Original Article

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Reduction Of Mortality In Children And Youth Due To Central Nervous System Tumors In Brazil

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Introduction: Mortality due to central nervous system (CNS) neoplasms is one of the leading causes of death in the pediatric population. Although Brazil has experienced a general decline in pediatric mortality from CNS neoplasms over the past decade, this trend has not been consistent across all regions of the country.
Methods: This study analyzed trends and regional variations in pediatric mortality from CNS neoplasms using data from the Mortality Information System (SIM) and the Brazilian Institute of Geography and Statistics (IBGE). Mortality rates among individuals aged 0 to 19 were examined and stratified by sex, race, and federal unit.
Results: CNS neoplasms accounted for 27.3% of all deaths from neoplasms in the pediatric population. An overall reduction in mortality was observed, with the Southeast and Midwest regions showing the most significant declines, while the South experienced a less pronounced reduction. Mortality was more prevalent among males, individuals of white race, and the 5 to 9-year age group—contrasting with international findings that report higher mortality in children under 5 years of age. The data also revealed a trend of decreasing mortality with increasing age.
Conclusion: Regional disparities in mortality may be associated with differences in diagnostic capabilities and access to treatment. The age-related discrepancies between Brazilian and international data may reflect regional demographic dynamics. These findings highlight the ongoing need for improvements in early diagnosis, specialized care, and health education to further reduce CNS neoplasm mortality rates in Brazil.

Keywords: Infant Mortality; Central Nervous System Neoplasms; Pediatric Tumors; Brazil.

INTRODUCTION

Central nervous system (CNS) neoplasms are the leading cause of cancer-related deaths in childhood and represent the most common solid tumors in children and adolescents under the age of 19 [1-3]. According to the Central Brain Tumor Registry of the United States (CBTRUS), the annual incidence of CNS tumors in individuals aged 0 to 19 years is 6.14 per 100,000 population [4]. In Brazil, CNS tumors account for slightly more than 20% of all neoplasms in children and adolescents. Supratentorial tumors predominantly occur during the first two years of life and adolescence, while infratentorial tumors are more frequent between the ages of 2 and 10 years [5]. CNS tumors include neoplasms located in the brain, brainstem, cranial nerves, spinal nerves, and meninges, forming a heterogeneous group characterized by distinct histopathological, molecular, and other parameters. Their incidence varies according to the patient's age, sex, and ethnicity [1,3, 6]. In 2016, the World Health Organization introduced a significant update to CNS tumor classification. This new approach integrates histological origin, malignancy grade, and, for the first time, molecular characteristics, offering a more precise understanding of CNS neoplasms and improving diagnosis, prognosis, and treatment strategies [5]. The main histological groups of CNS tumors in children and adolescents include gliomas, such as pilocytic astrocytoma and ependymoma, as well as tumors like pituitary adenoma and medulloblastoma [2-4]. Despite advancements in neuroimaging, including neuronavigation and tractography, molecular biology innovations identifying tumor-specific traits, and genetic progress enabling early diagnosis and targeted therapies, CNS tumors remain the leading cause of childhood deaths among solid tumors. Unlike adults, where environmental and behavioral factors are significant, genetic factors play a crucial role in CNS tumor development in children and adolescents. This is especially true in hereditary syndromes and genetic mutations that increase predisposition to these neoplasms. Conditions associated with CNS tumor development include Neurofibromatosis type 1 and type 2, Tuberous Sclerosis Complex, Li-Fraumeni Syndrome, Gorlin-Goltz Syndrome, Werner Syndrome, Von Hippel-Lindau Syndrome, Familial Adenomatous Polyposis, Lynch Syndrome and Turcot Syndrome [2-4,6-9]. Data on pediatric mortality from CNS neoplasms in Brazil, especially regarding age group, sex, ethnicity, and distribution by

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federative units, remain limited and fragmented [10-13]. Most existing studies focus on local or regional analyses, making it challenging to achieve a comprehensive understanding of disparities and trends nationwide. Furthermore, there is a lack of comparative studies on statistical indicators, limiting the ability to identify epidemiological patterns and evaluate the effectiveness of public health policies in the region. Given this context, the present study aims to conduct a comprehensive and comparative analysis of CNS tumor mortality rates in children and adolescents in Brazil from 2013 to 2023, providing deeper insights into regional variations, identifying inequalities and trends, and contributing to the development of prevention and treatment strategies.

