

Distribution of Children and Adolescent Mortality by Central Nervous System Tumors in the State of Ceará

doi: <https://doi.org/10.32635/2176-9745.RBC.2022v68n2.2134>

Distribuição da Mortalidade Infantojuvenil por Tumores do Sistema Nervoso Central no Estado do Ceará

Distribución de la Mortalidad Infantil y Juvenil por Tumores del Sistema Nervioso Central en el Estado de Ceará

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ABSTRACT

Introduction: Central nervous system (CNS) tumors are one of the most common types of solid tumors that affect children. Due to their heterogeneity, they comprise more than 100 defined histological types of cell origin-based and other histopathological characteristics. **Objective:** To analyze the spatial distribution of mortality by CNS tumors in children and adolescents in the State of Ceará in the period 2008-2018. **Method:** Ecological study, with secondary data of the period selected, available at the Mortality Information System (SIM). Crude rates, Moran Global and Local index, and relative risk for all deaths were calculated. **Results:** Of the 378 deaths, 197 were males (52%) mostly, 116 aged between 5-9 years (30.7%), 193 Brown (51%) and 354 died in the hospital (93.6%). The municipalities with the highest rates (49.94 and 99.88 deaths/1 million inhabitants) were Aracati, Barreira, Catunda, Coreaú and Fortaleza. The Moran Index showed the formation of a cluster with a high/high standard and statistical significance of distribution in the Metropolitana Fortaleza Mesoregion. The municipality of Pacujá had the highest relative risk (7.32) followed by the municipality of Catunda (6.94). **Conclusion:** The North and Northwest Regions of Ceará presented the higher mortality and risk rates by CNS tumors.

Key words: central nervous system neoplasms/mortality; demography; child; adolescent.

RESUMO

Introdução: Os tumores do sistema nervoso central (SNC) são um dos tipos mais comuns de tumores sólidos que acometem crianças. Apresentam heterogeneidade por compreender mais de 100 tipos histológicos definidos com base na origem da célula e outras características histopatológicas. **Objetivo:** Analisar a distribuição espacial da mortalidade por tumores do SNC em crianças e adolescentes no Estado do Ceará, no período de 2008-2018. **Método:** Estudo ecológico realizado com dados de fontes secundárias de 2008-2018 disponíveis no Sistema de Informação sobre Mortalidade (SIM). Foram calculadas as taxas brutas, o Índice de Moran Global e Local e o risco relativo para todos os óbitos. **Resultados:** Dos 378 óbitos, 197 eram do sexo masculino (52%), 116 apresentavam a faixa etária entre 5-9 anos (30,7%), 193 eram pardos (51%) e 354 morreram no hospital (93,6%). Os municípios que apresentaram as maiores taxas (49,94 e 99,88 óbitos/1 milhão de habitantes) foram Aracati, Barreira, Catunda, Coreaú e Fortaleza. Pelo Índice de Moran, observou-se a formação de um *cluster* com padrão alto/alto e significância estatística de distribuição na Mesoregião do Metropolitana de Fortaleza. O município de Pacujá apresentou o maior risco relativo (7,32) seguido do município de Catunda (6,94). **Conclusão:** As Regiões Norte e Noroeste do Ceará possuem taxas mais elevadas e risco maior para mortalidade por tumores do SNC.

Palavras-chave: neoplasias do sistema nervoso central/mortalidade; demografia; criança; adolescente.

