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Cancer incidence among children and adolescents in Brazil: first report of 14 population-based cancer registries

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The Brazilian Population-Based Cancer Registry (PBCR) was started in 1967; today there are 20 PBCRs in Brazil. We report the first descriptive analysis of the incidence of childhood cancer based on data from 14 PBCRs, corresponding to 15% of the child and adolescent population in Brazil. Data were obtained from registry databases, including information on population coverage and data quality indicators. The International Classification of Childhood Cancer was used. Age-adjusted rates were calculated by world population. Incidence by cancer registry, age, sex, and cancer type were calculated per 1,000,000 children. Age-adjusted rates per 1,000,000 children/adolescents ranged from 92 to 220 among the 14 PBCRs. The principal groups of cancers were leukemia, lymphoma and central nervous tumors. The median incidence rate of childhood cancer in the 14 PBCRs was 154.3 per million; children 1–4 years of age had the highest incidence rates. The Brazilian PBCRs provide important information about pediatric cancer incidence in an emerging country. The observed incidence rates of childhood leukemia were similar to previous reported rates, and the age-specific incidence rates of retinoblastoma (0–4 years of age) were higher than those for developed countries. These data can be used as baseline incidence rates of childhood and adolescent cancer in Brazil in future epidemiological studies.

Worldwide cancer incidence in children varies from 100 to 180 per million children under 15 years of age and 210.42 per million in the group of adolescents between 15 and 19 years-old. There are considerable variations in occurrence of different types of cancer according to lower and higher income countries around the world.[1–4]

In poor resource countries, incidence data for pediatric cancer are not well-documented, due in part to the lack of infrastructure on which cancer registries are built. As the largest country in South America, Brazil is composed of 5 geographical macro regions (North, Northeast, Central-West, Southeast, and South), with population density, climate, and socioeconomic inequalities, making the establishment of cancer registries a challenge. At the end of the 1960s, PBCRs appeared in Brazil as result of isolated initiatives. Some PBCRs have successfully documented the incidence of childhood cancer within a limited geographic area of Brazil since 1967.[2,5] Since the 1980s, the Instituto Nacional de Câncer has promoted the establishment of cancer registries in distinct cities of Brazil, and there are now 20 PBCRs distributed in major cities of all regions of Brazil (www.inca.gov.br/cgi/sisbasepop.asp). In order to disseminate the information gained from these efforts, we analyzed the incidence childhood cancers according to the data contained in 14 PBCRs, using quality criteria that allow us to report descriptive epidemiological data for Brazil.

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Material Methods

Data sources

Data were extracted from the databases of 20 PBCRs located in 17 Brazilian capital cities, the Federal District, and 2 non-capital cities (Campinas and Jaú in São Paulo state). The period and population coverage for each PBCR are displayed in Figure 1. Information contained in the registries for each patient included patient name, patient's mother's name, date of birth, diagnosis, sex, full residence address, histopathology, basis of diagnosis, and site of tumor. The underlying population-at-risk for each region was obtained from the Instituto Brasileiro de Geografia e Estatística (http://www.ibge.gov.br/home).

Case definition

Cases with confirmed diagnosis of cancer were collected and assigned a morphology and topography code as per the International Classifications of Disease for Oncology (ICD-02), except for Campinas' PBCR, which used the ICD-01 during 1991–1993.[6] The different types of cancer were then grouped into 12 major diagnostic groups according to the International Classification of Childhood Cancer (ICCC). Benign tumors were excluded except for those of the central nervous