MATERIALS AND METHODS

This is an ecological study based on secondary data obtained from the Mortality Information System, available on the Department of Informatics of the Unified Health System website. Records of deaths caused by central nervous system tumors in children and adolescents were analyzed, considering the place of residence of the victims during the period from 2013 to 2023. The selected cases followed the codes of the International Classification of Diseases, Tenth Revision (ICD-10): C70 (malignant neoplasm of meninges), C71 (malignant neoplasm of the brain), C72 (malignant neoplasm of the spinal cord, cranial nerves, and other parts of the CNS), D32 (benign neoplasm of meninges), D33 (benign neoplasm of the brain and other parts of the CNS), D42 (neoplasm of uncertain or unknown behavior of meninges), and D43 (neoplasm of uncertain or unknown behavior of the brain and CNS). The age groups analyzed included less than 1 year, 1–4 years, 5–9 years, 10–14 years, and 15–19 years. Data collection was conducted in September 2024. Descriptive analysis of the variables was performed to identify trends in mortality rates. Statistical analysis was carried out using Microsoft Excel software to calculate mortality rates and prepare charts and tables. Population projections for the age groups 0–4 years, 5–9 years, 10–14 years, and 15–19 years were considered for each federative unit. Statistical tests included linear regression to calculate the Beta coefficient (β), used to evaluate the trend of changes in mortality rates over the studied period. The standard deviation (SD) was calculated to measure variability in mortality rates across states, while the correlation coefficient (r) was applied to assess the intensity and direction of mortality trends over time, whether increasing or decreasing. Confidence intervals (CI) were generated to provide an estimate of the precision of mortality values. The p-value was used to test the statistical significance of observed trends, adopting a significance level of 5% ($p<0.05$).

RESULTS

Between 2013 and 2023, 6,995 deaths caused by CNS tumors in children and adolescents were recorded in Brazil, accounting for approximately 27.3% of all neoplasm-related deaths in individuals under 19 years old during this period. Throughout these years, the mortality rate from CNS tumors in the pediatric population fluctuated, peaking at 11.5 per million inhabitants in 2013, while the lowest rate was observed in 2020 at 9.7 per million inhabitants. Of the total deaths caused by CNS tumors among children and adolescents, 54.12% occurred in males (n=3,786), and 45.86% in females (n=3,208), while 0.01% (n=1) did not have sex information recorded. The age group of 5–9 years showed the highest frequency of deaths in both sexes. Regarding race, the highest prevalence was among white individuals, representing 49.94% (n=3,493), followed by mixed-race individuals with 39.76% (n=2,781). Geographically, the Southeast region had the highest concentration of deaths, accounting for 38.48% of the total. In terms of tumor behavior, a similar pattern was observed between the sexes, with malignant neoplasms predominating and accounting for 95.65% of deaths during the analyzed period. Malignant neoplasms of the brain (C71) were the leading cause, responsible for 78.08% of fatal cases (Table 1).

Annual trend analysis indicated a general reduction in mortality rates across all regions, with negative correlation coefficients indicating declines (Table 2). The North region showed the highest negative correlation ($r=-0.554$), suggesting a more consistent reduction, while the South had the lowest correlation ($r=-0.203$), reflecting a more stable trend over time, though without statistically significant decline ($p = 0.124$). Additionally, the South recorded the highest average mortality rate (11.13 per million inhabitants) and the highest standard deviation (SD=1.32), indicating greater variability across the years. The Midwest region showed the highest Beta coefficient ($\beta=-0.214$), suggesting a faster decline rate, while the Northeast had the lowest index ($\beta=-0.072$). Overall, Brazil demonstrated a decreasing trend in pediatric CNS tumor mortality rates between 2013 and 2023, with statistical significance ($p<0.001$) (Figure 1).

