if $1.5\leq SIR(r_i)<2.0$ then SIR is higher than the overall incidence of the geographical region by more than 50%; and if $SIR(r_i)\geq 2.0$ then it is two or more times higher than the total incidence of the geographical region[13]. So, the SIR of the geo-object r_i is given by the incidence ratios of the occurrence of CM of nervous system in that geo-object (municipality) with respect to the geographic region (the state of Paraíba).

Circular scan statistics were used for the detection of the spatial clusters of the CM[14]. The method searches the entire geographical region of study for geo-object clusters (composed by at least one geo-object), which are defined as clusters where the likelihood of case occurrence is significantly higher inside it than outside it. To this end, the information of the geo-object must be concentrated in a single point within it, called the centroid, which representes the center of mass of each region's area[14].

To identify these spatial clusters, the likelihood ratio test is used, which checks whether the observed number of cases in a geo-object exceeds the expected number of cases. If this does not occur, a circle centered around the centroid of that geo-object is increased so as to encompass its neighbors. The radius of the circle can vary from zero to a maximum percentage of 50% of the population under risk[14]. The radius of each circle created by the scan statistics is based on the total number of cases and the population size in the geographic region[15].

The ST scan was used for the detection of clusters that occur simultaneously in space and time. The method can be defined by a window with a cylindrical shape with its circular base representing the geographical dimension and its height the interval of time. As such, the cylindrical window is moved in space and time for each possible location and size of the circle as well as for each possible time interval. Although an infinite number of cylinder overlays is obtained, the epidemiological data contains a finite number of individuals, which means some of these cylinders will contain exactly the same number of people. This circumstance therefore leads to a finite number of cylinders for which the probability really has to be calculated. It is recommended that the size of the geographical dimension (circular base) and the time interval should be limited to half the number of expected cases and half of the total period, respectively[16].

That method can be used both retrospectively or prospectively. The prospective use seeks to detect clusters that are still active, *i.e.*, those that are still present during the last time period for which data is available. It is repeated periodically in time, for example, every day, week, month or year[16]. The retrospective study, meanwhile, detects clusters that began and ended before the beginning of the study. It is used in a single analysis, using historical data, for example[17]. The retrospective ST scan was used with historical data from SINASC with a persistence time of one, two and three years.

The discrete Poisson model was the most appropriate for the study since it uses occurrence count data[15]. It was used a significance level of 5% for the Monte Carlo simulations hypothesis tests with 999 random replications of the data with a null hypothesis of both spatial and ST randomness[14,16]. This study analyzed, 0.1%, 0.3%, 0.5%, 0.7%, and the values between 1.0 and 10% of the population at risk, and for the ST analysis persistence times of one, two and three years were used. Next, the scan statistics maps were analyzed for each year and ST scan, using the SIR maps as reference.

The data were stored in a electronic spreadsheet and analyzed in the SaTScanTM and R software. The project was approved by the Brazil Platforma under protocol number 082/17.

RESULTS

In the period from 2010 to 2016, 551 cases of CM of nervous system were reported in the state of Paraíba. Of these, 53.3% were females, with a mean weight of 2757

Table 1: Characteristics of live births with congenital malformation of the nervous system, state of Paraíba, Brazil, 2010-2016.