RESUMEN

Introducción: Los tumores del sistema nervoso central (SNC) son uno de los tipos más comunes de tumores sólidos que afectan a los niños. Presentan heterogeneidad al comprender más de 100 tipos histológicos definidos y basados en el origen celular y otras características histopatológicas. **Objetivo:** Analizar la distribución espacial de la mortalidad por tumores del SNC en niños y adolescentes en el Estado de Ceará en el período 2008-2018. **Método:** Estudio ecológico realizado con datos de fuentes secundarias de 2008-2018 disponibles en el Sistema de Información de Mortalidad (SIM). Se calcularon las tasas brutas, el Índice de Moran Global y Local y el riesgo relativo de todas las muertes. **Resultados:** De los 378 fallecidos, 197 eran varones (52%), 116 presentaban el grupo de edad entre 5-9 años (30,7%), 193 eran morenos (51%) y 354 murieron en el hospital (93,6%). Los municipios con mayores tasas (49,94 y 99,88 defunciones/1 millón de habitantes) fueron Aracati, Barreira, Catunda, Coreaú y Fortaleza. El Índice de Moran observó la formación de un *cluster* con un patrón alto/alto y significación estadística de distribución en la Mesoregión de Fortaleza Metropolitana. El municipio de Pacujá presentó el mayor riesgo relativo (7,32) seguido del municipio de Catunda (6,94). **Conclusión:** Las regiones del Norte y Noroeste de Ceará tienen tasas más elevadas y un mayor riesgo de mortalidad por tumores del SNC.

Palabras clave: neoplasias del sistema nervioso central/mortalidad; demografía; niño; adolescente.

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INTRODUCTION

Cancer is already the first cause of death (8% of the total) by disease among children and adolescents from 1 to 19 years of age in Brazil. The most frequent tumors for this population are leukemias (affecting white blood cells) in the CNS – Central Nervous System and lymphomas¹.

CNS tumors are heterogeneous with more than 100 histological types defined by the World Health Organization – WHO's Classification of Tumors of the Central Nervous System based in the origin of the cell and other histopathological characteristics².

These tumors are more incident in the first decade of life, account for 20% of the neoplasms in less than 15 years and 70%-80% originate from glial cells. Location of the tumor and child's age-range influence the clinical manifestations including vague and secondary symptoms to intracranial hypertension and in advanced disease, headache, brain seizure, vomits, gait and behavior disorders and visual changes³. Thus, childhood cancer requires targeted investigations due to differences in primary locations, histological origins, clinical evolution and latency period compared to cancer in adults to improve the prognosis and identify risk factors^{4,5}.

As they belong to a complex and heterogeneous group of primary tumors either malignant or benign and rarely affecting adults, they are one of the main causes of death by cancer in individuals aged <19 years⁶.

This study has the objective of analyzing the spatial distribution of death by CNS tumors in children and adolescents (0-19 years) in the State of Ceará from 2008 to 2018.

METHOD

Ecological study investigating a population of a group of persons living in a geographical area⁷, in the present case, the state of Ceará in Brazil's Northeast Region, with territorial extension of 148,894,442 km², the fourth larger of the Region⁸.

Secondary data available from “*Sistema de Informação sobre Mortalidade (SIM)*”⁹ collected from the Computer Information System of the National Health System (DATASUS) were utilized. Data from death by CNS tumors in children and adolescents from 2008 to 2018 were obtained. The following codes of the International Classification of Diseases and Related Health Problems – (ICD 10) were selected: C70 (malignant neoplasms of meninges), C71 (malignant neoplasm of brain) and C72 (malignant neoplasm of spinal cord, cranial nerves and other parts of central nervous system)¹⁰. Information was collected in March 2021.

Initially the data were described according to sex, age-range, race/color and place of deaths.

Crude mortality rate by CNS tumors was calculated as the number of deaths of residents in the period 2008 to 2018 divided by the population of the mid-year and multiplied by 1 million inhabitants.

Moran's Index was applied to verify the spatial autocorrelation. For the global evaluation (Global Moran's Index) it was attempted to identify the spatial autocorrelation and the pattern of spatial distribution and formation of clusters of the deaths by CNS according to the state regions.

In the local analysis (Local Moran's Index), it was found the existence of clusters and the level of spatial association for each municipality. This similarity is verified by normalized values (Z) and mean of the neighbors (WZ). The diagram is divided in four quadrants: Q1 (positive values, positive means), Q2 (negative values, negative means), Q3 (positive values, negative means) and Q4 (negative values, positive means)¹¹. All the analyzes (crude rate, Global and Local Moran's Index) were calculated with software Terraview 4.2.2.