Table 1 - Distribution of deaths caused by central nervous system tumors by sex, age group, race, ICD codes, and Brazilian region (2013–2023).

Sex	Female		Masculine		Ignored		Total	
	n	%	n	%	n	%	n	%
Age range (years)								
Under 1	184	2,63	166	2,37	-	-	350	5
1-4	737	10,54	875	12,51	-	-	1.612	23,05
5-9	971	13,88	1.029	14,71	-	-	2.000	28,59
10-14	727	10,39	844	12,07	1	0,01	1.572	22,47
15-19	589	8,42	872	12,47	-	-	1.461	20,89
Total	3.208	45,86	3.786	54,12	1	0,01	6.995	100
Race								
White	1.626	23,25	1.867	26,69	-	-	3.493	49,94
Black	139	1,99	190	2,72	-	-	329	4,70
Yellow	5	0,07	12	0,17	-	-	17	0,24
Mixed	1.255	17,94	1.525	21,80	1	0,01	2.781	39,76
Indigenous	13	0,19	24	0,34	-	-	37	0,53
Ignored	170	2,43	168	2,40	-	-	338	4,83
Total	3.208	45,86	3.786	54,12	1	0,01	6.995	100
ICD								
C70 - Malignant Neoplasm of Meninges	19	0,27	20	0,29	-	-	39	0,56
C71 - Malignant Neoplasm of Brain	2.476	35,40	2.985	42,67	1	0,01	5.462	78,08
C72 - Malignant Neoplasm of Spinal Cord, Cranial Nerves and Other Parts of CNS	578	8,26	612	8,75	-	-	1.190	17,01
D32 - Benign Neoplasm of Meninges	4	0,06	11	0,16	-	-	15	0,21
D33 - Benign Neoplasm of Brain and Other Parts of CNS	26	0,37	26	0,37	-	-	52	0,74
D42 - Neoplasm of Uncertain/Unknown Behavior of Meninges	1	0,01	3	0,04	-	-	4	0,06
D43 - Neoplasm of Uncertain/Unknown Behavior of the Brain and CNS	104	1,49	129	1,84	-	-	233	3,33
Total	3.208	45,86	3.786	54,12	1	0,01	6.995	100
Região								
North region	305	4,36	386	5,52	-	-	691	9,88
Northeast region	964	13,78	1.097	15,68	1	0,01	2.062	29,48
Southeast region	1.220	17,44	1.472	21,04	-	-	2.692	38,48
South region	462	6,60	515	7,36	-	-	977	13,97
Midwest region	257	3,67	316	4,52	-	-	573	8,19
Total	3.208	45,86	3.786	54,12	1	0,01	6.995	100

Table 2- Temporal trend of pediatric CNS tumor mortality rates by region in Brazil, adjusted per million inhabitants (2013–2023).

Year of death	Region					Brazil
	North	Northeast	Southeast	South	Midwest	
2013	10,5	10.3	11.7	13.1	14,3	11.5
2014	9.7	10.5	11.4	9.8	9.7	10.6
2015	9.7	10.8	9.6	11.9	11.6	10.4
2016	9.6	10.5	10.2	10.1	9.9	10.2
2017	9.8	10.9	10.2	12.2	11.4	10.7
2018	8.2	11.0	10.1	10.8	9.7	10.2
2019	9.2	11.5	9.8	12.4	10.6	10.6
2020	11.0	8.3	10.5	8.2	11.2	9.7
2021	9.3	11.2	10.0	11.0	10.8	10.5
2022	7.9	9.3	10.0	11.7	9.7	9.8
2023	8.3	10.2	10.4	11.0	9.7	10.1
Average	9.38	10.40	10.36	11.13	10.77	10.40
DP	0.92	0.87	0.62	1.32	1.30	0.48
r	-0.554	-0.264	-0.507	-0.203	-0.521	-0.688
β	-0.161	-0.072	-0.100	-0.085	-0.214	-0.105
IC 95%	-0.191 a -0.131	-0.105 a -0.040	-0.121 a -0.079	-0.136 a -0.034	-0.257 a -0.171	-0.119 a -0.091
p	0.002*	0.013*	0.002*	0.124	0.016*	<0,001*

Standard deviation (SD), correlation coefficient (r), Beta coefficient (β), 95% confidence interval (95% CI).
*p < 0.05, considered statistically significant.

