

Temporal Trend of Hospitalizations for Cancer Diagnosis in Children and Adolescents

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Tendência Temporal de Internações por Diagnóstico Oncológico em Crianças e Adolescentes

Tendencia Temporal de las Hospitalizaciones por Diagnóstico de Cáncer en Niños y Adolescentes

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ABSTRACT

Introduction: Pediatric cancer is considered a rare pathology, but it requires long periods of treatment in an oncology specialty center. One of the main challenges for the families is the distancing from treatment and hospital support facilities for hospitalizations in pediatric oncology. **Objective:** To analyze the time trend per places of residence and hospitalization of children and adolescents for cancer diagnoses occurred between 1998 and 2018 in the state of Rio Grande do Sul, Brazil. **Method:** Analytical documental epidemiological study, with collection of secondary data in a public domain database. The study is characterized as a historical series and spatial-geographical distribution of hospital admissions of children undergoing cancer treatment in Rio Grande do Sul. **Results:** Children under 4 years were the main demand for hospitalization for child and juvenile cancer diagnosis over the years. In about 80% of the health regions, patients end up admitted for cancer diagnosis out of their health regions and places of residence. In the last 20 years, there has been an increase in the prevalence of hospitalizations, which are still much concentrated in specialty centers. **Conclusion:** It is necessary the intervention of public policies and decentralization of specialized services for the treatment and hospitalization in pediatric oncology.

Key words: Neoplasms/epidemiology; Hospitalization/trends; Time Factors; Child; Adolescent.

RESUMO

Introdução: O câncer pediátrico é considerado uma patologia rara, porém requer longos períodos de tratamento em centros de especialidade oncológica. Um dos principais desafios das famílias é o distanciamento dos locais de tratamento e de suporte hospitalar para internações em oncologia pediátrica. **Objetivo:** Analisar a tendência temporal por locais de residência e internação de crianças e adolescentes por diagnósticos oncológicos, entre os anos de 1998 e 2018, no Estado do Rio Grande do Sul, Brasil. **Método:** Trata-se de um estudo epidemiológico documental analítico, com coleta de dados secundários em base de dados de domínio público. O estudo possui caráter de série histórica e de distribuição espaço-geográfica, das internações hospitalares de crianças em tratamento oncológico no Rio Grande do Sul. **Resultados:** Menores de 4 anos representaram a principal demanda de internação por diagnóstico oncológico infantojuvenil ao longo dos anos. Em cerca de 80% das regiões em saúde, os pacientes acabam internando, por diagnóstico oncológico, fora das suas regiões de saúde e locais de residência. Nos últimos 20 anos, houve aumento da prevalência nas internações, ainda muito localizadas em centros de especialidade. **Conclusão:** Há necessidade de intervenção de políticas públicas e descentralização de serviços especializados no tratamento e internação em oncologia pediátrica. **Palavras-chave:** Neoplasias/epidemiologia; Hospitalização/tendências; Fatores de Tempo; Criança; Adolescente.

RESUMEN

Introducción: El cáncer pediátrico se considera una patología rara, pero requiere largos períodos de tratamiento en un centro especializado en oncología. Uno de los principales desafíos para las familias es el distanciamiento de los sitios de tratamiento y apoyo hospitalario para hospitalizaciones en oncología pediátrica. **Objetivo:** Analizar la tendencia temporal por lugares de residencia y hospitalización de niños y adolescentes para diagnósticos de cáncer, entre los años 1998 y 2018, en el Estado de Rio Grande do Sul, Brasil. **Objetivo:** Analizar la tendencia temporal por lugares de residencia y hospitalización de niños y adolescentes para diagnósticos de cáncer, entre los años 1998 y 2018, en el Estado de Rio Grande do Sul, Brasil. **Método:** Estudio epidemiológico documental analítico, con recopilación de datos secundarios en una base de datos de dominio público. El estudio tiene el carácter de una serie histórica y de distribución espacial-geográfica, de ingresos hospitalarios de niños sometidos a tratamiento contra el cáncer en Rio Grande do Sul. **Resultados:** Los niños menores de 4 años representan la principal demanda de hospitalización por diagnóstico de cáncer para niños y adolescentes a lo largo de los años. En aproximadamente el 80% de las regiones de salud, los pacientes terminan internando, debido al diagnóstico de cáncer, en sus regiones de salud y lugares de residencia. En los últimos 20 años, ha habido un aumento en la prevalencia de hospitalizaciones, que todavía están muy ubicadas en centros especializados, en cinco de las siete macro regiones analizadas. **Conclusión:** Existe la necesidad de intervención de políticas públicas y descentralización de servicios especializados en el tratamiento y hospitalización en oncología pediátrica.