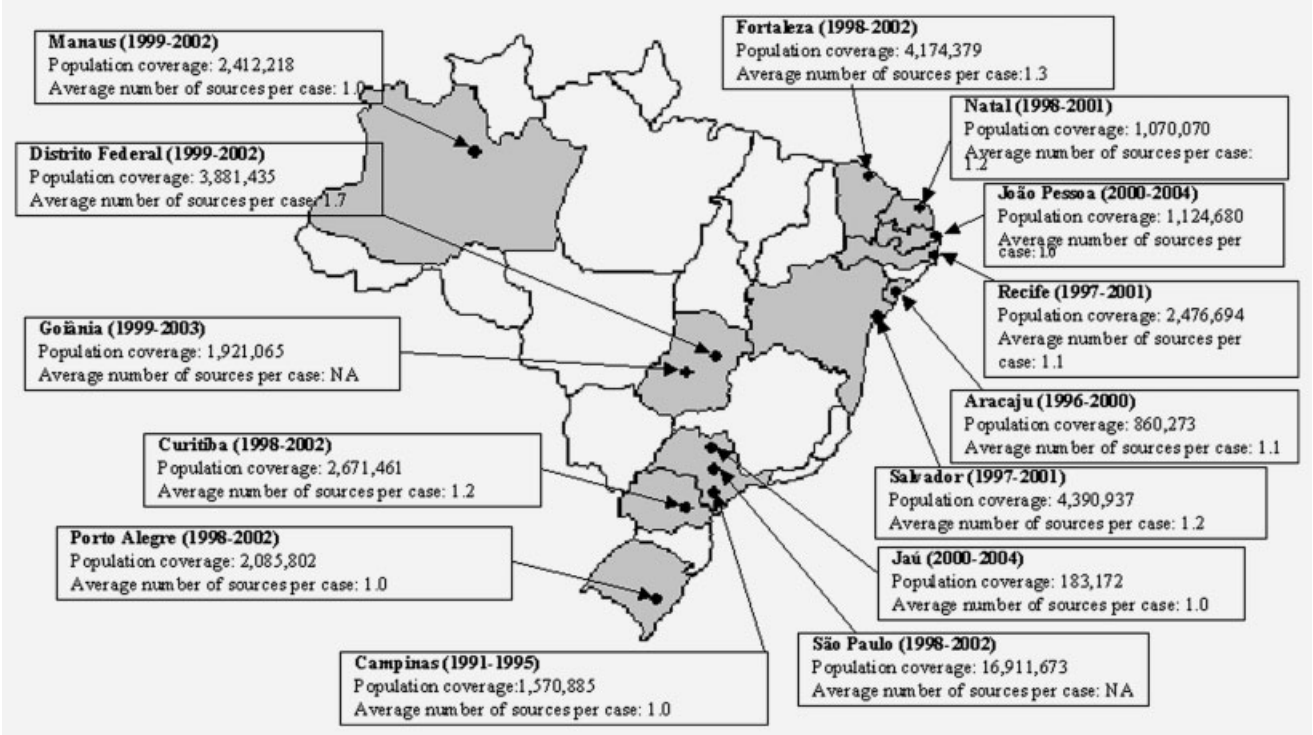

Figure 1. Illustration of the location of 14 Brazilian Population-Based Cancer registry.

system and miscellaneous intracranial and intraspinal neoplasm (ICCC group III), as per international recommendations.[7] The International Agency for Research in Cancer (IARC) parameters regarding quality data are proportion of cases diagnosed with microscopic verification greater than 70% and diagnosis performed only *via* death certificate less than 20%.

Data from all PBCRs included were reviewed from data entry to selection of eligible cases according to a consistency checklist. The variables evaluated were compatibility between anatomical site and sex, anatomical site and morphology, morphology and extension of the disease, date of birth and date of diagnosis, tumor site and age, morphology and age, date of death (if it had occurred), date of birth, and date of diagnosis.

To avoid mismatch between cases and population at risk a double check were performed by automated record linkage, comparing cases ascertainment according to home address included only covered area, mothers' names and child's date of birth, gender and disease characteristics. Then a second data check was performed manually.

Statistical methods

Age-adjusted incidence rates (AAIR) were estimated by the direct method using the world population proposed for age groups less than 20 years.[8] The incidence rate per 1,000,000 inhabitants refers to the risk of new cases. For all 14 PBCRs included, analyses included the number of new cases, the absolute and relative values, age-adjusted incidence rates (AAIR) and AAIRs according to tumor type, sex, and age range. Age range was stratified into five groups: younger than 1 year of age; 1–4 years of age; 5–9 years of age; 10–14 years of age, and 15–19 years of age.

Results

Six PBCRs were excluded from the analysis. Three did not meet the standards criteria recognized by the IARC (Belém, Palmas, and Cuiabá) and, 3 PCBRs because the data covered less than 3 years (Vitória, Belo Horizonte, and Campo Grande). The median incidence rate of childhood cancer in the 14 PBCRs was 154.3 per million; children 1–4 years of age had the highest incidence rate.

