revista de pesquisa

ISSN 2175-5361

CUIDADO É FUNDAMENTAL

Escola de Enfermagem Alfredo Pinto – UNIRIO

RESEARCH

DOI: 10.9789/2175-5361.rpcfo.v14.11542

CHARACTERIZATION OF CHILDHOOD CANCER IN BRAZIL FROM THE HOSPITAL-BASED CANCER REGISTRIES, 2000-2016

Caracterização do câncer infantojuvenil no Brasil a partir dos Registros Hospitalares de Câncer (RHC), 2000-2016

Caracterización del cáncer infantil en Brasil a partir de los Registros de Cáncer del Hospital (RCH), 2000-2016

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ABSTRACT

Objective: to characterize childhood cancer in Brazil, based on the national and regional investigation of hospital-based cancer registries, from 2000 to 2016. **Method:** observational, retrospective and secondary-based study, with a sample of 71,925 records containing information of children and adolescents (0 to 19 years old). **Results:** infant-juvenile cancer was more frequent in males with 39,049 (54.3%) cases, with 22,391 (31.1%) records of children aged 0 and 4 years and 19,892 (40.4%) with color of brown skin. Leukemias, myeloproliferative diseases and myelodysplastic diseases affected 20,744 (28.8%) individuals. Solid tumors were diagnosed in 42,087 (58.5%) children and adolescents,23,941 (48.7%) of which underwent chemotherapy at the beginning of treatment and 56,518 (78.6%) who started treatment within 60 days of the diagnosis. **Conclusion:** it was possible to know the demographic, clinical and care profile of children and adolescents with cancer in Brazil, and by region.

DESCRIPTORS: Child; Adolescent; Cancer; Epidemiology; Hospital registry.

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Received: 11/25/2021; Accepted: 01/25/2022; Published online: 10/07/2022

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How cited: Lucena NNN, Damascena LCL, Moreira MSC, Lima-Filho LMA, Valença AMG. Characterization of childhood cancer in Brazil from the hospital-based cancer registries, 2000-2016. *R Pesq Cuid Fundam* [Internet]. 2022 [cited year mouth day];14:e11542. Available from: https://doi.org/10.9789/2175-5361.rpcfo.v14.11542

RESUMO

Objetivo: caracterizar o câncer infantojuvenil no Brasil, a partir da investigação nacional e regional dos registros hospitalares de câncer, no período de 2000 a 2016. **Método:** estudo observacional, retrospectivo e de base secundária, com amostra de 71.925 registros contendo informações de crianças e adolescentes (0 a 19 anos). **Resultados:** o câncer infantojuvenil foi mais frequente no sexo masculino com 39.049 (54,3%) casos, existindo 22.391 (31,1%) registros de crianças de 0 e 4 anos de idade e 19.892 (40,4%) com cor de pele parda. As leucemias, doenças mieloproliferativas e doenças mielodisplásicas acometeram 20.744 (28,8%) indivíduos. Os tumores sólidos foram diagnosticados em 42.087 (58,5%) crianças e adolescentes, sendo 23.941 (48,7%) submetidas a quimioterapia no início do tratamento e 56.518 (78,6%) que iniciaram o tratamento até 60 dias após comprovação diagnóstica. **Conclusão:** foi possível conhecer o perfil demográfico, clínico e assistencial das crianças e adolescentes com câncer no Brasil, e por regiões.

DESCRITORES: Criança; Adolescente; Câncer; Epidemiologia; Registro hospitalar.

RESUMEN

Objetivo: caracterizar el cáncer infantil en Brasil, con base en la investigación nacional y regional de registros hospitalarios de cáncer, de 2000 a 2016. **Método:** estudio observacional, retrospectivo y secundario, con una muestra de 71,925 registros que contienen información de niños. y adolescentes (0 a 19 años). **Resultados:** el cáncer infantil-juvenil fue más frecuente en el sexo masculino con 39.049 (54,3%) casos, con 22.391 (31,1%) registros de niños de 0 y 4 años y 19.892 (40,4%) con color de piel morena. Las leucemias, enfermedades mieloproliferativas y enfermedades mielodisplásicas afectaron a 20.744 (28,8%) individuos. Se diagnosticaron tumores sólidos en 42.087 (58,5%) niños y adolescentes, 23.941 (48,7%) de los cuales se sometieron a quimioterapia al inicio del tratamiento y 56.518 (78,6%) que iniciaron el tratamiento dentro de los 60 días del diagnóstico. **Conclusión:** fue posible conocer el perfil demográfico, clínico y de atención de niños y adolescentes con cáncer en Brasil y por región.

DESCRIPTORES: Niño; Adolescente; Cáncer; Epidemiología; Registro hospitalario.

INTRODUCTION

Childhood cancer, although considered a rare event when compared to tumors that affect adults, is the leading cause of death by disease in the age group zero to 19 years.[1] It is a little known disease with different characteristics, which makes its prevention difficult.[2]

In Brazil, it is estimated for 2020 and subsequent years, 8,460 new cases of childhood cancer, with the estimated risk of 137.87 cases per million for males and 139.04 per million for females. In 2017, 2,553 deaths were recorded.[1] These are relevant data, given that about 33% of the Brazilian population is made up of children and adolescents.