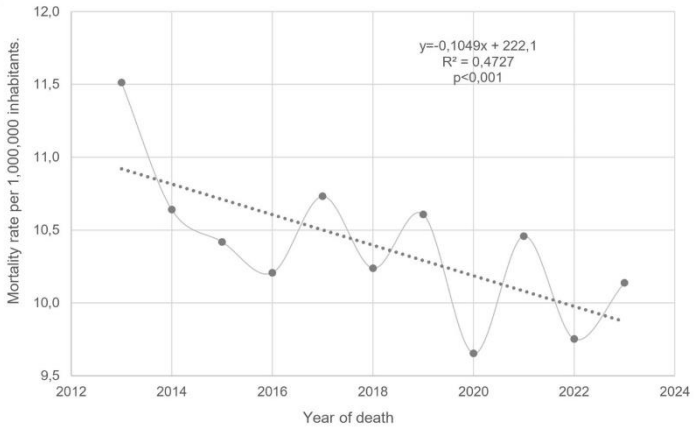


Figure 1- Temporal trend of pediatric CNS tumor mortality in Brazil from 2013 to 2023.

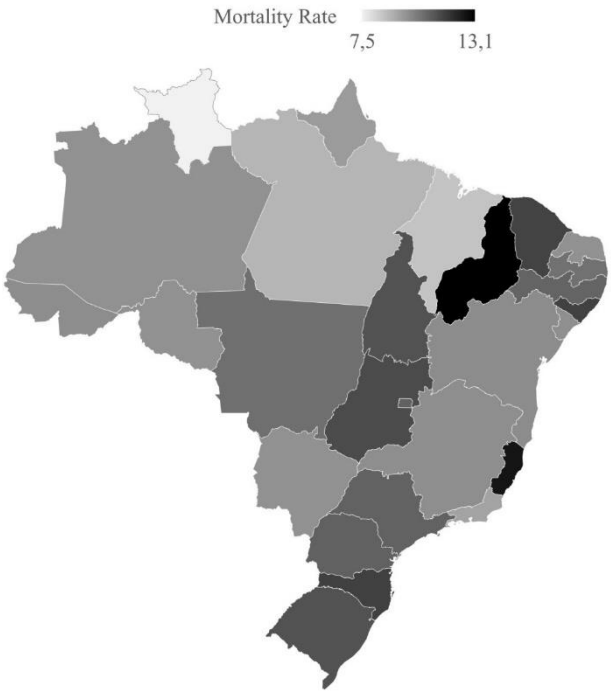


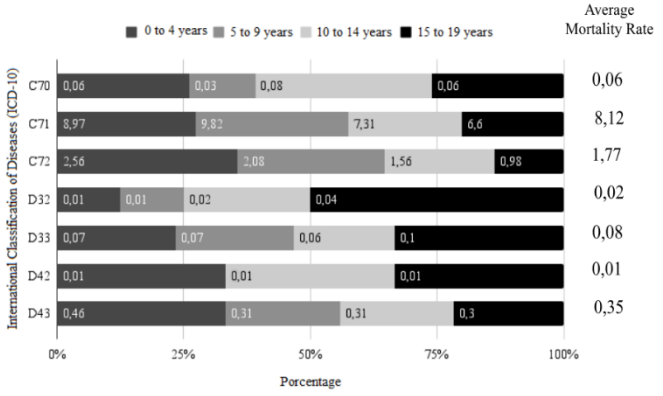
Figure 2- Distribution of pediatric CNS tumor mortality rates per million inhabitants in Brazil (2013–2023).

