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Cancer survival among children and adolescents in a brazilian reference service

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Abstract

Few studies have been found that report cancer survival in children and adolescents in Brazil over the years due to limited information. We aim to analyse the cancer survival time of children and adolescents (0-19 years) residents in Campinas, Southeastern Brazil diagnosed in 1996-2005, attended in the reference service of childhood cancer. This is a cohort retrospect study and the follow-up censored date was December 31, 2011. Cancers were classified according to the International Classification of Childhood Cancer Groups. By design, just the 4 most common groups were studied: Group I, Group II, Group III and Group IX. Kaplan-Meier estimation methods, log-rank test and Cox regression were used for survival analysis. A total of 180 cases were diagnosed during the study period. Significant differences in survival times were found by diagnostic groups adjusted for age and sex (p=0.001). In conclusion, five-year survival was higher in children than in adolescents similar to the findings reported in the literature.

Keywords

Neoplasms, survival, child health, adolescent's health

Introduction

Cancer is the name of group over than one hundred diseases with disorder cells grow (maligned) spread cells to organ and tissues (metastasis) for different body parts. The causes of cancer are variant, can be extern or intern related (Amador 2011).

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Childhood cancers (age at diagnosis 0–19 years) comprise a variety of malignancies, with incidence varying worldwide by age, sex, ethnicity and geography, which provide insights into cancer etiology (Gatta et al. 2014; Steliarova-Foucher 2017).

In developed countries, over the last four decades, advances in cancer treatment and in diagnostic techniques have resulted in an increased survival for children (ages 0-14 years) and adolescents (ages 15-19 years). It has been reported that in developed countries the 5-year survival increased from less than 30% in the 60s to approximately 80% in the 2000s for all childhood cancers (Gatta et al. 2014; Stiller et al. 2012).

In developing countries, the mortality rates are higher in Brazil, neoplasms corresponded to the second leading cause of death in children only surpassed by external causes INCA (2016).

Few studies have been found that report cancer survival in children and adolescents in Brazil over the years due to limited information on the date of death and the lack of active monitoring Silva et al. (2016) . Only from the historical knowledge about the occurrence of events will it be possible to implement care policies in order to understand the survival rates in specific regions.

In Brazil, the childhood cancer statistics have been less studied in the national medic literature, despite the existence of database liked by the Mortality Information System (SIM) from Health of Ministry and the Population Based-cancer registries (PBPCR) Morais De (2017).

For implementation of a qualified cancer registry, providing the access to care information as identification of epidemiological profile, providing comprehensive and accurate management.5

Epidemiological studies about the childhood cancer are rare in Brazil. This is resulted from the insufficient number of primary notice and registry that difficult to describe the clinical and epidemiological characteristics from these cases Grabois et al. (2011).

It is known that for cases of malignant neoplasms, the use of information about death is not enough to know the problem impact, because there are different types of cancer, and each of them has a different lethality and survival (Gatta et al. 2005). The knowledge respect of the and the profile of the incidence, clinical characteristics and survival depend of the

In the same way, some rare diseases, such as childhood cancer, need to be monitored. Although they have a low occurrence, their incidence can negatively affect the quality of life of children and adolescents, and a worse prognosis is found when there is no structured care network based on the needs population's. Thus, the production of information about the cancer survival and improvement of cancer registries contributes to the formulation of public health policies consistent with reality.

Therefore, this study analyses survival among children (0–14 years) and adolescents (15–19 years) residents in a Brazilian city, attended in the reference service of childhood cancer.

Material and methods

An observational retrospective study of a longitudinal cohort of children and adolescents (0 - 19 years), diagnostic with the Leukemias, Lymphomas, Central Nervous System tumors and soft tissue and other extra osseous sarcomas was conducted in Campinas, São Paulo, Brazil. This is an industrial city with approximately 1.1 million inhabitants IBGE (2022), located in the State of São Paulo. About 30% of the population living in Campinas is aged less than 19 years.

This retrospective coorth was conducted in the High Complexity Care Unit for Pediatric Oncology in Campinas, that is a main cancer care for children and adolescents, and was conducted with cases diagnosed in the period of 1996-2005, and mortality identified between 1996 and 2011.