In this aspect, it is important to highlight the differences between the Brazilian regions, with an estimated higher incidence in the Southeast region (43.6%), and the North with 7.4%, being considered the region with the lowest incidence of childhood and adolescent cancer.[1] In turn, the country has several geographical differences, which are related to access to goods and health services, being a barrier for those living in peripheral areas and areas lacking development.[3–4]

Several aspects must be considered in childhood and juvenile neoplasms, such as the biological origin, histological type, forms of development, clinical presentation, and the need for precise and early care.[5]

Faced with the particularities of the disease, the need for cure, the need for monitoring in patient care, the fragility of health services, and the little investment in public policies, in 2012 Law no.12,732 was instituted, which determines the deadline for the start of oncological treatment, after diagnostic proof.[6] Early diagnosis and appropriate specialized treatment are able to improve the prognosis, increase the chances of cure, and positively impact the quality of life of children and adolescents.[7–8]

One of the great challenges for developing countries is to plan strategies and implement policies for the control of childhood and adolescent cancer, since the information is neglected due to the lack of data that expresses the reality, being most often omitted from statistics or grouped with neoplasms in adults.[8]

Thus, the monitoring of cancer cases in Brazil is done by systematized morbidity and mortality information made available by Population-Based Cancer Registries (PBCR), Hospital Cancer Registries (HCR) and the Mortality Information System (SIM), which help in the epidemiological description and support research involving cancer in different age groups.[1]

The studies involving children and adolescents aged 0-19 years with cancer in Brazil, for the most part, address incidence, mortality, and specific types of neoplasms, without verifying the involvement of the assistance provided to these individuals and without considering the regional differences that exist in the country. Thus, this study addressed the information from Hospital Cancer Registries, since it is essential to verify the gaps and the quality of cancer information in the Brazilian territory.

Given the context presented, this research aimed to characterize childhood and adolescent cancer in Brazil, from the national and regional investigation of cancer hospital registries, in the period from 2000 to 2016.

METHOD

This is an observational, retrospective, secondary study with a quantitative approach. Data were collected from the information on childhood cancers (0-19 years) in the Brazilian states, including the Federal District, contained in the Integrating Module of Hospital Cancer Registries, made available by the National Cancer Institute José Alencar Gomes da Silva (INCA) at https://irhc.inca.gov.br/RHCNet/visualizaTabNetExterno.action, and also from data offered by the Oncocentro Foundation of São Paulo (FOSP) at http://www.fosp.saude.sp.gov.br/publicacoes/acessobancodados.

A total of 71,925 records were included in the study, being considered eligible only those cases registered as analytic, and those who had their first consultation in the hospital unit in the period from 2000 to 2016. The information was obtained from the websites of each institution, and downloads were performed on September 30, 2020.

Analytical cases are understood as those with a therapeutic plan, treatment and follow-up performed in the hospital that registered them in the Hospital Cancer Registry System SisRHC, making it possible to evaluate the quality of care by the hospital.[9]

The variables analyzed were extracted from the tumor registration form of the analytical cases of the RHC and were grouped, according to their classification into sociodemographic variables (sex, age, race/color, federation unit (UF) of the patient's residence, age range, Brazilian regions), clinical and treatment variables (location of the primary tumor, histological type, tumor type, clinic of treatment initiation, origin of referral, diagnosis and previous treatments, initial hospital treatment, basis for diagnosis, time between diagnosis and start of treatment, disease status at the end of the first hospital treatment).

The variable "time between diagnosis and start of treatment" was categorized into ≥ 60 days and < 60 days from what is recommended by Law 12,732/2012, i.e., the deadline for starting antineoplastic treatment should be up to 60 days after diagnostic confirmation with pathological report.[6]

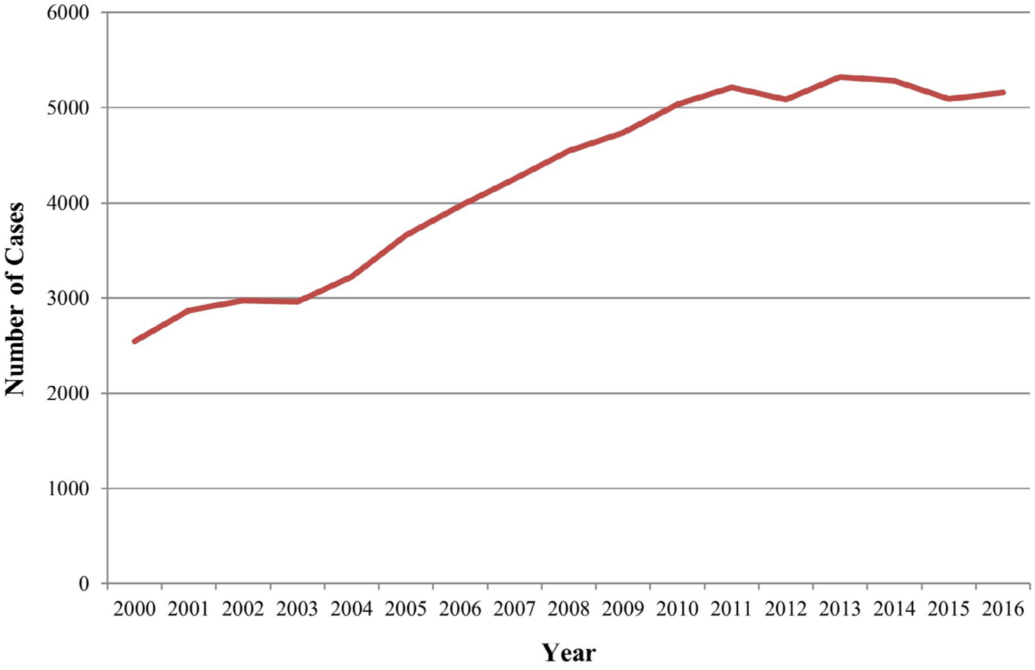
The information contained in the database that had the response "not evaluated; not applicable; no information" or even absence of information were grouped in the category "No information" for further analysis of data completeness.

The data were analyzed descriptively as to their incompleteness, i.e., the determination of the percentage of ignored or unfilled information. The degree of completeness was classified according to a stratified score system as follows: Excellent (< 5% incompleteness), Good (5 ≤ 10%), Fair (10 ≤ 20%), Poor (20 ≤ 50%) and Very Poor (≥ 50%).[10] The public domain software R was used.

The research does not require an Ethics Committee because it is a study with secondary data integrated into the Hospital Cancer Registry System (SisRHC), provided by (INCA) and the Hospital Cancer Registry provided by (FOSP), making it freely accessible.

RESULTS

In total, 71,925 records of children and adolescents with cancer met the inclusion criteria for the study. Graph 1 shows an increase until 2011, followed by stability, with a peak in 2013, with 5,322 new cancer records.