Region	Age range				
	0 to 4 years	5 to 9 years	10 to 14 years	15 to 19 years	Total
North	11,36	10,94	7,14	8,28	9,38
Northeast	12,25	12,55	9,29	8,03	10,40
Southeast	11,99	12,19	9,73	7,83	10,36
South	12,94	13,38	9,80	8,73	11,13
Midwest	12,32	12,49	10,06	8,37	10,77
Total	12,15	12,33	9,35	8,10	10,40

Table 3- Pediatric CNS tumor mortality rates by age group and Brazilian region, adjusted per million inhabitants (2013–2023).

Despite the observed reduction, the highest mortality rate during the analyzed period was registered in the State of Piauí, with 13.1 deaths per million inhabitants, followed by then State of Espírito Santo, with 12.6 deaths per million inhabitants (Figure 2). The application of Moran's Index to verify spatial autocorrelation revealed that the distribution of deaths caused by CNS tumors was relatively dispersed among the states, with a Moran's Index value of I=0.0699, confirming the absence of a significant spatial pattern (p=0.861). Furthermore, mortality rates for malignant tumors of the brain and CNS varied by age group, being highest among younger children, with rates of 12.15 per million inhabitants for the 0–4 age group and 12.33 per million inhabitants for the 5–9 age group. From the age of 10, mortality rates showed a declining trend, reaching the lowest value in the 15–19 age group, with 8.10 per million inhabitants (Table 3).

Mortality rates for malignant neoplasms of the brain (ICD-10 code C71) were the primary cause of death across all age groups, with the highest rates concentrated in the 5–9 age group (9.82 per million inhabitants) and the 0–4 age group (8.97 per million inhabitants). Mortality rates for malignant neoplasms of the spinal cord and other parts of the CNS (ICD-10 code C72) progressively decreased with age, dropping to 0.98 per million among adolescents aged 15–19 years. Conversely, benign neoplasms (ICD-10 codes D32 and D33) and neoplasms of uncertain behavior (ICD-10 code D43) showed much lower mortality rates, below 0.1 per million inhabitants (Figure 3).



C70: Malignant Neoplasm of the Meninges; C71: Malignant Neoplasm of the Brain; C72: Malignant Neoplasm of the Spinal Cord, Cranial Nerves, and Other Parts of the CNS; D32: Benign Neoplasm of the Meninges; D33: Benign Neoplasm of the Brain and Other Parts of the CNS; D42: Neoplasm of Uncertain/Unknown Behavior of the Meninges; D43: Neoplasm of Uncertain/Unknown Behavior of the Brain and CNS; CNS: Central Nervous System.

Figure 3- Pediatric CNS tumor mortality rates by age group and ICD classification, adjusted per million inhabitants (2013–2023).