Scan statistics was adopted to analyze the formation of purely spatial clusters by deaths of CNS with software SaTScan™ version 9.6. The circular scanning window corresponding to 50% of the risk with level of significance of 5% to identify clusters of high mortality rate was applied⁴. Relative risk (RR) of mortality was analyzed when RR<1 (risk of a certain place is lower than the whole region) and RR>1 (risk of an area is bigger than the whole region).

Aggregate unidentified public domain data were utilized, reason for which the submission to the Institutional Review Board (IRB) was waived.

RESULTS

From 2008 to 2018, 378 deaths by CNS tumors were identified in children and adolescents in Ceará. In this period, 197 (52%) of them were males. The age-range from 5 to 9 years concentrated the highest number of deaths, 116 (30.7%). 193 (51%) of the deaths were of Brown color/race. Hospital was where the great number of deaths – 354 (93.6%) – occurred as shown in Table 1.

The spatial analysis by crude rates of mortality revealed that a significant part of the municipalities presented rates between 0.01 and 24.97 deaths/1 million inhabitants and irregular distribution of the spatial pattern. The municipalities of *Aracati*, *Barreira*, *Catunda*, *Coreaú* and *Fortaleza* (Figure 1) presented rates between 49.94 and 99.88 deaths/1 million inhabitants.

Table 1. Sociodemographic characteristics of deaths by CNS tumors in children and adolescents. Ceará, Brazil, 2008-2018

Variable	N	%
Sex		
Male	197	52
Female	181	48
Total	378	100
Age-range		
<1 year	9	2.3
1-4 years	97	25.7
5-9 years	116	30.7
10-14 years	80	21.2
15-19 years	76	20.1
Total	378	100
Race/Color		
White	108	28.6
Black	5	1.3
Yellow	1	0.3
Brown	193	51
Ignored	71	18.8
Total	378	100
Place of occurrence		
Hospital	354	93.6
House	21	5.5
Thoroughfare	1	0.3
Others	2	0.6
Total	378	100

Source: SIM⁹.

Global Moran's Index of death rates ($I=0.054$) showed positive spatial association although no value close to one has been generated. The level of significance $p=0.11$ was obtained, indicating the hypothesis of spatial correlation. The Local Moran's Index was utilized to find the areas with high spatial dependence.

In Figure 2 (Map A) it was found a cluster with high-high pattern in the Mesoregion of *Fortaleza* (municipalities of *Aquiraz* and *Eusébio*). In Lisa Map, Figure 2 (Map B), the cities with high death rates and statistical significance ($p<0.05$) concentrated in the Mesoregion of *Centro-Sul Cearense* (*Antonina do Norte*), *Jaguaribe* (*Ererê* and *Iracema*), *Noroeste Cearense* (*Alcântara*, *Frecheirinha*, *Hidrolândia*, *Ubajara* and *Uruoca*), of *Sertões Cearenses* (*Monsenhor Tabosa*), *Sul Cearense* (*Potengi* and *Altaneira*), Metropolitan of *Fortaleza* (*Aquiraz*, *Eusébio*, *Pacajus* and *Pacatuba*) and *Norte Cearense* (*Capistrano*, *Chorozinho*, *Mulungu* and *Redenção*).

There was more heterogeneity of RR for mortality by CNS tumors in the state regions. The municipality of *Pacujá*