Palabras clave: Neoplasias/epidemiología; Hospitalización/tendências; Factores de Tiempo; Niño; Adolescente.

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INTRODUCTION

Currently, cancer is a chronic disease, a complex public health issue and is the second cause of death in Brazil. Its physiopathology is provoked by the uncontrolled multiplication of cells, most of them young cells that give origin to tumors that replace the normal cells of one or more organs and harm their vital functions¹.

The epidemiological data of neoplasms in Brazil reflect in its high rate of mortality since 21% of the deaths by non-communicable chronic diseases were related to malignant neoplasms. The distribution of the incidence per Brazilian geographic region strengthens the local disparity because the Southeast and South regions concentrate 70% of the occurrence of new cases¹.

Within a pediatric perspective according to the National Cancer Institute José Alencar Gomes da Silva (INCA)², childhood cancer corresponds to a group of several diseases having in common the uncontrolled spread of abnormal cells reaching any part of the organism in children and adolescents until 19 years. Childhood cancer is considered a rare pathology, relatively, for reaching one in every ten thousand children from 0 to 14 years old. However, according to INCA, in Brazil, cancer represents the first cause of deaths in children and adolescents. It is estimated that in 2020, 8,460 new cases of malignant neoplasms are diagnosed in the children and youth population².

International and national studies emphasize that most common neoplasms in childhood are leukemias, tumors of the central nervous system and lymphomas¹. Contrary to cancer in adults, children and youth cancer usually affects blood system cells and supporting tissues².

In Brazil, between 2018-2019, 420 thousand new cases of cancer occurred. According to the Population-Based Cancer Registries (PBCR)³, the mean percentage of tumors for this age range is 3%. It is estimated that 12,500 cases of cancer occurred in children and adolescents until 19 years old. At this level in this period 1,300 new cases were anticipated in the South Region in Brazil. For developing countries, the proportion of childhood cancer represents from 3% to 10% of the total of neoplasms and in developed countries, 1%³.

Initially, one of the main obstacles of the pathway of the treatment is delayed early diagnosis⁴. Different from adult cancer, the risk factors related to the lifestyle do not influence the odds of children and adolescents to develop cancer. Occasionally, children can present genetic alterations that make them prone to have some sort of cancer⁵.

Even after the oncologic diagnosis in childhood, the child and its family cross several scenarios of care

and consultation with professionals who will define the therapeutic pathway with the determination of the protocol adopted. The protocols aim the uniformization of diagnostic methods and cancer treatment in childhood and adolescence and provide forms of evaluation during survival, of toxicity and adherence to the treatment. Most of them demand in-person frequent attendance in specialized facilities, large health centers or macro-regions, which compels the parents to ask for leave of absence from their jobs constantly and change social routines to accompany the child which causes social and economic impact to the family⁶.

Due to the distance from treatment facilities and oncology pediatrics hospital support for admission during the treatment or as a result of it, parents and main caretakers face financial difficulties to pay for their trip and lodging in the large specialized medical care centers when needed. This condition reiterates the necessity of access to health services considering the demand associated to the disease and the protocol adopted⁶.

In this perspective, it is clear to acknowledge the temporal trend of admissions resulting from oncologic diagnosis in children and adolescents and places with more prevalence of hospitals and origin of these patients in oncologic treatment. The description of this geographical organization allows to establish priorities for the care centers and decentralize them to minimize the distance, costs, and social impact of the oncologic treatment. For that purpose, the present study has the objective of analyzing the temporal trend and places of origin and admission of children and adolescents by oncologic diagnosis between 1998 and 2018 in the state of Rio Grande do Sul, Brazil.