DISCUSSION

The sociodemographic characteristics of deaths due to CNS neoplasms in the pediatric population, from 2013 to 2023, reveal that these tumors accounted for 27.3% of all deaths from neoplasms. This percentage is consistent with international studies, such as those conducted in Austria [14] and the United States [15, 16]. In this study, it was observed that the majority of deaths occurred in males, predominantly in the white race (49.94%), with the 5–9 age group being the most affected. This corroborates findings from studies conducted in the United States [15, 16] and Colombia [17], as well as in different regions of Brazil [10-13]. One possible explanation for the prevalence in this age group is that signs and symptoms, such as strabismus, headache, and imbalance [3], are more easily recognized and verbalized by children themselves or observed by educators in schools, while in younger age groups, these findings are less noticeable. However, there are discrepancies compared to studies conducted in other countries, such as China [18], Costa Rica [19], and Canada [20], which reported a higher prevalence of cases in children under 5 years of age. These findings may be attributed to demographic dynamics, such as birth rates, maternal and child health policies, and access to pediatric services, which can impact early disease detection, resulting in a higher prevalence of cases in children under 5 years. The data show a trend of decreasing mortality with increasing age, highlighting that younger age groups, especially those under 9 years, are more vulnerable to death from CNS neoplasms, particularly malignant brain tumors [11]. In general, a significant reduction in mortality rates was observed across the country ($p<0.001$), although with variations in the pace and consistency among different regions. This heterogeneity is reinforced by Moran's Index, which indicates the absence of a consistent concentration of deaths in specific areas of the country, suggesting a dispersed spatial distribution. The North region presented the greatest negative correlation ($r=-0.554$), indicating a more pronounced reduction in mortality rates over the years. This trend can be attributed to advances in public health policies, such as the expansion of the “Mais Médicos” program, which brought healthcare professionals to remote areas, and the implementation and strengthening of High Complexity Oncology Centers (CACON) and High Complexity Oncology Assistance Units (UNACON), promoting greater access to diagnosis and specialized treatment. Despite these advancements, absolute mortality values in the region remain significant, with states such as Tocantins (11.2 per million inhabitants) and Amapá (9.5 per million inhabitants) presenting some of the highest mortality rates. On the other hand, the South region showed the lowest negative correlation ($r=-0.203$) and a slight downward trend that was not statistically significant ($p=0.124$), despite having the highest average mortality rate of 11.13 per million inhabitants. This stability suggests that, although the South has the best health indicators in the country, mortality from CNS tumors has not shown a consistent reduction. The high average mortality rate in the region and the highest standard deviation (SD=1.32) indicate considerable variability across states, with Santa Catarina (11.6 per million inhabitants), Rio Grande do Sul (11.2 per million inhabitants), and Paraná (10.8 per million inhabitants) showing high values. This scenario may reflect differences in access to and quality of diagnosis and specialized treatment, as well as environmental factors, such as the intensive use of pesticides associated with the region’s agriculture, which could contribute to the high prevalence of CNS tumors in these three states. Meanwhile, the Southeast region, which houses most of the pediatric oncology reference centers and accounted for the highest concentration of deaths during the studied period due to its large resident population, showed an overall decreasing trend in CNS tumor mortality. However, the negative correlation was intermediate. The variability in mortality rates was significant, with Espírito Santo (12.6 per million inhabitants) presenting one of the highest rates, while Rio de Janeiro had the lowest (9.3 per million inhabitants). São Paulo (10.8 per million inhabitants), despite having the leading treatment centers, still reported a considerable mortality rate. This pattern of deaths may reflect intraregional disparities in access to and quality of healthcare, emphasizing the need for targeted actions to reduce these discrepancies between states.

Furthermore, the South and Southeast regions, by concentrating most of the reference centers for pediatric oncology and having better infrastructure, greater availability of neuropediatricians, neuro-oncologists, and access to advanced diagnostic tools such as magnetic resonance imaging and molecular diagnostics, ultimately attract patients from other regions of the country for clinical follow-up, also contributing to the high mortality rates recorded in these regions. The Central-West region stood out with the highest Beta coefficient ($\beta=-0.214$), indicating a