Graph 1 – Evolution of the number of cases of childhood cancer in Brazil, 2000-2016
Source: Hospital Cancer Registries (HCR): 2000-2016.

Although it is not possible to calculate the incidence of the disease due to the HCR including institutional cases and not population cases, the prevalence coefficient was determined. Thus, it can be seen that the South region had higher prevalence coefficients when compared to the other regions, both for sex and age groups, with males (1,526.9) and the 0-4 age group (1,875.4) as the most prevalent (Table 1).

In the records analyzed, 39,049 (54.3%) are related to males, with a M/F ratio of 1.18 boys for each girl, and a greater representation in the North with 3,139 (56.8%) cases. The disease in females was more present in the Center-West region when compared to the other regions, with 1,578 (46.3%) records.

The age of the individuals ranged from 0 to 19 years, with a mean of 9.31 years (± 6.19). The most affected age group was 0 to 4 years, with 22,391 (31.1%) affected individuals, and the Midwest region had 1,161 (34.1%) records, followed by the North with 1,833 (33.2%), and the South with 3,664 (31.7%).

The skin color brown was more representative with 19,892 (40.4%) of the analyzed data, being more expressive in the Northeast with 10,846 (59.7%) cases, while the skin color white was more frequent in the records of the South region with 9,572 (84.2%).

Regarding the regions that presented the most children and adolescents with cancer, the Southeast region had 32,802 (45.6%) with the most cases, followed by the Northeast with 8,650 (25.9%) (Table 2).

The most commonly affected anatomical sites were the hematopoietic system and endothelial reticulum with 21,830 (30.4%) records, followed by lymph nodes with 7,987 (11.1%), and the brain with 7,383 (10.3%), but there were considerable differences among the regional percentages. In the North, there were 2,323 (42.0%) cases affecting the hematopoietic and endothelial reticulum system, while the Midwest presented 917 (26.9%) (Table 3).

The most relevant diagnosis classification was Group I – Leukemias, myeloproliferative disorders, and myelodysplastic diseases with 20,744 (28.8%) occurrences, being more prevalent in the North with 2,227 (40.3%) and less prevalent in the Midwest with 876 (25.7%). In turn, solid tumors were more frequent with 42,087 (58.5%) records when compared to hematological neoplasms with 29,817 (41.5%), but in the North, solid tumors were diagnosed in smaller quantity, with 2,577 (46.6%) events.

Regarding the care characteristics, 37,515 (76.1%) referrals were offered by the Unified Health System to units and centers specialized in cancer, and the Center-West region was the one that most used the service with 2,249 (79.2%) referrals (Table 4).

As for previous diagnosis and treatment, 46,556 (64.7%) patients arrived in the qualified centers without diagnosis and without previous treatment; however, the North region was the least representative, with 2,613 (47.3%) individuals with these characteristics. This region stands out for having the highest percentage of children and adolescents who arrived in the oncologic network with diagnosis but no treatment (40.1%; n = 2,217). Regarding diagnosis, microscopic confirmation was the diagnostic strategy used by 65,720 (91.4%) of patients with childhood and adolescent cancer, being more pronounced in the North with 5,161 (93.3%) records, while in the Midwest 316 (9.3%) children and adolescents used non-microscopic resources for this purpose. The time between diagnosis and start of treatment ranged from 0 to 4,627 days, with a median of 8 days and a mean of 44.15 days (±160.19). The Brazilian regions presented more than 70% of the cases diagnosed and with the beginning of treatment up to 60 days after proven diagnosis, with the Southeast region offering the most treatment on time, with 27,228 (83.0%) records.

Pediatric Oncology attended 28,490 (39.6%) individuals, and is the specialty that works most with this disease, followed by Clinical Oncology with 13,635 (19.0%) and Hematology with 7,383 (10.3%). Clinical Oncology was used by 1,764 (31.9%) children and adolescents assisted in the North region. The therapeutic modalities vary according to the patient's needs, in this case, chemotherapy was the most administered at the

Table 1 – Prevalence coefficient of childhood and adolescent cancer, according to sex and age group, in Brazilian geographic regions, according to hospital cancer registries, Brazil, 2000-2016

Variables		North	Northeast	Midwest	Southeast	South
Gender	Male	909,8	1.065,0	742,2	1.451,6	1.526,9
	Female	721,7	951,2	666,2	1.283,7	1.321,6
	Total	817,7	1.009,2	705,0	1.369,4	1.426,5
Age Group	0-4 years old	1.133,5	1.380,9	971,5	1.725,8	1.875,4
	5-9 years old	722,5	870,5	580,7	1.145,5	1.152,8
	10-14 years old	659,7	831,9	588,8	1.194,5	1.160,5
	15-19 years old	771,3	990,4	677,1	1.404,2	1.496,9
	Total	817,7	1.009,2	705,0	1.369,4	1.426,5

Source: IBGE/Diretoria de Pesquisas. Population and Social Indicators Coordination. Gerência de Estudos e Análises da Dinâmica Demográfica. Population projection for Brazil and states by sex and age, July 1, 2010-2060
Note: Prevalence coefficient adjusted per 1,000,000 inhabitants

Table 2 – Demographic characteristics of childhood and adolescent cancer in Brazilian geographic regions and in Brazil, according to hospital cancer registries, Brazil, 2000-2016