METHOD

Analytical, documental, epidemiologic study with secondary data collection in public domain databases with characteristics of historical series and spatial-geographical distribution of hospital admissions of children in oncologic treatment in Rio Grande do Sul. The study population consisted of children and adolescents in the age range from 0 to 19 years old and determined by the databases itself. The Computer Information System of the Brazilian Health Service (DATASUS) utilizes the age range from 0 to 19 years old which covers the periods of childhood and adolescence for the classification.

The data were collected in the online database DATASUS, available from: <http://tabnet.datasus.gov.br/cgi/defthtm.exe?sih/cnv/mrrs.def>, at the webpage TabNet. The search followed the steps: TABNET → Epidemiologic and morbidities → SUS hospital morbidity

→ General per place of admission (1998-2018) and General per place of residence (1998-2018).

The filters utilized were: place of residence (Brazil and Rio Grande do Sul); chapter ICD 10: II neoplasms (tumors); and age range (0-19 years). Raw data were collected manually and transcribed to Excel spreadsheet (version 2010). Population calculations for analysis of prevalence were collected at the site of the Brazilian Institute of Geography and Statistic (IBGE). Census 2000 and 2010 were the base for the calculation of the prevalence.

The formula $p = \text{number of individuals affected in a certain moment} / \text{total of individuals}$ was used for the calculation of the prevalence.

Simple statistical analysis (calculation of the prevalence and simple descriptive analysis) and analytical statistical analysis through the correlation of the prevalence during the years (Pearson correlation – non-parametric data – utilizing $p < 5\%$ for statistical association in the correlation) were used for the data. The comparison between the spatial distribution of the difference between the place of admission and residence was performed after the calculation of the prevalence (of treatment and origin, prevalence index for each one thousand inhabitants of the age range). The population data were determined for 2018 according to estimates for Rio Grande do Sul (IBGE). The places of residence and admission were classified according to the health micro-regions and macro-regions of the State of Rio Grande do Sul distributed and classified as shown in Chart 1.

The norms for human and social clinical trials disposed in Resolution 510 dated April 7, 2016⁷ were complied with. For being a search in public domain databases, the present study waived review. The commitment of the investigators with the trustworthiness of the data and how they reflect in the results presented is worth mentioning.

RESULTS

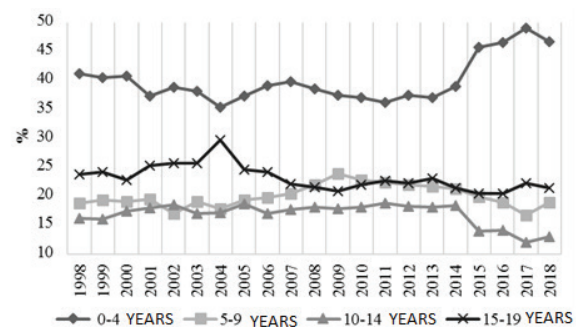
The data are presented as distribution of temporal trend and defining characteristics according to place of hospitalization and residence and distribution per age range. In Graph 1, the temporal trend of the hospitalizations per oncologic diagnostic of children and adolescents in the State of Rio Grande do Sul stratified per age range is shown.

Younger than 4 years old were the most prevalent in hospitalizations along the 20 years analyzed. In the last five years, there is an increase for the younger than 4 years old age range. In the age range from 10 to 14 years the prevalence dropped, especially in the last three years

Chart 1. Description of the health micro-regions of the State of Rio Grande do Sul

Macro-region	Number	Micro-region
Centro-Oeste	01	Verdes Campos
	02	Entre Rios
	03	Fronteira Oeste
Metropolitana	04	Belas praias
	05	Bons Ventos
	06	Paranhanna
	07	Vale dos Sinos
	08	Vale do Caí
	09	Carbonífera
	10	Porto Alegre/ Metropolitana
Missioneira	11	Sete Povos das Missões
	12	Portal das Missões
	13	Região da Diversidade
	14	Fronteira Noroeste
Norte	15	Caminho das Águas
	16	Alto Uruguai Gaúcho
	17	Região do Planalto
	18	Região das Araucárias
	19	Região do Botucaraí
	20	Rota da Produção
Sul	21	Região Sul
	22	Pampa
Serra	23	Caxias
	24	Campos de Cima da Serra
	25	Vinhedos
	26	Uvas e Vales
Vales	27	Jacuí/Centro
	28	Santa Cruz do Sul
	29	Vale das Montanhas
	30	Vale da Luz

Source: Council of Municipal Health Secretaries of Rio Grande do Sul⁸.