faster decline in mortality rates. Factors such as improved access to specialized treatment centers, particularly in the Federal District (10.8 per million inhabitants), may have influenced this trend. However, the mortality rate still remains concerning in states like Goiás (11.3 per million inhabitants). In the Northeast, the negative correlation was less pronounced (β=-0.072), indicating a slower reduction. Despite the most populous states, Bahia and Pernambuco, recording the highest absolute number of deaths in the region [13], Piauí (13.1 per million inhabitants) and Ceará (11.5 per million inhabitants) presented some of the highest mortality rates in the country. In contrast, Maranhão (8.6) showed the second-lowest rate in Brazil, highlighting regional heterogeneity within the Northeast region [12, 13]. Malignant neoplasms accounted for 95.65% of deaths during the analyzed period, a percentage similar to that observed in another Brazilian ecological study [11], which reported 94.7% from 1979 to 2019. This data aligns with findings from several countries, such as the United States [15], which also recorded high mortality rates from malignant neoplasms. In contrast, countries like Austria [14] (72%) and Canada [20] (86%) had slightly lower but still significant proportions. Malignant brain neoplasms (C71) were the leading cause of CNS tumor-related mortality across all age groups. Similar results were observed in a descriptive study from the Northeast region [13], with greater vulnerability in younger age groups, from 0 to 9 years old. This pattern can be explained by the high aggressiveness of these tumors and, possibly, by late diagnosis and difficulties in accessing specialized treatments. On the other hand, neoplasms of the spinal cord and other parts of the CNS (C72) showed a gradual reduction in mortality rates with increasing age. This decline may be explained by better prognoses and greater treatment efficacy in older individuals, whose nervous systems are more developed, allowing for a better response to therapies. In contrast, benign neoplasms (D32 and D33) and neoplasms of uncertain behavior (D43) presented considerably lower mortality rates, reflecting their less aggressive nature and the greater availability of effective treatments. In this context, gliomas are the most common primary CNS tumors in children, encompassing both malignant and benign forms, and they represent 52.9% of cases in the 0 to 14-year age group, as reported by Ostrom et al. [9]. Originating from glial cells, the most frequent types in pediatrics are pilocytic astrocytoma, diffuse midline glioma, and ependymomas [9, 21]. Embryonal tumors follow, with medulloblastoma being the most prevalent, accounting for approximately 60% of embryonal cases and around 20% of malignant CNS tumors in children [9,21-24]. The results of this study highlight the complexity of pediatric CNS tumor mortality in Brazil, emphasizing significant regional variations. The unequal pace of mortality rate reduction across states reflects not only disparities in access to specialized services and advanced treatment technologies but also differences in healthcare infrastructure and health education for parents, caregivers, and educators. These inequalities underscore the urgent need for more effective public policies that not only seek to minimize regional disparities but also ensure consistent and equitable reductions in pediatric CNS tumor mortality nationwide. To this end, it is crucial to prioritize strengthening the primary healthcare network, continuous training of healthcare professionals, and the implementation of awareness and health education programs involving all sectors of society, particularly schools.

CONCLUSION

This study clearly demonstrates that central nervous system tumors remain the leading cause of cancer-related death in childhood, particularly in the early years of life. The analysis of pediatric CNS tumor mortality in Brazil from 2013 to 2023 reveals a decreasing trend (r=-0.688; p<0.001), with significant regional differences that deserve attention. The Southeast region, despite having a more robust healthcare infrastructure, accounted for the highest concentration of deaths in the country (38.38%). On the other hand, the most consistent reduction was observed in the North (r=-0.554), while the Midwest region showed the sharpest decline (r=-0.521; β=-0.214), offering more optimistic prospects for these regions. However, the South, with high variability among states (SD=1.32) and the highest mortality rate (11.13 per million inhabitants), and the Northeast, which shows a slower reduction (r=-0.264; β=-0.072), still highlight existing regional disparities. These data reflect inequalities in public health policies, such as access to basic healthcare networks and specialized centers that promote efficient diagnosis and treatment, as well as in health education, which enables early diagnosis by educators, parents, and caregivers based on children's signs and symptoms. Such disparities emphasize the urgent need for improvements in these areas, especially in early diagnosis and expanding access to quality treatment, so that the reduction of CNS tumor mortality becomes more consistent across the entire country.

DISCLOSURES

Ethical approval

Since this study used aggregated, publicly available, non-identifiable data, it was exempt from ethical review by a Research Ethics Committee (REC).

Consent to participate

Not applicable, as this is an epidemiological study based entirely on secondary data sources.

Conflict of interest

The authors declare no conflicts of interest with respect to the content, authorship, and/or publication of this article.

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Artificial intelligence

During the preparation of this work, the authors used ChatGPT to enhance the cohesion and formality of the scientific writing. After using the tool, the content was reviewed and edited by the authors, who take full responsibility for the final text.

CONTRIBUTIONS

-**Thamara Vieira Bitencourt**: Conceptualization, Data curation, Formal Analysis, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing
-**Guilherme Xavier Wensing**: Formal Analysis, Software, Visualization, Writing – review & editing
-**Jucélia Jeremias Fortunato**: Data curation, Formal Analysis, Methodology, Supervision, Validation, Visualization, Writing – original draft

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