Variables		North	Northeast	Midwest	Southeast	South	Brazil
		n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
Gender	Male	3.139 (56,8)	10.027 (53,8)	1.831 (53,7)	17.745 (54,1)	6.307 (54,7)	39.049 (54,3)
	Female	2.390 (43,2)	8.622 (46,2)	1.578 (46,3)	15.057 (45,9)	5.227 (45,3)	32.874 (45,7)
	No Information	00 (0,0)	01 (0,0)	00 (0,0)	00 (0,0)	01 (0,0)	02 (0,0)
	Total	5.529 (100,0)	18.650 (100,0)	3.409 (100,0)	32.802 (100,0)	11.535 (100,0)	71.925 (100,0)
Age Group	0-4 years old	1.833 (33,2)	5.756 (30,9)	1.161 (34,1)	9.977 (30,5)	3.664 (31,7)	22.391 (31,1)
	5-9 years old	1.201 (21,7)	3.825 (20,5)	666 (19,5)	6.426 (19,6)	2.136 (18,5)	14.254 (19,8)
	10-14 years old	1.128 (20,4)	3.952 (21,2)	711 (20,8)	7.068 (21,5)	2.313 (20,1)	15.172 (21,1)
	15-19 years old	1.367 (24,7)	5.117 (27,4)	871 (25,6)	9.331 (28,4)	3.422 (29,7)	20.108 (28,0)
	Total	5.529 (100,0)	18.650 (100,0)	3.409 (100,0)	32.802 (100,0)	11.535 (100,0)	71.925 (100,0)
Skin Color*	White	598 (12,6)	3.325 (18,3)	702 (24,8)	5.511 (45,5)	9.572 (84,2)	19.708 (40,0)
	Black	82 (1,7)	642 (3,5)	83 (2,9)	1.013 (8,4)	228 (2,0)	2.048 (4,2)
	Yellow	14 (0,3)	285 (1,6)	06 (0,2)	46 (0,4)	42 (0,4)	393 (0,8)
	Brown	2.711 (56,5)	10.846 (59,7)	1.141 (40,2)	4.543 (37,5)	651 (5,7)	19.892 (40,4)
	Indigenous	83 (1,7)	25 (0,1)	15 (0,5)	13 (0,1)	27 (0,2)	163 (0,2)
	No Information	1.306 (27,2)	3.049 (16,8)	892 (31,4)	987 (8,1)	847 (7,5)	7.081 (14,4)
	Total	4.794 (100,0)	18.172 (100,0)	2.839 (100,0)	12.113 (100,0)	11.367 (100,0)	49.285 (100,0)

Source: Hospital Cancer Registries (HCR): 2000-2016.
* Variable presenting information for Brazilian states with the exception of São Paulo.

beginning of the course of the disease with 23,941 (48.7%) records, followed by surgery with 6,320 (12.8%) and radiotherapy with 2,049 (4.2%).

After completion of the first treatment, complete remission of the disease was observed in 11,082 (22.5%) of the cases, with the Southern region showing the most individuals without signs of the disease with 3,575 (31.5%) and the Northern region the one where complete remission was less frequent with 402 (8.4%). Deaths reached 16,338 (2.9%) of children and adolescents in the first phase of cancer treatment, with higher values represented by 807 (16.8%) cases in the North, 2,924 (16.1%) in the Northeast, and 397 (14.0%) in the Midwest.

Regarding the completeness of the data, there is lack of information in some variables, and we can classify "sex" (0.0%), "age group" (0.0%), "primary tumor location" (0.0%), "type of neoplasm" (0.0%), "diagnosis classification" (0.7%), "treatment clinic" (2.3%), "previous diagnosis and treatment" (1.6%) and "basis of diagnosis" (0.7%) as excellent. In contrast, the variable "time between diagnosis and start of treatment" (7.5%) was characterized as good completeness, "origin of referral" (11.1%) and "skin color" (14.4%) were filled out regularly, and "first hospital treatment" (30.5%) and disease status at the end of the first hospital treatment (28.0%) were not fully complete, being described as poor.

Table 3 – Clinical characteristics of childhood cancer in Brazilian geographic regions and in Brazil, according to hospital cancer registries, Brazil, 2000-2016

Variables		**North**	**Northeast**	**Midwest**	**Southeast**	**South**	**Brazil**
		n(%)	**n(%)**	**n(%)**	**n(%)**	**n(%)**	**n(%)**
Primary Tumor LocationSouth	Hematopoietic System E Reticulum End.	2.323 (42,0)	5.833 (31,3)	917 (26,9)	9.305 (28,4)	3.452 (29,9)	21.830 (30,4)
	Lymph nodes	629 (11,4)	2.214 (11,9)	379 (11,1)	3.428 (10,5)	1.337 (11,6)	7.987 (11,1)
	Encephalon	372 (6,7)	1.756 (9,4)	435 (12,8)	3.662 (11,2)	1.158 (10,0)	7.383 (10,3)
	Bones, joints and cartilage art.	398 (7,2)	1.399 (7,5)	220 (6,4)	1.986 (6,1)	619 (5,4)	4.622 (6,4)
	Kidney	299 (5,4)	1.014 (5,4)	207 (6,1)	1.648 (5,0)	526 (4,6)	3.694 (5,1)
	Other	1.508 (27,3)	6.433 (34,5)	1.251 (36,7)	12.773 (38,8)	4.423 (38,3)	26.388 (36,7)
	No Information	00 (0,0)	01 (0,0)	00 (0,0)	00 (0,0)	20 (0,2)	21 (0,0)
	Total	5.529 (100,0)	18.650 (100,0)	3.409 (100,0)	32.802 (100,0)	11.535 (100,0)	71.925 (100,0)
Diagnostic Classification (CICI)	Group I	2.227 (40,3)	5.520 (29,6)	876 (25,7)	8.828 (26,9)	3.293 (28,5)	20.744 (28,8)
	Group II	858 (15,5)	3.050 (16,4)	547 (16,1)	5.455 (16,6)	1.907 (16,5)	11.817 (16,4)
	Group III	377 (6,8)	1.749 (9,4)	451 (13,2)	4.119 (12,6)	1.193 (10,3)	7.889 (11,1)
	Group IV	123 (2,2)	577 (3,1)	114 (3,4)	1.374 (4,2)	469 (4,2)	2.657 (3,7)
	Group V	168 (3,1)	578 (3,1)	127 (3,7)	1.007 (3,1)	222 (1,9)	2.102 (2,9)
	Group VI	289 (5,2)	975 (5,2)	200 (5,9)	1.590 (4,8)	504 (4,4)	3.558 (4,9)
	Group VII	56 (1,1)	174 (0,9)	37 (1,2)	328 (1,0)	105 (0,9)	700 (1,1)
	Group VIII	489 (8,9)	1.730 (9,3)	280 (8,2)	2.510 (7,7)	828 (7,2)	5.837 (8,1)
	Group IX	257 (4,6)	1.081 (5,8)	222 (6,5)	2.318 (7,1)	664 (5,8)	4.542 (6,3)
	Group X	229 (4,2)	763 (4,1)	175 (5,1)	1.780 (5,4)	698 (6,1)	3.645 (5,1)
	Group XI	350 (6,3)	1.885 (10,1)	288 (8,4)	3.082 (9,4)	1.333 (11,6)	6.938 (9,6)
	Group XII	90 (1,6)	338 (1,8)	68 (2,0)	268 (0,8)	199 (1,7)	953 (1,3)
	No Information	11 (0,2)	217 (1,2)	22 (0,6)	130 (0,4)	107 (0,9)	487 (0,7)
	Total	5.529 (100,0)	18.650 (100,0)	3.409 (100,0)	32.802 (100,0)	11.535 (100,0)	71.925 (100,0)
Type of Neoplasm	Solid Tumor	2.577 (46,6)	10.602 (56,9)	2.113 (62,0)	20.069 (61,2)	6.726 (58,3)	42.087 (58,5)
	Hematologic Neoplasia	2.952 (53,4)	8.047 (43,1)	1.296 (38,0)	12.733 (38,8)	4.789 (41,5)	29.817 (41,5)
	No Information	00 (0,0)	01 (0,0)	00 (0,0)	00 (0,0)	20 (0,2)	21 (0,0)
	Total	5.529 (100,0)	18.650 (100,0)	3.409 (100,0)	32.802 (100,0)	11.535 (100,0)	71.925 (100,0)