Variables	2010		2011		2012		2013		2014		2015		2016	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Gender														
Female	25	45.45	18	40.90	20	55.56	25	55.56	35	59.32	98	55.05	73	54.48
Male	29	52.73	26	59.10	14	38.89	20	44.44	24	40.68	80	44.95	61	45.52
Ignored	1	1.82	0	0.00	2	5.56	0	0.00	0	0.00	0	0.00	0	0.00
Weight (grams)														
Less than 2500	17	30.90	11	25.00	14	38.89	17	37.78	18	69.50	58	32.59	36	27.87
2500 and more	38	69.10	33	75.00	22	61.11	28	62.22	41	30.50	120	67.41	98	73.13
Apgar score 1st minute														
0 to 3	8	14.55	9	20.45	12	33.33	10	22.22	16	27.12	23	12.92	15	11.19
4 to 6	11	20.00	10	22.72	4	11.11	7	15.56	13	22.03	19	10.68	16	11.94
7 to 10	34	61.82	23	52.28	19	52.78	28	62.22	30	50.85	134	75.28	101	75.37
Not provided	2	3.63	2	4.55	1	2.78	0	0.00	0	0.00	2	1.12	2	1.50
Apgar score 5th minute														
0 to 3	5	9.10	6	13.63	9	25.00	7	15.56	10	16.95	13	7.30	9	6.72
4 to 6	8	14.54	5	11.37	4	11.11	4	8.89	7	11.86	12	6.74	10	7.46
7 to 10	40	72.72	31	70.45	22	61.11	34	75.55	42	71.19	151	84.84	113	84.32
Not provided	2	3.64	2	4.55	1	2.78	0	0.00	0	0.00	2	1.12	2	1.50

Continuation - Table 1: Characteristics of live births with congenital malformation of the nervous system, state of Paraíba, Brazil, 2010-2016.

Variables	2010		2011		2012		2013		2014		2015		2016	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Types														
Anencephaly and similar malformations	13	23.63	10	22.72	13	36.11	9	20.00	13	22.03	12	6.74	9	6.72
Encephalocele	4	7.28	4	9.10	6	16.67	4	8.89	1	1.70	4	2.25	1	0.74
Microcephaly	6	10.91	2	4.54	3	8.33	3	6.67	5	8.47	133	74.71	75	55.97
Congenital Hydrocephalus	17	30.91	22	50.00	7	19.44	16	35.56	21	35.60	16	9.00	28	20.90
Other congenital malformations of the brain	1	1.82	3	6.82	1	2.78	2	4.44	3	5.08	3	1.68	4	2.98
Spina bifida	13	23.63	3	6.82	6	16.67	7	15.56	14	23.72	9	5.05	15	11.19
Other congenital malformations of the spinal cord	0	0.00	0	0.00	0	0.00	2	4.44	1	1.70	0	0.00	0	0.00
Other congenital malformations of the Central Nervous System	1	1.82	0	0.00	0	0.00	2	4.44	1	1.70	1	0.56	2	1.50
Total	55	100.00	44	100.00	36	100.00	45	100.00	59	100.00	178	100.00	134	100.00

grams. Approximately 70% of live births had an Apgar score greater than or equal to seven in the first minute and 78.5% in the fifth minute. The malformations with a higher frequency included microcephaly, hydrocephalus, anencephaly and similar malformations, representing 76.5% of the sample, as can be seen in Table 1.

In relation to the detection of spatial clusters through the circular Scan statistic, 0.3% of the at-risk population was listed for the years 2010, 2011, 2012 and 2014, obtaining 10, 12, 8 and 8 spatial clusters, respectively, distributed throughout the state. 14 spatial clusters were identified in the year 2013 with a higher number in the center-west region of the state, under na at-risk population of 1%. With an at-risk population of 7% in the year 2015, 23 were detected with a greater concentration in the northwest of the state. In the year of 2016, 16 spatial clusters were detected with an at-risk population of 1% (Figure 1).

A retrospective approach was used in the ST scan for the period from 2010 to 2016, with an at-risk population of 2% and a persistence time of two years, using the SIR maps as reference, obtaining three clusters that persisted simultaneously in space and time (Figure 2).