Case definition

Data were retrieved of all children and adolescents residing in Campinas, aged 0–19 years who were diagnosed between January 1st, 1996 and December 31st 2005. Confirmed diagnosis of cancer was obtained from medical records, using the date of diagnoses of first primary tumors.

Cancers were classified according to the International Classification for Childhood Cancer, third edition (ICCC-3) (Inca, 2016). Benign tumors were excluded. By design, just the most common 4 groups were studied: Group I – Leukemias, myeloproliferative diseases, and myelodysplastic diseases, Group II - Lymphomas and reticuloendothelial neoplasms, Group III - CNS and miscellaneous intracranial and intraspinal neoplasms and, Group IX - Soft tissue and other extraosseous sarcomas.

Survival Analysis

Mortality data from 1996 to 2011 were confirmed, by examining the medical records linked to the Campinas's Mortality Registry and Health Mortality Information System, Department of Data and Information Technology, the information and statistics office of the Unified National Health System (SUS), representing the Ministry of Health (DATASUS, 2021).

The survival time was calculated as the difference between the date of diagnosis and the date of death or loss to follow-up. The analysis was performed with all cases followed until December 31, 2011. The follow-up for vital status was collected from the hospital medical records.

To calculate the lower and upper limits of the 95% confidence interval for a proportion. Survival in each group was analysed using Kaplan-Meier estimation methods. Log rank test was used to compare the survival curves (Kaplan 1958). The probability of five-year survival was estimated by Kaplan Meier method. Cox regression models were used for the uni and multivariable analyses, and assumptions of proportionality of hazards was verified by inspection of the log-hazard plots versus time (Kleinbaum 1995).

The analyses were performed using the software SPSS and R version 2.14.1 (Project for Statistical Computing).

Ethics approval and consent to participate

The study was conducted in accordance with the Resolution 466/2012 of the Brazilian National Health Council and was approved by CAAE number 0566.0.000.144-11 from Research Human Research Ethics Committee.

Results

A total of 180 cases were diagnosed, 85.6% children (n=154) and 14.4% adolescents (n=26). The median follow-up time in the cohort was 7.5 years (percentile 25:1.3; percentile 75: 11.5). Death was observed for 68 cases (37.8%). **Figure 1** shows the cumulative survival of children and adolescents by ICCC-3 and age groups. Statistically significant differences in the probability of survival were observed

according to diagnostic Group (p = 0.001), but not to age groups (p = 0.071). Group IX and Group III showed lowest survival rates with median estimated survival 2.89 years and 2.91 years, respectively.