Source: Hospital Cancer Registries (HCR): 2000-2016.

Table 4 – Care and treatment characteristics of childhood and adolescent cancer in the Brazilian regions, Brazil, 2000-2016

Variables		North	Northeast	Midwest	Southeast	South	Brazil
		n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
Source of Referral*	SUS	3.746 (78,1)	13.604 (74,8)	2.249 (79,2)	9.183 (75,8)	8.733 (76,8)	37.515 (76,1)
	No SUS	476 (9,9)	1.310 (7,2)	114 (4,0)	1.316 (10,9)	1.256 (11,0)	4.472 (9,1)
	Own Account	46 (1,0)	1.265 (7,0)	186 (6,6)	197 (1,6)	156 (1,4)	1.850 (3,7)
	No Information	526 (11,0)	1.993 (11,0)	290 (10,2)	1.417 (11,7)	1.222 (10,8)	5.448 (11,1)
	Total	4.794 (100,0)	18.172 (100,0)	2.839 (100,0)	12.113 (100,0)	11.367 (100,0)	49.285 (100,0)
Previous diagnosis and treatment	No diag/no treatment	2.613 (47,3)	11.442 (61,4)	2.155 (63,2)	22.908 (69,8)	7.438 (64,5)	46.556 (64,7)
	With diag/ without treatment	2.217 (40,1)	5.496 (29,5)	1.016 (29,8)	8.917 (27,2)	2.283 (19,8)	19.929 (27,7)
	With diag/ with treatment	464 (8,4)	1.223 (6,6)	161 (4,8)	843 (2,6)	1.082 (9,4)	3.773 (5,3)
	Other	75 (1,4)	313 (1,7)	22 (0,6)	89 (0,3)	37 (0,3)	536 (0,7)
	No information	160 (2,8)	176 (0,8)	55 (1,6)	45 (0,1)	695 (6,0)	1.131 (1,6)
	Total	5.529 (100,0)	18.650 (100,0)	3.409 (100,0)	32.802 (100,0)	11.535 (100,0)	71.925 (100,0)
Basis for diagnosis	Clinic	72 (1,3)	189 (1,0)	61 (1,8)	227 (0,7)	251 (2,2)	800 (1,1)
	Non-microscopic resources	279 (5,1)	1.332 (7,1)	316 (9,3)	1.946 (5,9)	1.024 (8,9)	4.897 (6,8)
	Microscopic Confirmation	5.161 (93,3)	16.963 (91,0)	2.966 (87,0)	30.534 (93,1)	10.096 (87,5)	65.720 (91,4)
	No Information	17 (0,3)	166 (0,9)	66 (1,9)	95 (0,3)	164 (1,4)	508 (0,7)
	Total	5.529 (100,0)	18.650 (100,0)	3.409 (100,0)	32.802 (100,0)	11.535 (100,0)	71.925 (100,0)
Time between diagnosis and treatment	≤ 60 days	3.894 (70,4)	13.618 (73,0)	2.734 (80,2)	27.228 (83,0)	9.044 (78,4)	56.518 (78,6)
	> 60 days	1.184 (21,4)	3.016 (16,2)	480 (14,1)	3.795 (11,6)	1.540 (13,4)	10.015 (13,9)
	No Information	451 (8,2)	2.016 (10,8)	195 (5,7)	1.779 (5,4)	951 (8,2)	5.392 (7,5)
	Total	5.529 (100,0)	18.650 (100,0)	3.409 (100,0)	32.802 (100,0)	11.535 (100,0)	71.925 (100,0)
Treatment Clinic	Pediatric Oncology	1.439 (26,0)	8.126 (43,6)	1.643 (48,2)	13.718 (41,8)	3.564 (30,9)	28.490 (39,6)
	Clinical Oncology	1.764 (31,9)	4.066 (21,8)	549 (16,1)	5.048 (15,4)	2.208 (19,1)	13.635 (19,0)
	Clinical Hematology	1.214 (22,0)	752 (4,0)	142 (4,2)	4.077 (12,4)	1.198 (10,4)	7.383 (10,3)
	Pediatrics	52 (0,9)	407 (2,2)	109 (3,2)	2.022 (6,2)	243 (2,1)	2.833 (3,9)
	Radiology	221 (4,0)	973 (5,2)	227 (6,7)	641 (2,0)	511 (4,4)	2.573 (3,6)
	Other	774 (14,0)	4.061 (21,8)	694 (20,3)	7.091 (21,6)	2.709 (23,5)	15.329 (21,3)
	No Information	65 (1,2)	265 (1,4)	45 (1,3)	205 (0,6)	1.102 (9,6)	1.682 (2,3)
	Total	5.529 (100,0)	18.650 (100,0)	3.409 (100,0)	32.802 (100,0)	11.535 (100,0)	71.925 (100,0)

Table 4 – Cont.