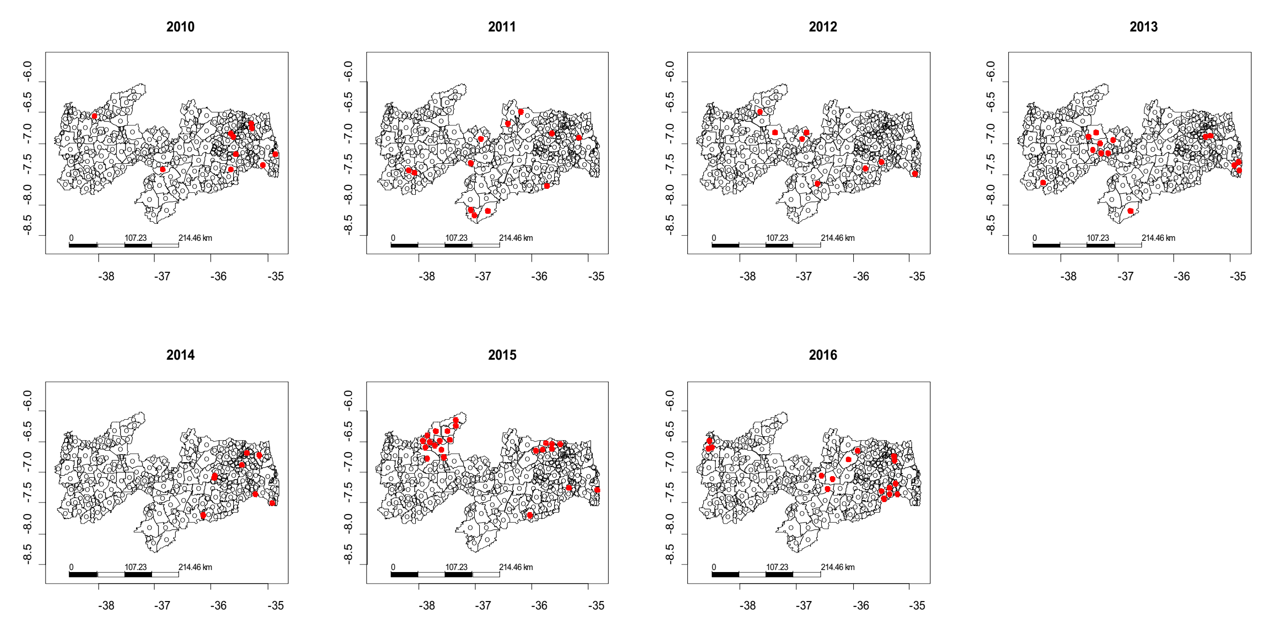

Figure 1: Circular Scan statistics maps of the congenital malformations of nervous system for the period 2010 to 2016, state of Paraíba, Brazil.