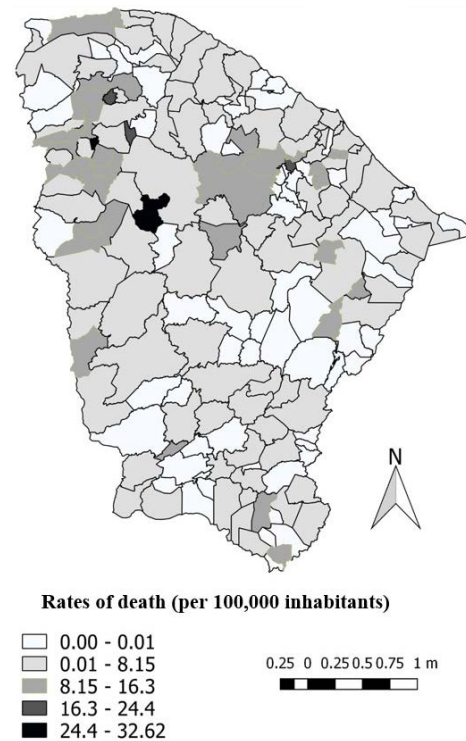


Figure 1. Crude death rates. Ceará, Brazil, 2008-2018

had the highest RR (7.32) followed by the municipality of *Catunda* (6.94) according to Figure 3 (Map A).

Through purely spatial scan statistic, five high-risk mortality spatial clusters by CNS tumors were identified, but only one presented statistical significance ($p<0.001$). The primary cluster included 36 municipalities in the Mesoregions *Norte Cearense*, *Noroeste Cearense* and *Sertões Cearenses*. The secondary clusters not statistically significant were found in the Mesoregions of *Sul Cearense*, Metropolitan of *Fortaleza*, *Norte Cearense* and *Noroeste Cearense*, as shown in Figure 3 (Map B).

Table 2 presents the detailed information of clusters of deaths by CNS tumors identified by spatial scan alone.

DISCUSSION

The sociodemographic characteristics of the deaths for the period 2008-2018 indicate that most of the deaths were in males, similar to other studies about childhood and adolescent cancer in Brazil^{12,13} and in other countries as Austria, USA and Colombia¹⁴⁻¹⁶. The deaths were more incident in the age-range from 5 to 9 years for CNS tumors unlike the data by cancer in Brazil where high risk of death is between 15 and 19 years of age¹⁷. The findings of death for race/color by CNS tumors in Ceará were different from other analyzes where White race was more predominant than Brown¹⁴ instead.