Variables		North	Northeast	Midwest	Southeast	South	Brazil
		n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
First Hospital Treatment*	None	152 (3,2)	306 (1,7)	72 (2,5)	298 (2,5)	226 (2,1)	1.054 (2,1)
	Surgery	339 (7,1)	2.109 (11,6)	417 (14,7)	1.657 (13,7)	1.798 (15,8)	6.320 (12,8)
	Radiotherapy	130 (2,7)	778 (4,3)	198 (7,1)	428 (3,5)	515 (4,5)	2.049 (4,2)
	Chemotherapy	2.746 (57,3)	8.854 (48,7)	1.462 (51,5)	5.184 (42,8)	5.695 (50,1)	23.941 (48,7)
	Hormone Therapy	05 (0,1)	19 (0,1)	04 (0,1)	06 (0,0)	24 (0,2)	58 (0,1)
	Bone Marrow Transplant	03 (0,1)	21 (0,1)	01 (0,0)	27 (0,2)	17 (0,1)	69 (0,1)
	Immunotherapy	01 (0,0)	08 (0,0)	01 (0,0)	03 (0,0)	10 (0,1)	23 (0,0)
	Other	104 (2,1)	315 (1,8)	44 (1,6)	128 (1,1)	135 (1,2)	726 (1,5)
	No Information	1.314 (27,4)	5.762 (31,7)	640 (22,5)	4.382 (36,2)	2.947 (25,9)	15.045 (30,5)
	Total	4.794 (100,0)	18.172 (100,0)	2.839 (100,0)	12.113 (100,0)	11.367 (100,0)	49.285 (100,0)
Disease status at the end of the first hospital treatment*	Full Remission	402 (8,4)	3.529 (19,4)	769 (27,1)	2.807 (23,2)	3.575 (31,5)	11.082 (22,5)
	Partial Remission	385 (8,0)	920 (5,1)	105 (3,7)	1.098 (9,1)	1.350 (11,9)	3.858 (7,8)
	Stable Disease	1.751 (36,5)	3.831 (21,1)	483 (17,0)	2.424 (20,0)	1.657 (14,6)	10.146 (20,6)
	Progressing Disease	594 (12,4)	1.058 (5,8)	197 (6,9)	1.074 (8,9)	686 (6,0)	3.609 (7,3)
	Oncological Therapeutic Support	47 (1,0)	178 (1,0)	13 (0,5)	158 (1,2)	70 (0,6)	466 (0,9)
	Death	807 (16,8)	2.924 (16,1)	397 (14,0)	1.162 (9,6)	1.048 (9,2)	6.338 (12,9)
	No Information	808 (16,9)	5.732 (31,5)	875 (30,8)	3.390 (28,0)	2.981 (26,2)	13.786 (28,0)
	Total	4.794 (100,0)	18.172 (100,0)	2.839 (100,0)	12.113 (100,0)	11.367 (100,0)	49.285 (100,0)

Source: Hospital Cancer Registries (HCR): 2000-2016.
* Variable presenting information for Brazilian states except São Paulo.

DISCUSSION

This study characterizes the population of children and adolescents affected by cancer in Brazil, exposing epidemiological, clinical, and care aspects that contribute to a systemic view of access to diagnosis and treatment.

Only analytical registries were considered to avoid overestimation of information.[11] Thus, data were selected from the year 2000, due to the systematic standardization of data incorporation in the system[11], until the year 2016, for being the most recent year with data records in all months of the year, corresponding to the approximate amount of data from the previous year (2015). It should be noted that the process of updating the database and filling in the most recent years represent limitations for current data analysis.

That said, it can be seen that the number of cancer cases in children and adolescents has increased over time at all ages, varying their incidence rates in different continental regions. Despite the lack of knowledge about this phenomenon, it is believed that there is a link between the types of exposure and genetic factors culminating in the disease.[1]

The present research mobilized information that does not depend only on new cases, but on those who consulted and had the diagnosis in the period studied, thus it was possible to visualize a growth in the frequency of childhood cancer diagnosis, which may be related to a greater national coverage of cancer registries, since in the year 2000 there were only 45 HCR in the country, and in recent years it has reached 321 registries.[1] Another factor to be analyzed is the implementation of the Health Care Network (RAS) in oncology, which has expanded the training of professionals, technologies, institutions, and specialties qualified for diagnosis and adequate treatment.

In Brazil, the estimate of childhood and adolescent cancer for the triennium 2020-2021 shows that 4,310 new cases are expected in males, with an estimated risk of 137.87 cases per million, with females prevailing.[1] Male predominance was observed in this study and in another study involving children and adolescents, which covered the entire Brazilian territory[9] and isolated studies directed at states in different regions of the country.[4,12–16] Males are more likely to have congenital diseases (chromosomal anomalies, monogenic syndromes, and nonsyndromic birth defects), which is associated with the risk of childhood cancers.[18]

A higher number of records were found in the 0 to 4 years age group, corroborating a national study[9] and from different Brazilian states,[4,13,15–16,18] as well as an international study.[8] Age is an important factor of analysis, because the occurrence of some tumors is higher in certain age groups, with patients in the first years of life being the most affected.[18] Thus, leukemias are the most common hematologic neoplasms among children and adolescents, being more present in children under 5 years of age.[19]

The study shows a greater predominance of individuals with brown skin color, being in agreement with studies developed in the state of Piauí[20], Alagoas[13], Minas Gerais[14], and Acre[15]. Research developed in the South region observed white individuals as the most affected by childhood and adolescent cancer.[12,16] Finally, a study carried out with the RHC records from all the units of the federation, in the period from 2000 to 2015, also verified a predominance of white children and adolescents.[21] This fact can be explained by the differences in human groups distributed in the country.