Graph 1. Distribution of relative frequency per age range of hospital data of children and adolescents per oncologic diagnosis in the State of Rio Grande do Sul, 1998-2018

analyzed, the other age ranges remained steady with weak and non-significant correlation (CC<0.3).

Regarding gender, males are more prevalent in the admissions, representing 52.9% of the total; 47.1% of the admissions were of females from 1998 to 2018. Table 1 shows the distribution per macro-region and place of residence.

In the macro-regions *Norte* and *Missioneira*, the proportions dropped nearly 4% during the last 20 years; for such, there was expressive growth for the regions *Metropolitana* and *Sul*, considering that in the *Sul* region, the number of cases nearly doubled. While analyzing the distribution of frequency of admission per health macro-region in the last 20 years, there was growth of the number of admissions per place of residence in the macro-regions 01 (CC 0.982), 02 (CC 0.826), 05 (CC 0.759), 06 (CC 0.826) and 07 (CC 0.973), but with non-significant difference (p<0.05). For the macro-regions 03 and 04, prevalence decreased with strong correlation coefficients and non-significant data (p<0.05).

In Table 2, it stands out the difference between the prevalence of the places of admissions and residence of children and adolescents in oncologic treatment distributed per place of admission and place of residence stratified per age-range.

It is clear that as poor the relation between the place of admission and place of residence, greater is the necessity of children of the micro-region to travel from their municipality to be admitted. Micro-regions 16, 18 and 20 present the lowest relation between the number of hospitalized and the demand. The micro-region 16 has the highest prevalence and many patients need to travel. However, the micro-regions with higher prevalence per place of admission, 01, 10 and 17, are considered regional and reference health centers.

Of the 30 micro-regions, 10% meet their demand and other referrals. Two micro-regions meet their demand (PA-PR=0) and 83% of the municipalities present more prevalence of children in oncologic treatment who are hospitalized according to its own local admission demand. Table 3 presents the distribution per age-range.

Younger than 4 years old are the main demand of admissions per oncologic diagnosis in Rio Grande do Sul in 2018, more than the double of the state mean. The age-range from 10 to 14 years is the less prevalent in admissions.

DISCUSSION

The magnitude of the global burden of cancer in childhood and adolescents remains poorly quantified. There are no global estimates of incidence, survival, and mortality for children with cancer in most low income countries⁹. INCA highlights that childhood cancer has nearly 12 thousand new diagnoses each year with peak of incidence in the age range from 4 to 5 years and a second peak between 16 and 18 years in Brazil. This data of the peak of the diagnosis differs from the percent of hospitalizations presented in the study because the higher prevalence of hospitalizations occurs in the age range from 0 to 4 years¹. The study of Silva et al¹⁰ corroborates these findings due to highest development of cancer and need of hospitalizations in the earlier age ranges¹⁰.

Children and juvenile cancer represented 3% of all the neoplasms treated at the oncology reference hospitals over the total hospitalizations in Brazil by oncologic treatment in SUS. The most frequent diagnosis were leukemias (30.6%), lymphomas (16.6%) and central nervous system (9.3%). These hospitalizations generally occur in specialized centers approved for pediatric oncology¹¹.

Table 1. Distribution of the number of hospitalizations per oncologic diagnostic in children and adolescents of the health macro-regions of the State of Rio Grande do Sul, 1998-2018

Year		MR01	MR02	MR03	MR04	MR05	MR 06	MR07	Total
2018	n	417	1.337	3.614	3.309	1.735	268	308	10,988
	%	3.8	12.2	32.9	30.1	15.8	2.4	2.8	100
2008	n	416	1.746	4.401	4.276	2.322	341	317	13,819
	%	3.0	12.6	31.8	30.9	16.8	2.5	2.3	100
1998	n	232	1.294	6.202	6.540	1.951	221	183	16,623
	%	1.4	7.8	37.3	39.3	11.7	1.3	1.1	100
1998-2018	CC	0.982	0.826	-0.756	-0.903	0.759	0.826	0.973	
	p*	0.121	0.381	0.454	0.283	0.452	0.381	0.149	

Captions: CC: Correlation Coefficient; MR01: Centro-Oeste; MR02: Metropolitana; MR03: Missioneira; MR04: Norte; MRO5: Sul; MRO6: Serra; MR07: Vales, *p-value.