For children younger than 1 year of age, the highest rate was seen in Campinas with AAIR of 223.5 per million. Among adolescents 15–19 years of age, the highest rates were in São Paulo (264 per million), Goiânia (251 per million), and Porto Alegre (229 per million). Children 1–4 years of age had the highest rates in the majority of PBCRs (Table 1). As shown in Table 1, in all PBCRs except in Fortaleza and Jaú, the AAIR of childhood cancer was slightly higher in males (M) than females (F), with an M/F ratio of 0.81–1.37.The AAIRs of all pediatric cancers for both genders varied from 92 per million (Salvador, Bahia) to 231 (Goiania, Goiás) per million.

Table 1. Incidence of cancers in children and adolescents according to age and gender

	Rate per million									
Region	0	1–4 yrs	5–9 yrs	10–14 yrs	15–19 yrs	0–14 yrs	0–19 yrs	Ratio M/F	%MV	Total Number of Cases*
South										
Curitiba	145.12	268.89	186.57	113.68	216.29	187.69	194.13	1.17	83.4	538
Porto Alegre	152.54	251.96	150.64	169.88	229.18	187.75	197.07	1.37	82.1	436
Southeast										
Campinas	223.55	180.66	98.66	101.69	115.97	134.61	130.41	1.24	90.9	208
Jaú	0.00	289.60	132.74	100.97	141.39	168.29	157.22	0.81	100.0	29
São Paulo	188.80	231.41	163.99	161.38	264.10	186.03	203.60	1.17	83.7†	3,667
Northeast										
Aracaju	75.04	191.34	108.97	123.87	141.89	136.18	137.46	1.05	84.6	123
Fortaleza	82.02	144.29	104.17	105.90	186.96	115.38	131.49	0.88	88.4	587
João Pessoa	93.23	213.50	92.88	88.12	171.76	128.88	138.53	1.31	95.1	162
Natal	116.31	193.37	104.61	148.90	158.31	145.86	148.66	1.06	80.8	167
Salvador	79.15	137.22	69.39	81.66	83.55	94.72	92.20	1.21	93.4	417
Recife	129.82	222.07	137.57	162.65	164.47	170.42	169.08	1.07	85.1	436
North										
Manaus	125.50	209.84	159.40	118.03	150.95	160.39	158.26	1.30	79.5	397
Middle-West										
Distrito Federal	77.67	183.98	148.30	138.66	152.42	151.08	151.38	1.06	84.1	620
Goiânia	315.19	274.20	221.14	157.03	251.40†	226.24	230.98†	1.16†	92.0†	435
Total Number of Cases	338	1,917	1,630	1,677	2,660	5,562	8,222			

MV, microscopic verification; yrs, years.
*The total number of cases does not represent Brazil as a whole; the PBCR were mainly in capital cities. †Include only up to 18 years old.

Overall, the most common cancer types were leukemia (18–41%), lymphoma (13–24%), and central nervous system (CNS) tumors (7–17%). The highest AAIRs of leukemia were seen in Goiania (67.5 per million), Manaus (67 per million), and Curitiba (64 per million), whereas, the lowest AAIRs were seen in Salvador (21 per million) and Aracaju (27 per million). The highest AAIRs for lymphomas were in Jaú (39 per million), followed by Goiânia (34 per million; Table 2). CNS tumors were more common in Porto Alegre and Goiania (32 per million). CNS tumors were the third most common tumor in all PBCRs except those in Porto Alegre, Campinas and Aracaju. Retinoblastoma had a relatively high incidence in almost all registries. The AAIRs of retinoblastoma varied from 2.4 in Distrito Federal to 9.8 in Natal. Among children 0-4 years of age, higher AAIRs for retinoblastoma were found in Natal (27.0 per million), Jaú (23.0 per million), Goiania (21.5 per million), São Paulo (21.5 per million), Porto Alegre (19.4 per million), Manaus (15.0 per million), and Salvador (14.6 per million). The AAIRs of bone cancer were highest in São Paulo (18.2 per million), João Pessoa (12.4 per million), and Goiania (16 per million). Among adolescents 15–19 years of age, the AAIR in São Paulo was 35.5 per million (data not shown).