Childhood and adolescent cancer is embryonic in nature, with involvement of cells of the blood system and supporting tissues, with short latency periods, good response to treatment, and good prognosis when diagnosed early, thus differing from adult cancer.[1,5] Thus, cancer registries consider the International Classification of Diseases for Oncology (ICD-O) to group neoplasms according to their topography and histology.

In this aspect, the present study shows a higher number of cases in the Hematopoietic System and Endoplasmic Reticulum in all regions of Brazil. However, it is important to highlight a higher proportion in the North region, which may be related to a wider range of diagnoses of hematological neoplasms due to the fact that exams to prove the disease are less complex and of better access when compared to the difficulty of investigation of solid tumors. Information from the HCR of a reference hospital in the state of Piauí, as well as data from hospital records in the state of Minas Gerais, point to a predominance of the impairment of such system[14,20], corroborating the results of the present study.

When considering the International Classification of Cancer in Childhood (ICICI-3), the present study identified results consistent with other national[9,12–13,22] and international[5], 8 studies, which considered leukemias, lymphomas, and CNS tumors as the most incident neoplasms. For the international studies, CNS tumors come second, followed by lymphomas.[5,6]

As for the most prevalent types of neoplasms in this population, we have leukemias (28%), central nervous system tumors (26%) and lymphomas (8%, being Non-Hodgkin – 5% and Hodgkin – 3%), corresponding to 62% of all childhood cancers. Central Nervous System (CNS) tumors are the second most frequent type of neoplasm in the pediatric range in developed countries, followed by lymphomas.[19]

Taking into consideration the types of neoplasms, solid tumors were the most prevalent in Brazil, with the exception of the Northern region. Based on this classification, a survey in the state of Paraná identified hematological tumors as the most prevalent.[18]

When analyzing these clinical characteristics, it is observed that the Northern region presents more diagnoses of hematological neoplasms. This fact could be attributed to simpler methods of diagnosis of this group of tumors, which mostly involve routine exams. The diagnosis of hematological neoplasms requires a clinical examination and less complex complementary exams (hemogram, myelogram, cytology and immunophenotyping) when compared to the exams for the diagnosis of solid tumors (imaging exams such as ultrasonography, computed tomography, magnetic resonance imaging), which allows for greater surveillance by primary care and subsequent referral to specialized services.[7] This scenario points to the need to expand the oncologic network in this region, because the fragility in the availability of qualified services hinders mainly the diagnosis of solid tumors, thus lengthening the treatment time, which can impact the prognosis and survival of these patients.

Brazil has 317 units and centers qualified for the diagnosis and treatment of cancer distributed throughout the country, with at least one establishment with the necessary attributions per state. The North region has about 5% of these services, among these, 02 High Complexity Oncology Assistance Centers (CACON) for the entire region[22], which shows the precariousness of comprehensive care for the user in a regionalized and decentralized manner from these establishments.

In view of the unequal geographical distribution of qualified services, data from this study indicate that SUS-funded institutions are responsible for about 75% of referrals throughout Brazil. Another important fact is that the Southeast and South regions present a proportion higher than 10% of people who are referred from places that are not public health services, which may be associated with a higher purchasing power of the population, since they are the regions with higher economic development. Therefore, it is assumed that people with higher purchasing power use private health plans.

From this perspective, it is essential to guarantee access to specialized centers through referral and social support, especially for those patients who have more difficulty in obtaining oncologic care.[3] A study developed in 352 health regions in Brazil verified the real regional differences for the care of childhood cancers, one of them being the great distances traveled by some individuals residing in the North region. These individuals, to have access to the qualified centers, needed to travel about 1,000 km, and for the effective treatment, about 1,600 km.[3]

With this, one of the major bottlenecks is the delay in treatment due to the limitations faced, such as the difficulties of primary care professionals to identify the first signs and symptoms and refer these individuals to cancer centers, the access to specialized sites, either by geographical barriers or by the financial restriction of families, as well as the lack of necessary supplies for the initiation and continuity of oncological care. In this scenario, there is a need for sharing responsibilities, establishing agile and resolutive flows, favoring referral to specialized centers, as well as early diagnosis and adequate treatment.[7]

Studies developed in the states of Minas Gerais14 and Piauí20, aiming to know the clinical-epidemiological and care profile of children and adolescents with cancer, revealed a greater use of microscopic exams for the diagnosis of the disease. These findings were also found in this study, being more evident in the North, Northeast and Southeast regions. A greater demand for non-microscopic exams was also observed in the Midwest and South regions. Thus, microscopic exams are essential to guide the professional in charge about the suspicion of childhood and adolescent cancer and thus allow referral to specialized oncology centers for further diagnostic or complementary exams, responsible for concluding the definitive diagnosis.

It is important to report that the results of this study indicate that about 90% of children and adolescents had the diagnosis based on less complex laboratory tests, but most cancers in this population were solid tumors, which require imaging tests for diagnostic confirmation.

Given the above, and the need to implement cancer control policies, in 2012, Law No.12,732 was published, establishing a maximum time limit of 60 days for the start of treatment, after diagnostic proof of cancer.[6] Thus, the present study quantified the proportion of individuals who started treatment up to the limit of days stipulated by law, demonstrating that all regions of Brazil reached 70% or more of the child and adolescent population with cancer, ranging from 0 to 4,627 days, with a median of 08 and a mean of 44.15 days. The Midwest, Southeast, and South regions showed percentages around 80% compliance with the federal law, while the North was the region where the highest frequency of delays was observed, followed by the Northeast.

It was also possible to visualize the time between diagnosis and treatment in a study conducted with all HRCs in Brazil between 2000 and 2015, taking into account individuals without diagnosis and treatment. A range of 01 to 1,455 was observed, with a median of 02 and a mean of 15 days. In the analysis by region, the Midwest region presented the shortest time followed by the South region, and the North and Northeast regions presented the longest median times.[21] The results of this study diverge from these findings regarding the range of days from diagnosis to treatment (0 and 2,461 days), however, the mean and median times are similar among the studies.