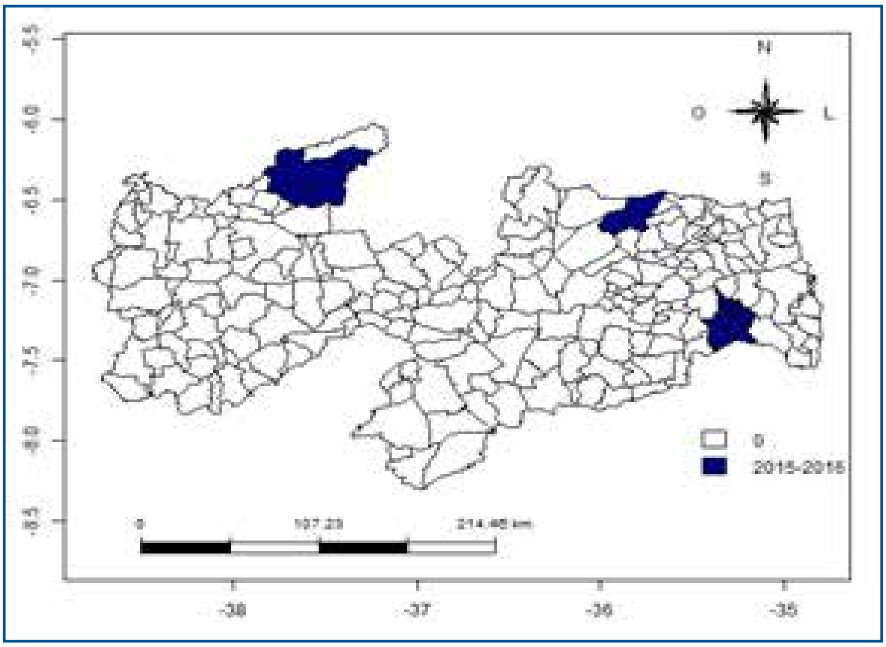

Figure 2: Spatio-temporal scan of the congenital malformations of nervous system in the state of Paraíba, Brazil, in the period between 2010 and 2016.

Table 2: Spatio-temporal clusters of congenital malformations of nervous system in the state of Paraíba, Brazil, 2010-2016.

Clusters	Municipalities	Persistence (years)	Observed cases	Expected cases	Likelihood Ratio	p - value
Cluster 1	São José do Brejo do Cruz, São Bento, Catolé do Rocha, Riacho dos Cavalos, Brejo do Cruz.	2	19	2.99	19.38	6.6×10^{-7}
Cluster 2	Gurinhém, Mogeiro, Itabaiana, Juripiranga, Pilar, Sobrado, Riachão do Poço, São José dos Ramos, Caldas Brandão, São Miguel de Taipu.	2	14	3.18	10.04	$6.6x10^{-3}$
Cluster 3	Cacimba de dentro, Araruna, Damião.	2	9	1.31	9.73	$1.0x10^{-2}$

Table 2 shows the information related to the ST clusters, such as the, the municipalities making up the clusters, persistence time, the expected and observed number of cases, the likelihood ratio and the p-value.

DISCUSSION

The spatial analysis revealed that the clusters were dispersed in different regions of the state, except in the years 2013 and 2015, which showed a higher concentration in the central-west and northwest regions of the state, respectively, representing the Sertão Paraibano. Cardoso *et al*.[10] mapped genetic diseases and CM in Brazil and observed a high percentage of CM in the region of the Sertão Paraibano, albeit not in the same locations as in the present study.

In the year of 2010, ten spatial clusters scattered throughout the state were identified, but most were located in the eastern region near the capital of the state. In 2011, the spatial clusters present were not in the same regions as in the previous year. The eight identified in 2012 were well dispersed. In the following year of 2013, meanwhile, there was a greater concentration in the center-west portion of the state, in the region of the Sertão. In 2014, the spatial clusters were detected near the major cities of the state. It is worth mentioning that this is the only year in which they were not identified in the central-west and western regions of the state. In the year 2015, the Sertão Paraibano region had a larger numbers, which were in different locations than in the year 2013. The 15 spatial clusters observed in the year of 2016 were mostly between the northeast and southeast of the state. It is worth noting that when referring to the purely spatial analysis, the spatial clusters cannot be compared in relation to years, so one could not say that a change or displacement between them occurred.

With respect to the ST analysis, a approach was used in which clusters that began and ended before the beginning of the study were pointed out, detecting three, which are concentrated in the northeast, southeast and northwest of the state, which persisted during the years of 2015 and 2016. Cluster 1, located to the northwest of the state, is far from the state capital (more than 350 kilometers). This negatively affects the access to the main reference centers, especially the hospitals and maternity units specialized in high-risk pregnancies. Cluster 2 is located to the southeast of the state, close to the capital and major cities in the state, which offer more adequate care support. Finally, cluster ST 3 is located about 200 kilometers from the capital city near the border with the state of Rio Grande do Norte, being composed of small-sized municipalities.