Table 2. Difference between prevalence per place of admission and residence of children and adolescents in oncologic treatment in the health micro-regions of the State of Rio Grande do Sul, in 2018

Micro-region	Place of residence (PR)	Place of Admission (PA)	PR-PA
	Prevalence/thousand inhabitants		
01	0.4	3.6	3.2
02	0.9	0	-0.9
03	0.4	0.1	-0.3
04	1.1	0.1	-1
05	0.4	0.1	-0.3
06	0.3	0.1	-0.2
07	0.9	0.1	-0.8
08	1	0.2	-0.8
09	0.8	0.1	-0.7
10	1.1	2.9	1.8
11	1.2	0.2	-1
12	1.1	0.3	-0.8
13	1.3	0.3	-1
14	49.8	48.6	-1.2
15	1	0.2	-0.8
16	42.7	38.3	-4.4
17	1.3	4.8	3.5
18	1.4	0.1	-1.3
19	1.2	0.1	-1.1
20	1.4	0.1	-1.3
21	0.9	0.2	-0.7
22	0.6	0	-0.6
23	0.9	0.9	0
24	0.9	0.2	-0.7
25	0.8	0.2	-0.6
26	0.4	0	-0.4
27	1	0	-1
28	0.8	0.2	-0.6
29	1.2	1.2	0
30	1.3	0.1	-1.2

The number of hospitalizations can portray and present, in addition to the hospital profile, the characteristics of children and adolescents who sicken in the State. Because of this, the figures of this study highlight that the prevalence of admissions by childhood cancer in the State of Rio Grande do Sul is higher for males, data similar to the results encountered in China, USA, Canada and Brazil¹².

The incidence of many childhood cancers reported since the decade of 1970 is actual and particularly remarkable for more prevalence of leukemia, type of cancer of great complexity and with treatment demanding focus and investment from SUS¹³, especially in regard to time of hospitalization. Although acute lymphoid leukemia can occur at any age, its incidence is higher among children from 2 to 5 years, nearly 70% reducing among adolescents and young adults for whom acute leukemias incidence is 20%⁹. This data can justify higher prevalence of admissions in younger than 4 years old.

Studies highlight that the rate of hospitalizations were higher in children from 0 to 4 years and adolescents from 15 to 19 years, but it is still premature to affirm or describe the highest local prevalence rate. It is assumed that for the age range lower than 4 years, clinical vulnerability and higher leukemia rates are the possible justifications for high prevalence¹⁴. The variation of the total incidence of childhood cancer worldwide is quite unknown, although probably is related to exposure to risk factors as contact with chemicals and carcinogenics (air pollution, passive smoking, drinking water or food), genetic variations and place of residence¹⁵.

In addition, the geographic variation of the findings indicates that the higher rates are in the micro-region *Fronteira Noroeste* (14) and this can be affected by age, economic status or rural/urban classification. According to data of Rio Grande do Sul State, this micro-region has high proportion of farming and industry activities and this can ensue potential genetic-risk environment interactions as air pollution and use of pesticides¹⁶.

The mean volume of pesticides is worrying in the micro-region 14 reaching 755,57-874,75 L/km²/year in comparison with the micro-regions with the lower rates of childhood cancer diagnosis *Vale do Paranhana* (06) and *Uva/Vale* (26), with 187,83-214,58 L/km²/year. The association between exposure to pesticides and development of cancer is still controversial, mainly because the individuals are submitted to several substances, in addition to genetic factors, but these hypotheses should not be rebutted, they should be better studied instead¹⁷.

The indicators of mapping of use of the SUS-funded services of pediatric cancer care – hospitalization, chemotherapy, and radiotherapy – showed inequalities of access, however, it must not be misled with disproportion of SUS-funded services. In more than 80% of the micro-regions, children and adolescents leave their health regions seeking for hospitalization because of cancer. This data is confirmed as much as many regions have more prevalence of ill who need hospitalization, which consequently entails the necessity of seeking other health services and facilities¹⁸.