In João Pessoa – PB, a study developed in a reference hospital found that pediatric patients with solid tumors had a range of 0 to 77 days from diagnosis to start of treatment, with a median of 14 and a mean of 18.6 days (±16.6). In contrast, in children and adolescents with hematologic neoplasms, this time ranged from 0 to 37 days, with a median of 02 and a mean of 6.1 days (±9.5). 23 Taking into consideration the types of tumors, the present study also found that solid tumors presented a greater median and mean number of days between diagnosis and start of treatment (12 and 48 days, respectively) when compared to hematological neoplasms (04 and 38 days, respectively), but the number of days was less than that observed in the reference hospital in Paraiba.[23]

These differences can be explained from the territorial dimension studied, in addition to the services involved in oncopediatric treatment, since the city of João Pessoa has a CACON with Pediatric Oncology service, while some states, especially in the North and Northeast, do not have centers specialized in childhood and adolescent cancer, thus enabling a delay in diagnosis and adequate treatment.

The variations in time elapsed between diagnosis and initiation of treatment may have happened due to the periods analyzed in each study and the prevalence of tumor types in each sample. The North and Northeast regions recorded a lower number of children and adolescents who started treatment within 60 days, suggesting that in these regions there are greater weaknesses in the cancer care network.

There are factors inherent to the patient and the cancer that contribute to the prognosis of cancer, as well as factors related to oncologic care offered to these children and adolescents, which often compromise this process, such as the lack of specialized centers, oncopediatric specialists and a health network trained for early diagnosis, and these weaknesses are found in several Brazilian regions.[4]

The data from this study reveal that, for treatment, the most active specialty is oncology pediatrics followed by clinical oncology; however, in the North region, clinical oncology was the most frequent specialty. Thus, it is suggested that, due to the reduced number of qualified institutions in the North region and the restriction of centers and units specialized in pediatrics, there is also a lack of professionals with expertise in pediatric oncology. In spite of this, the care for this population is not restricted only to specialized oncology centers, but can be offered in other qualified institutions.

Corroborating the findings of this study, a study developed in a reference hospital in Teresina – PI20 also shows Pediatric Oncology as the most frequent specialty in treatment.

It is noteworthy that one of the difficulties in diagnosing childhood cancer is the similarity of signs and symptoms with other common diseases in this age group, requiring a team of trained professionals to identify changes and refer to specialized centers.[4,7] Therefore, primary care professionals need to be well trained and have resources to suspect the disease, referring these patients to specialized services.[24]

After the diagnosis, and with the expertise of the oncologic team, the planning and initiation of treatment is carried out, a difficult, cautious, and self-denying moment for children or adolescents and their families. Thus, according to the data analyzed in this study, there was a predominance of the chemotherapy modality in all Brazilian regions, followed by surgery and radiotherapy as the first hospital treatment, with immunotherapy being the least used treatment. These findings are corroborated by other studies carried out in the Northeast[13] and Southeast[14] regions, while those developed in the North of the country show radiotherapy as the second most used modality.[4,15]

A study that evaluated the flows of children and adolescents with cancer between their places of residence and health services showed that chemotherapy and radiotherapy treatment occurs similarly in Brazil, but there was a deficiency in access to these modalities in the North and in the poorest regions of the Northeast (Maranhão, south of Piauí, west of Bahia) when compared to the Southeast, South, and Center-West regions.[24]

From the findings of this study, the efficacy and effectiveness of the first hospital treatment was satisfactory in approximately 23% of the patients, as there was complete remission of the cancer, followed by stability of the pathology. The South and Midwest regions had the highest percentage of individuals with disappearance of all signs and symptoms of the disease, while the North and Northeast had the most stabilized cases. It is important to report that the North region registered a higher number of cases with disease progression at the end of the first treatment, and was also the region where most deaths occurred, followed by the Brazilian Northeast. A study in the state of Minas Gerais corroborates, in part, the results of the present study, because it shows a higher number of individuals with disease stability followed by complete remission of the disease.[14]

Finally, the completeness of the data made available in the RHCs (INCA and FOSP) was analyzed; most of them were considered excellent to good according to the classification adopted. However, it should be noted the lack of information on important variables that characterize the treatment assistance offered to these children and adolescents. Another factor to be discussed is the divergence of information between the databases, which have important epidemiological characterizations that could complement each other favoring a greater knowledge of the population studied and the course of treatment offered by the qualified centers.

The importance given to cancer registries corresponds to the reliability of the information base to print the reality of the facts, being considered pillars for epidemiological surveillance. Thus, it is necessary to monitor the information in a systematic and standardized way, in addition to the qualification of professionals responsible for filling out the information systems.

The limitations of this study were due to the fact that it is a survey with secondary data, and should consider possible biases of information and selection. Follow-up for a prolonged time (16 years) may cause changes in the standardization of data collection, as well as in the classifications used for completion, and in the turnover of professionals responsible for the records.11 Most of the variables listed for analysis were mandatory, and even with this particularity, they presented levels of incompleteness. Another aspect is the difference in characteristics distributed in the databases of the INCA and FOSP hospital registries, making some national-level conclusions impossible. As for the potentialities of the study, are the size of the sample analyzed and the territorial coverage, allowing the knowledge of oncopediatric care in the country.

The study proposed to characterize the population affected by childhood cancer in Brazil, and in its regions, in a time series not yet presented in other studies, contributing not only for scientific knowledge, but also for the improvement of public policies and the application of specific and assertive strategies according to the reality of each location, from those less favored by the precariousness and difficulty of a quality oncologic assistance, to those that can meet the demands of cancer patients.

CONCLUSION

Analyzing the information contained in the HCR made it possible to know the demographic, clinical, and care representation of children and adolescents with cancer in Brazil and by regions, understanding the disease and identifying weaknesses in access to adequate treatment for this population. Finally, it is evident the importance of the completeness of the HCR data, in the perspective of translating the reality of the problem studied, assisting in the decision making by managers and professionals involved in the care of pediatric oncology patients.

ACKNOWLEDGEMENTS

Foundation for Research Support of the State of Paraíba (FAPESQ) – (Term nº 010/19), (process nº 23038.004264/2015-03).

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