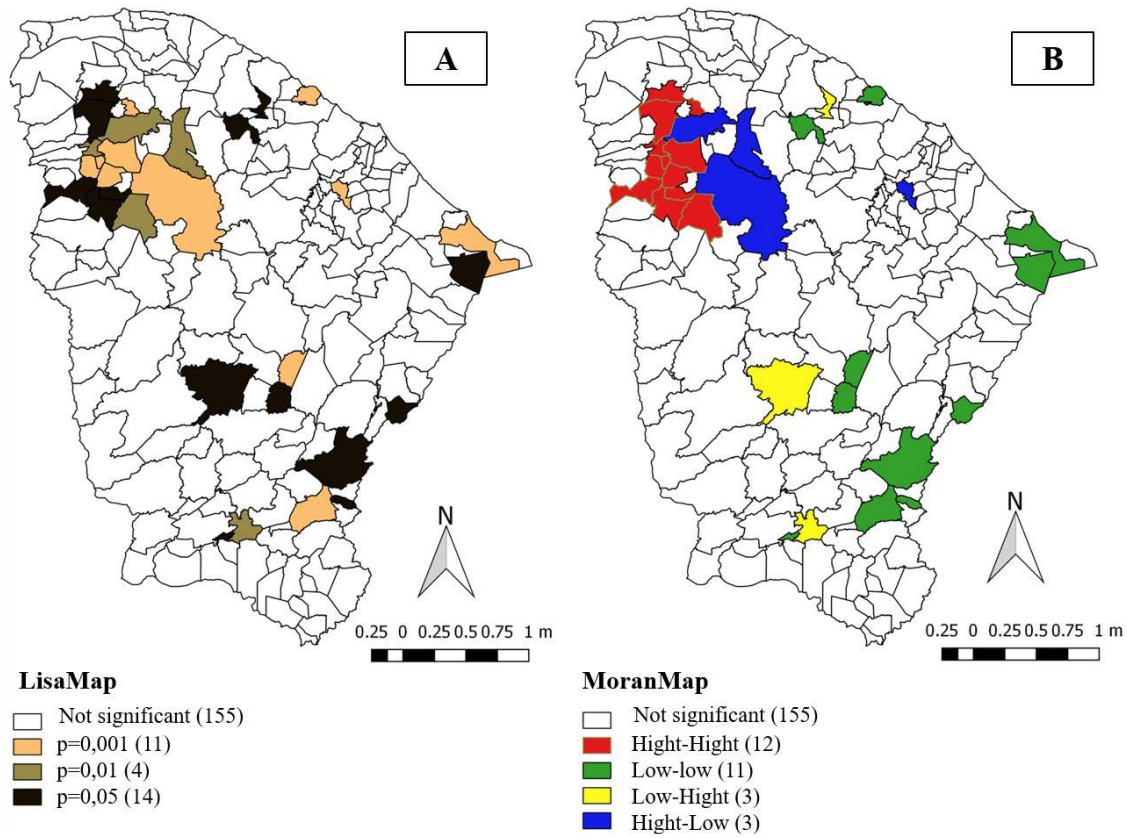


Figure 2. Deaths map. Ceará, Brazil, 2008-2018. A. Moran Map; B. Lisa Map

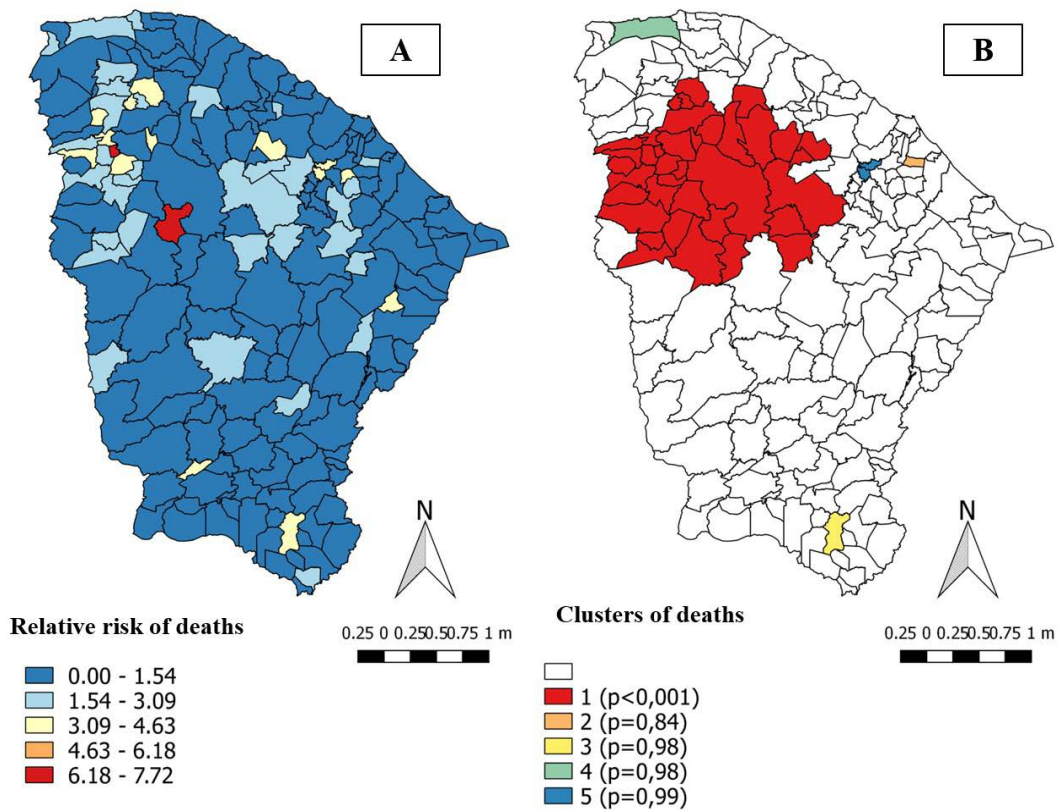


Figure 3. Relative risk maps and of clusters of the deaths by CNS tumors. Ceará, Brazil, 2008-2018. A. Map of relative risk of deaths; B. Map of clusters of deaths