Only two of the seven years under study showed the occurrence of persistent cases for these CM, which were the years of 2015 and 2016. This period was marked by a change in the historical series of microcephaly at the SINASC. Since the year 2000, the prevalence of microcephaly in newborns was 5.5/100,000 live births, with this frequency holding steady until 2010 (5.7/100,000 live births). At the end of 2015, the incidence increased to 99.7/100,000 live births, corresponding to a 20-fold increase in comparison with the rate observed in previous years[18]. According to Barreto *et al.*[19], issues related with the magnitude of this problem project new health care patterns, needs and demands into the following years that should be investigated. Adequate resources, training and qualifications will have to be defined to deal with this current situation. The increase in these cases of microcephaly has been attributed to the probable intrauterine exposure to the Zika virus[20].

Groisman *et al.*[21] highlight the importance of studying clusters by stating that the maps used in conjunction with statistical tests may be useful for researchers in the health care sector by focusing attention on areas for further research. They further state that, because these maps show general disease patterns, they generate hypotheses about the role of environmental, genetic or life style factors in the etiology of a disease.

Circular scan statistics have been used in different studies on CM[22-24]. ST scan in the health care sector have been employed to identify clusters for tuberculosis[25], hand-foot-mouth disease[26], breast cancer[27,28] and CM[21]. These methods can be used in geographic patterns with different types of diseases, demonstrating their legitimacy. The studies showed a clustering analysis using the circular or ST scan statistics, but did not use both methods at the same time, as in the present study, which therefore reinforces its relevance. The limitation of this study is similar to all the studies that work with secondary data and depend on the good and accurate recording of information. In addition, no studies were found involving all CM of nervous system in the context of spatial and ST analysis.

The findings contributed to the field of public health by revealing the patterns of spatial and ST distribution of CM of nervous system in state of Paraíba, and especially by indicating the regions that must be prioritized for their monitoring. This information can assist public managers in maintaining or expanding the access to health services for this population and may support public policy actions involving maternal and child health.

Among the malformations present in this study, anencephaly and similar malformations stand out for being part of the neural tube defects that are responsible for the greatest proportion of CM of nervous system. However, the incidence of these defects can be reduced with the supplementation of folic acid in the periconceptional period and during pregnancy, mainly in the first quarter. It should be noted that neural tube defects may also be due to other factors, including genetic or multifactoral ones[29].

CONCLUSION

This study enabled the detection of the spatial and ST clusters of CM of nervous system in the state of Paraíba, in the period from 2010 to 2016. In addition, it demonstrated the use of a suitable and useful methodology in the analysis of health information in this territory. The findings presented in the study indicate areas that should be prioritized for monitoring of congenital anomalies of nervous system cases, supporting public managers in the decision making process regarding this subject.

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Resumo

Introdução: No Brasil, a anomalia congênita do sistema nervoso tem sido a mais frequente dentre as anomalias. O conhecimento da sua distribuição geográfica, tanto no espaço quanto ao longo do tempo, pode auxiliar os gestores públicos no processo de tomada decisão sobre as áreas que devem ser priorizadas no monitoramento dessa doença.

Objetivo: Detectar aglomerados espaciais e espaço-temporais das anomalias congênitas do sistema nervoso.

Método: Estudo ecológico a partir de dados secundários do Sistema de Informações sobre Nascidos Vivos no período de 2010 a 2016 no estado da Paraíba. Foram estimadas as Razões de Incidências Espacial e aplicada a estatística Scan circular e Scan espaço-temporal para a detecção dos aglomerados das anomalias citadas anteriormente.

Resultados: O padrão espacial foi diferente ao longo dos anos da ocorrência destas anomalias, uma vez que os aglomerados espaciais foram detectados em diferentes regiões do estado, exceto nos anos 2013 e 2015 que foi verificada uma maior concentração nas regiões do centro-oeste e noroeste do estado.

Conslusão: Os achados indicaram as áreas que devem ser priorizadas para o monitoramento de anomalias congênitas do sistema nervoso no estado da Paraíba, tanto no tempo quanto no espaço.

Palavras-chave: análise espacial, análise espaço-temporal, análise por conglomerados, defeitos congênitos.