Among all 14 PBCRs, there were 11 cases of adrenocortical carcinoma (ACT) (five in São Paulo, three in Curitiba, two in Campinas, and one in Manaus), with AAIRs ranging from 0.34 in São Paulo to 1.57 in Campinas.

Discussion

This report is the first descriptive analysis of PBCR data on childhood cancer in Brazil, covering 15% of Brazil's child and adolescent population. Children and adolescents make up 38% of the entire population of Brazil, and the North and Central-West regions have the highest population growth rates. The successful institution of multiple PCBRs in different regions of Brazil demonstrates the feasibility of establishing these types of registries in other countries subject to various cultural and socioeconomic constraints. Cancer registries in developing countries are vulnerable to several common technical problems that could jeopardize the quality of the data collected. However, since 1990, support provided by the Brazilian government has allowed for the implementation of quality control

Table 2. Incidence rates of cancer in children and adolescents (≤19 years) in 14 PBCR in brazil according to ICCC-3 groups

Region	Leuk. AAIR	Lymph. AAIR	CNS tu. AAIR	Neurobl. AAIR	Retinobl. AAIR	Renal AAIR	Liver AAIR	Bone AAIR	Soft tissue AAIR	Germ cell AAIR	Carcinomas AAIR	Others AAIR	Neoplasms AAIR	Cases
South														
Curitiba	64.22	26.59	25.98	10.98	2.73	5.21	0.57	9.44	11.80	16.63	16.33	3.66	194.13	538
Porto Alegre	48.01	28.91	32.45	9.16	5.86	13.25	2.15	9.79	15.75	10.14	14.09	7.50	197.07	436
Southeast														
Campinas	35.51	17.09	20.62	4.41	5.90	7.44	1.17	6.48	16.00	3.76	10.99	1.04	130.41	208
Jaú	53.77	39.01	21.00	0.00	6.95	0.00	0.00	0.00	8.52	11.49	16.47	0.00	157.22	29
São Paulo	47.50	30.58	29.41	7.72	7.04	9.19	1.31	18.20	12.92	8.79	17.83	13.09	203.60	3667
Northeast														
Aracaju	26.84	19.60	21.81	5.43	5.43	10.95	1.50	9.37	10.89	7.03	16.57	2.05	137.46	123
Fortaleza	37.91	18.97	13.40	1.86	2.76	5.75	0.24	9.96	6.69	4.02	15.21	14.73	131.49	587
João Pessoa	34.63	22.53	15.74	2.74	3.34	9.59	0.00	12.41	8.82	2.80	19.02	6.91	138.53	162
Natal	47.45	29.67	9.60	4.29	9.82	4.02	0.00	6.89	3.32	4.90	19.52	9.17	148.66	167
Salvador	21.36	13.57	10.92	3.82	5.11	8.22	2.42	5.90	7.12	3.58	7.27	2.92	92.20	417
Recife	48.53	24.13	22.85	8.67	3.87	10.42	1.58	8.25	9.39	4.60	10.08	16.71	169.08	436
North														
Manaus	67.36	24.56	18.43	1.80	4.53	4.90	1.57	10.12	4.27	3.84	7.48	9.39	158.26	397
Middle-West														
Distrito Federal	29.03	22.69	22.91	4.67	2.40	8.64	0.79	9.62	6.63	7.39	16.53	20.08	151.38	620
Goiânia*	67.51	34.21	31.98	9.34	6.78	15.32	2.77	15.98	15.41	7.80	18.21	5.68	230.98	435
Number of Cases	2,044	1,291	1,106	250	207	352	58	669	514	375	837	519		8,222

AAIR, Age-ajusted incidence rate (per million); Leuk., Leukemia; Lymph., lymphomas; CNS Tu., central nervous system tumors; neurobl., neuroblastoma; Retinobl., retinoblastoma.
*Include only up to 18 years old.