Table 3. Prevalence per place of residence of children and adolescents in oncologic treatment in the health micro-regions of the State of Rio Grande do Sul stratified per age-range in 2018

Age-range (years)/ micro-region	00-04	05-09	10-14	15-19	Total
	Prevalence/thousand inhabitants				
01	1.5	2.5	1.8	0.5	0.4
02	0.1	1.3	1	1.2	0.9
03	1.8	1.1	1.2	1.5	0.4
06	1	1.6	1.1	0.6	0.3
07	1.1	1.1	0.4	0.9	0.9
08	1.9	0.7	0.7	0.6	1.0
09	0.7	1	1	0.6	0.8
10	1.6	1.1	0.9	0.7	1.1
04	1.3	0.6	0.2	2.2	1.1
05	0.3	0.1	0.2	1	0.4
12	0.1	0.4	2.5	1.3	1.1
11	1.7	0.7	1.4	1	1.2
14	130.3	32.6	17.3	36.8	49.8
13	0.1	1	0.6	3.1	1.3
17	0.7	1.2	1	2.2	1.3
18	2.1	0.1	1.3	1.9	1.4
19	0.4	1.1	1.9	1.3	1.2
20	3	2.2	0.4	0.7	1.4
15	1.5	0.9	0.4	1.3	1
16	100.3	23	19	39.6	42.7
21	1.3	0.9	0.6	1	0.9
22	1.3	0.1	0.8	0.2	0.6
23	2	0.8	0.6	0.4	0.9
24	2	0.3	0.3	1.2	0.9
25	0.3	1.4	0.8	0.7	0.8
26	0.2	0.2	0.8	0.4	0.4
27	0.9	2.1	0.7	0.4	1
28	1	0.4	0.8	1	0.8
29	1.6	0.6	1.2	1.6	1.2
30	1.5	1.1	1	1.7	1.3
Σ	8.8	2.7	2.1	3.6	4.0

Sickening by cancer and oncologic treatment routines are complex and cause suffering to the entire family. The repercussion can intensify when children and adolescents are involved because of the perception of the situation and consequently the increasing necessity of finding health specialized facilities². Clinical repercussions, invasive exams, hospital admissions far from their cities, weakness, swelling, and alopecia bring social and emotional distress to the child, adolescent and their families. Reorganizing

the routine according to the therapy, hospital demands and geographical distancing is required¹⁹.

Inconsistencies and/or sub-notifications of the health systems exist, since the study analyzed secondary data registered at the virtual platform and in SUS admission system, leaving out the admission in non-public hospitals. There may be differences among prevalence because the study calculated the prevalence through data of populational estimates of the Census 2000 and 2010.

CONCLUSION

The admissions due to oncologic diagnosis of Rio Grande do Sul are the most prevalent in males in the age-range from 0 to 4 years. Prevalence increased along the years in five of the seven macro-regions analyzed. The health micro-regions with high rates of admission due to pediatric oncologic diagnosis are *Fronteira Noroeste* (14) and *Alto Uruguai Gaúcho* (16). In addition, more than 80% of the admissions happen out of the health macro-regions, which is still related to the necessity of travels of children and adolescents and their families during the oncologic treatment.

This study contributed to show the increase of the rates of admission of younger than 4 years old, most vulnerable and present population in the health services and the necessity of displacement and nomadism of the patients to be hospitalized due to oncologic diagnosis along the last 20 years analyzed. It is noticed that intervention of public policies and decentralization of specialized services are needed in the treatment and admission in pediatric oncology. The figures are raising and indicate the necessity of displacement, economic expenditures, and changes of life routine for those who live far from the specialized health facilities.

CONTRIBUTIONS

Luisa Pradié Algayer and Larissa Luma Tomasi Febras contributed substantially for the conception and design of the study, collection, analysis and interpretation of data and wording. Bruna Segabinazzi Scheid and Jordana Ferreira Signori contributed for the collection, analysis and interpretation of the data and wording of the article. Leonardo Bigolin Jantsch contributed substantially for the conception and design of the study, analysis and interpretation of the data, wording and critical review. All the authors approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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