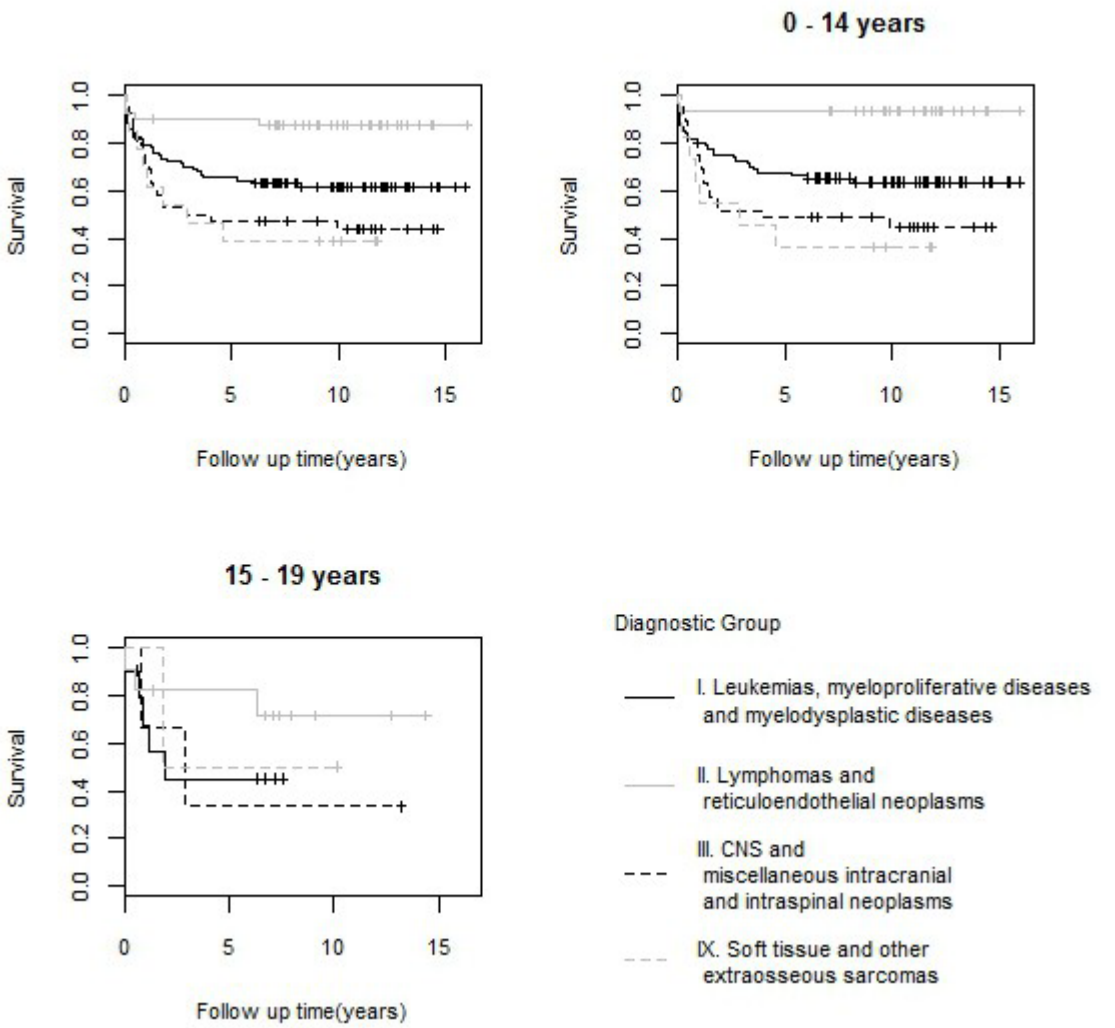

Figure 1. Estimates of survival probabilities by diagnostic and age groups among children and adolescents between 1996-2011 in Campinas, São Paulo, Brazil.

Overall, 5-year survival was 65.6% (95% CI: 57.4% - 72.9%) among children and 53.8% (95% CI: 33.7% - 72.8%) among adolescents (Table I).

The 5-year survival was higher than 80% for Group II, both in children and adolescents. The most favourable prognosis was observed for those with non-Hodgkin lymphomas except Burkitt lymphoma, with 91.7 % of children and 100% of adolescents alive 5 years after the diagnosis. The 5-year survival was lower than 40% among children for the diagnostic Group - IX, and among adolescents for the diagnostic Group III.

Table 1. Five-Year Survival children and adolescents residing in Campinas, São Paulo, Brazil: 1996-2011.