procedures and staff training and has increased number of PBCRs providing crucial information about the cancer burden in Brazil. Comparing the present data analysis with previous rather scanty publications on childhood cancer in Brazil,[2] more information's were added representing registries across most regions of the country. For instances, the increase of incidence in Goiania (120 to 226.2 per million)[2] in the age range 0–14 years old were clearly observed herein. One of the possible explanations for such differences within the Brazilian population could be the recent improvement of access to health care and modern diagnostic procedures. Well-established cooperative groups with ongoing protocol for treatments of acute leukemia, Wilms' tumor, retinoblastoma, osteossarcoma and other rare tumors have potential impact on the recognition of such diseases.[9,10]

Data from 39 National Program of Cancer Registries and five Surveillance, Epidemiology, and End Results (SEER) registries, representing more than 90% of the United States population, reported an AAIR of 151 per million for children 0–14 years of age and 210 per million for adolescents 15–19 years of age.[1] In Eastern Europe, the AAIR of childhood cancer was slightly higher than that in the Western European countries (143 per million *vs.* 140 per million), but among adolescents, the AAIR was slightly lower in the east than in the west (166 per million *vs.*198 per million).[4]

In Brazil, the highest AAIRs were seen in Goiânia and São Paulo and the lowest were seen in Salvador, Fortaleza, and Campinas. Leukemia, lymphoma, and CNS tumors were the most frequent malignancies in all registries. Despite the small number of cases and the short data collection period, the PBCR in Jaú reported a very high incidence of childhood leukemia (52 per million) and lymphoma (41 per million), suggesting the influence of some region-specific environmental factor. Shoe manufacturing is the main economic activity in Jaú. Although previous reports have suggested that shoemaker occupation is associated with leukemia in adults the association with childhood and adolescent remain to be elucidated.[11] Certainly, the data reported herein underscore the need for further epidemiological studies in this regard.

In some of the Brazilian PBCRs, CNS tumors were the second most common childhood tumor. This observed increase in incidence could be due to increased access to better imaging facilities. Indeed, since the late 1990s there has been an increasing demand for brain computer tomography studies (www.datasus.gov.br).

Previously reported data from the São Paulo PBCR showed elevated incidence rates of osteosarcoma and Wilms tumors in that region, and according to our analysis, these rates remain high.[12,13] Interestingly, data from this current analysis indicate that Goiania had an even higher incidence of Wilms tumors than did São Paulo.

There are considerable worldwide variations in the incidence of retinoblastoma. In the United States and Europe, the incidence rate in children 0–14 years of age is 4.0 per million; among children age 0–4 years of age, the incidence rate is 10–12 cases per million.[14,15] Higher incidence rates have been reported for other developing areas such as Malawi, Africa, and Colombia.[2,16,17] In Chiapas, Mexico, the incidence of retinoblastoma has been reported as high as 21 per million.[18] In seven of the 14 Brazilian PBCRs, the AAIR of retinoblastoma for children 0–4 years of age was greater than 11 cases per million (range: 15 in Salvador to 27 in Natal).

In general, childhood carcinomas are rare, with an incidence rate less than one per million. The incidence rate of adrenocortical carcinoma (ACT) in São Paulo was 1.5 per million, more than three times the rate in most registries.[19] Almost all cases of ACT registered were diagnosed in the Southern cities. This data corroborate with previous report.[20]

The incidence, prevalence, mortality, and survival rates for the various cancers are important indicators of the quality of the healthcare system. Thus, data from the PBCR initiative provide important benchmarks for pediatric oncology care in Brazil. The data reported herein provide baseline incidence rates of childhood and adolescent cancer for use in future epidemiological studies.

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References

1. Li J, Thompson TD, Miller JW, Pollack LA, Stewart SL. Cancer incidence among chil and adolescents in the United States, 2001–2003. *Pediatrics* 2008;121:e1470–77.
2. Parkin DM, Kramarova E, Draper G, Masuyer E, Michaelis J, Neglia J, Qureshi S, Stiller C, editors. International incidence of childhood cancer. Lyon (France): International Agency for Research on Cancer; 1998. v. II. Scientific Publications No.: 144. 391 p.
3. Ries LAG, Smith A, Gurney JG, Linet M, Tamra T, Young JL, Bunin GR, editors. Cancer incidence and survival among children and adolescents. Bethesda MD (United States): SEER Program 1975–1995, National Cancer Institute; 1999. NIH Pub. No.: 99–4649.
4. Steliarova-Foucher E, Stiller C, Kaatsch P, Berrino F, Coebergh JW, Lacour B, Parkin DM. Geographical patterns and time