Table 2. Spatial clusters of deaths by CNS tumors in children and adolescents defined by spatial scan alone per municipality of residence, Ceará, Brazil, 2008-2018

Cluster	Number of municipalities	Radius (km)	Number of deaths	Number of expected deaths	RR*	LRT	Value of p
1	36	94.20	76	42	2.0	12.9	<0.001
2	1	0	8	3.0	2.9	3.3	0.84
3	1	0	5	1.5	3.4	3.6	0.97
4	1	0	7	2.6	2.7	2.5	0.98
5	2	12.3	4	1.0	3.8	2.4	0.99

Source: SIM⁹.

Captions: RR = Relative Risk; LRT = Likelihood ratio test.

(*) RR for the cluster compared to the rest of the state.

Crude mortality rate for most of Ceará municipalities ranged from 0.01 to 24.97 deaths/1 million inhabitants and higher than the crude rate for Brazil (9.23 per 1 million inhabitants) and for Northeast (1 million inhabitants) between 2009-2013¹⁸. The results of a study in Paraná in the biennium 2012-2013 indicated highest death rate of 1.9/100 thousand inhabitants in the age-range of 0-4 years¹⁹.

Crude mortality rates presented in the map are fragmented and higher number of municipalities with rates equal to zero which makes the interpretation of the results difficult because of biases. The Mesoregions of *Jaguaribe*, Metropolitan of *Fortaleza*, *Noroeste* and *Norte Cearense* presented high rates from 49.9 to 99.88 deaths/1 million inhabitants. These findings concur with mortality analysis by childhood cancer in Ceará which revealed that municipalities located in the Mesoregion of *Noroeste Cearense* (63 deaths/1 million inhabitants) and Metropolitan of *Fortaleza* (53 deaths/1 million inhabitants) have also presented high death rates²⁰.

Moran's thematic maps showed that the distribution of deaths in Ceará is heterogenous. The Metropolitan Region of *Fortaleza* presented high-high pattern surrounded by neighboring municipalities with low-high pattern; this distribution may be related to the location of oncological pediatric services since *Barbalha*, *Fortaleza* and *Sobral* are references for the treatment of childhood and adolescent cancer and some patients inform their addresses in these cities²¹.

The municipality of *Catunda* had the highest RR of deaths by CNS tumors in children and adolescents. RR was also higher in the regions of *Noroeste* and *Norte Cearense*. Another hypothesis discussed in the literature is that the exposure to pesticides may be associated with the development of childhood and adolescent cancer, including CNS tumors. Studies conducted in the state evaluating the areas with high number of cases and deaths

for this type of cancer are located in farming areas²⁰. The regions *Noroeste* and *Norte Cearense* with the highest rate of deaths are poles of irrigation of *Ibiapaba* and *Baixo Acaraú*.

The high rates of death investigated can be explained by the improvement of the notification system and diagnosis. However, the hypothesis that the increase of fertilizers utilization in food production in the Mesoregion of *Jaguaribe* influenced the concentration of childhood and adolescents deaths by CNS tumors is reinforced by articles that revealed the presence of pesticides in 100% of the samples collected from house water wells and tanks in this area²².

CONCLUSION

The spatial distribution of deaths presented in this article indicates that some regions of the state have higher rates and risk for CNS tumors. Additionally, it is necessary to improve the notification systems to investigate environmental, genetic and gestational factors of cases notified.

CONTRIBUTIONS

All the authors contributed substantially to the study design, analysis and interpretation of the data, wording and critical review. They approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

FUNDING SOURCES

None.

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Recebido em 22/6/2021
Aprovado em 8/11/2021

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