	Age (0 - 14 years)			Age (15-19 years)			Total (0 - 19 years)		
Diagnostic group	Nr. of cases	Survival* (%)	(CI95%)	Nr. of cases	Survival* (%)	(CI95%)	Nr. of cases	Survival* (%)	(CI95%)
I. Leukemias	**80**	**67.5**	**56.0 - 77.3**	**10**	**50**	**23.6 - 76.3**	**90**	**64.5**	**53.5 - 74.0**
Ia. Acute lymphoblastic	58	79.3		4	33.3		62	77.2	
Ib. Acute non-lymphoblastic	20	40.0		6	50		26	42.3	
Ic, d, e. Unspecified and other specified leukemias	2	0		0	_		2	0	
II.Lymphomas and reticuloendothelial neoplasm	**28**	**92.9**	**75.0 - 98.7**	**11**	**72.7**	**39.3 - 92.6**	**39**	**87.1**	**71.7 - 95.1**
IIa. Hodgkin lymphomas	8	87.5		5	100		13	92.3	
IIb. Non-Hodgkin lymphomas except Burkitt lymphoma	12	91.7		3	100		15	93.3	
IIc. Burkitt lymphoma	7	100		3	33.3		10	80	
IId, e. Unspecified lymphomas and miscellaneous lymphoreticular neoplasm	1	100		0	_		1	100	
III. CNS and miscellaneous intracranial and intr. neoplasm	**35**	**48.6**	**31.7 - 65.7**	**3**	**33.3**	**1.7 - 87.4**	**38**	**47.4**	**31.3 - 63.9**
IIIa. Ependymomas and choroid plexus tumor	8	62.5		0			8	62.5	
IIIb. Astrocytomas	17	58.8		1	100		18	61.1	
IIIc. Intracranial and intraspinal embryonal tumors	7	14.3		2	0		9	11.1	
III d, e, f. Other specified and unspecified intrarcranial and intraspinal neoplasms	3	33.3		2	_		5	33.3	
IX. Soft tissue and other extra osseous sarcomas	**11**	**36.4**	**12.3 - 68.3**	**2**	**50**	**2.6 - 97.3**	**13**	**38.5**	**15.1 - 67.7**
IXa. Rhabdomyosarcomas	9	33.3		2	50		11	36.4	
IXd, e. Other specified and unspecified soft tissue sarcomas	2	50.0		0	_		2	50	
Total	**154**	**65.6**	**57.4 - 72.9**	**26**	**53.8**	**33.7 - 72.8**	**180**	**63.9**	**56.3 - 70.8**

* Kaplan Meier 5-year survival estimate.

Table 2 shows the main results of Cox Regression models. The probabilities of overall survival for girls, adolescents, mother's and father's profession not specified, private health service, white ethnic group, were higher than those for other categories of these covariates, but not statistically different ($p > 0.05$).

Regarding the survival time, statistically significant differences were observed according to the diagnostic Groups adjusted for age and sex ($p=0.001$), with lower survival in the Group IX (HRadj =6.38 - Group IX vs Group II) followed by Group III (HRadj =6.27 Group III vs Group II) (Table 2).

Table 2. Cox Regression Analysis for Survival among children and adolescents residing in Campinas, São Paulo, Brazil: 1996-2011.

	Unadjusted hazard ratio				**Cox adjusted* hazard ratio (n= 180)**			
Covariates	**HR (exp(b1))**	**95% CI**		***p-value***	**HR (exp(b1))**	**95% CI**		***p-value***
Diagnostic Groups				*< 0.001*				***0.001***
II. Lymphomas	1				1			
IX: Soft tissue	6.22	2.031	19.045		6.388	2.084	19.580	
III. CNS Tumors	5.372	2.220	14.271		6.271	2.293	17.153	
I. Leukemias	3.408	1.333	8.717		3.851	1.480	10.020	
Sex				*0.86*				*0.529*
Male	1				1			
Female	1.041	0.644	1.685		0.851	0.498	1.381	
Age group				*0.518*				*0.154*
0-14	1				1			
15-19	1.237	0.648	2.362		1.620	0.790	32.010	
Mother's profession				*0.57*				
Low Level	1							
High Level	0.777	0.354	1.701					
Not specified	1.653	0.518	5.28					
Father's profession				*0.907*				
Low Level	1							
High Level	0.873	0.454	1.676					
Not specified	1.037	0.470	2.288					
Public Health service				*0.299*				
Yes	1							
No	1.301	0.787	2.151					
Ethnic group				*0.214*				
Not White	1							
White	1.526	0.780	2.986					

*Adjusted for age and sex

Discussion

This study analysed the childhood cancer survival in Campinas, São Paulo, Brazil, showing that adolescents survive less than children. The most frequent childhood cancer adjusted by age was Group I – Leukaemia (28.8 per million), followed by Group III - CNS and miscellaneous intracranial and intraspinal neoplasm (11.9 per million).

Considering that characteristics such as frequency and cancer type distribution in children and adolescents are unique and different from those observed at any other age-group, it has been recommended that epidemiological studies of childhood cancer are performed separately from other age groups (Carreira et al, 2012).