trends of cancer incidence and survival among children and adolescents in Europe since the 1970s (the ACCIS project): an epidemiological study. *Lancet* 2004;364: 2097–105.
5. Parkin DM, Stiller CA, Draper GJ, Bieber CA. The international incidence of childhood cancer. *Int J Cancer* 1988;42: 511–20.
6. Percy C, Van Holten V, Muir C, editors. International Classification of Diseases for Oncology. 2nd ed. Geneva (Switzerland): World Health Organization; 1990. 144 p.
7. Kramarova E, Stiller CA. The international classification of childhood cancer. *Int J Cancer* 1996;68:759–65.
8. Doll R, Payne P, Waterhouse JAH, editors. Cancer incidence in five continents. Geneva, UICC; Berlin: Springer, 1966. vol. 1.
9. Petrilli AS, de Camargo B, Filho VO, Bruniera P, Brunetto AL, Jesus-Garcia R, Camargo OP, Pena W, Péricles P, Davi A, Prospero JD, Alves MT, et al. Brazilian Osteosarcoma Treatment Group Studies III and IV. Results of the Brazilian Osteosarcoma Treatment Group Studies III and IV: prognostic factors and impact on survival. *J Clin Oncol* 2006;24:1161–8.
10. Pombo de Oliveira MS, Koifman S, Vasconcelos GM, Emerenciano M, de Oliveira Novaes C. Brazilian Collaborative Study Group of Infant Acute Leukemia. Development and perspective of current Brazilian studies on the epidemiology of childhood leukemia. *Blood Cells Mol Dis* 2009;42:121–5.
11. Fu H, Demers PA, Costantini AS, Winter P, Colin D, Kogevinas M, Boffetta P. Cancer mortality among shoe manufacturing workers: an analysis of two cohorts. *Occup Environ Med* 1996;53: 394–8.
12. Parkin DM, Stiller CA, Nectoux J. International variations in the incidence of childhood bone tumours. *Int J Cancer* 1993;53:371–6.
13. Stiller CA, Parkin DM. International variations in the incidence of childhood renal tumours. *Br J Cancer* 1990;62: 1026–30.
14. Broaddus E, Topham A, Singh AD. Incidence of retinoblastoma in the USA: 1975–2004. *Br J Ophthalmol* 2009;93:21–3.
15. MacCarthy A, Draper GJ, Steliarova-Foucher E, Kingston JE. Retinoblastoma incidence and survival in European children (1978–1997). Report from the Automated Childhood Cancer Information System Project. *Eur J Cancer* 2006;42: 2092–102.
16. BenEzra D, Chirambo MC. Incidence of retinoblastoma in Malawi. *J Pediatr Ophthalmol* 1976;13:340–3.
17. Koulibaly M, Kabba IS, Cisse A, Diallo SB, Diallo MB, Keita N, Camara ND, Diallo MS, Sylla BS, Parkin DM. Cancer incidence in Conakry, Guinea: first results from the Cancer Registry 1992–1995. *Int J Cancer* 1997;70:39–45.
18. Fajardo-Gutiérrez A, Juarez-Ocana S, Gonzalez-Miranda G, Palma-Padilla V, Carreon-Cruz R, Ortega-Alvarez MC, Mejia-Arangure JM. Incidence of cancer in children residing in ten jurisdictions of the Mexican Republic: importance of the cancer registry (a population-based study). *BMC Cancer* 2007;7:68.
19. Parkin DM, Stiller CA, Draper GJ, Bieber CA, Terracini B, Young JL, editors. International incidence of childhood cancer. Lyon (France): International Agency for Research on Cancer; 1988. Scientific Publications No.: 87.
20. Pianovski MA, Maluf EM, de Carvalho DS, Ribeiro RC, Rodriguez-Galindo C, Boffetta P, Zancanella P, Figueiredo BC. Mortality rate of adrenocortical tumors in children inder 15 years of age in Curitiba, Brazil. *Pediatr Blood Cancer* 2006;47: 56–60.