In Campinas, similarly to results from previous European Registries reports, the most frequent childhood cancer is Group I, representing standardized incidence rates lower than those of the majority of European countries but similar to Portugal (28.0 per million), Poland (29.9 per million) and Romania (28.3 per million) (Who, 2014). In addition, the distribution of cases among sex, age and the four most common Groups of disease are similar to those found in other Brazilian studies and reported by 14 Brazilian Population-based Cancer Registries – PBCRs (Oliveira et al, 2020; Saraiva, Santos & Monteiro, 2018).

Acute lymphoblastic - ALL, Acute non-lymphoblastic, Astrocytomas, Hodgkin lymphomas were the most frequent diagnoses in Campinas, both in children and adolescent's studies, findings already reported in the literature (Oliveira et al, 2020; Steliarova-Foucher et al, 2018).

Compared to European countries, the largest differences in incidences were observed for Group III and Group IX, besides might indicate a deceleration in the increase of cancer incidence, although the registry datasets included differ somewhat between the studies (Steliarova-Foucher et al, 2018). In other hand, that's lower rate could suggest the reduced reporting discipline or other factors. For the knowledge reference on epidemiological profile of incidence and cancer survival is important to improve the studies for populations of smaller sizes, as been done in Europe (Steliarova-Foucher et al, 2018).

These differences may be explained by the type of tumour (solid) affecting mainly adolescents, who could have been treated elsewhere or confounded as young adult cases and not referred to the High Care Unit complexity in Pediatric Oncology.

Although incidence rates in the four diagnostic groups studied differs from the observations of PBCRs from developed countries, they are similar to those found in the literature for developing countries, including Brazil (Oliveira et al, 2020; Steliarova-Foucher et al, 2018).

A limitation of the study is the data source because a single childhood oncology service was used, and even though it had an 85% coverage of the cases of city dwellers, there were still other possible individuals who were not included in the analysis.

The creation of efficient monitoring system for cancer, in particular for rare cases of childhood cancer, is necessary across the healthcare networks and would greatly potentiate the value of spatial analysis permitting for more precise results. When investigated the cancer Incidence rates and the Standardized Morbidity Rates (SMR) spatial patterns in the same Brazilian city, the showed that results are agreement with previous reports from other cancer study and can be paramount in the definition of intervention programs for the region (Oliveira-Friestino et al, 2018).

Data from the EUROCARE-5 (Gatta et al, 2005; Gatta et al, 2009; Gatta et al, 2014), involving children under 15 years diagnosed with cancer between 1978 and 2007, pointed slightly higher Five-year survival. Nevertheless, in our study, the 5-year survival of children diagnosed with ALL (79.3%) and Non-Hodgkin lymphomas (87.5%), were substantially higher than those reported for the Eastern Europe countries (69.7% and 64.2%, respectively) and for all Group III not much different from those observed in the present study (Gatta et al, 2014).

In the Cox Regression analysis for survival of these four major groups significant differences in survival time were found in terms of diagnostic Groups adjusted for age and sex (p=0.001), similar to studies in developing countries (Gatta et al, 2014; Zouain-Figueiredo, Zandonade & Amorim, 2013).

It is known that for cases of malignant neoplasms, the use of information about death is not enough to know the problem impact, because there are different types of cancer, and each of them has a different lethality and survival (Inca, 2016). Thus, early diagnosis and initiation of immediate treatment can influence cancer patients' survival, as it is often possible that the outcome of treatment may lead to a good prognosis (Lima, 2018).

However, the inclusion of children and youth cancer in Public Health becomes a useful strategy to improve Health Information Systems, seeking to assess health conditions in different cancer groups, as well as contributing to early diagnosis and also to monitor the survival of existing cases (Silva, 2016).

In conclusion, incidence in the majority diagnostic groups in Campinas was similarly to previous reports from other Cancer Registries. The Five-year survival estimated for adolescents was higher than in children. The study of the cancer incidence rates can be used as baseline indicators of the quality of the healthcare system and as a framework for future improvements and health planning.

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