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Lymphoma subtype incidence rates in children and adolescents: First report from Brazil

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ABSTRACT

Background: Lymphoma is the third most common pediatric malignancy. The purpose of this study was to analyze the incidence rates of lymphoma in children and adolescents in Brazil.
Methods: All cases of Hodgkin lymphoma (HL), non-Hodgkin lymphoma (NHL), and Burkitt lymphoma (BL) were extracted from 14 population-based cancer registries (PBCRs) from 2000 to 2005, and included children and adolescents 0–19 years old. Analyses included age-adjusted incidence rates (AAIRs) and age-specific incidence rates (ASIRs) by each PBCR. A social exclusion index (SEI) was built and used as proxy for socioeconomic status (SES) levels. Correlations between SES and incidence rates were investigated using Spearman's test.
Results: The median incidence of lymphoma was 22.7/million. AAIRs of lymphomas varied from 12.9 (Salvador) to 34.5 per million (São Paulo). Median AAIR was 8.8/million, 9.8/million, and 2.9/million for NHL, HL, and BL, respectively. In all PBCRs except that of Recife, AAIR was slightly higher in males than females. The median ASIR was highest for HL (18.5/million) at 15–19 years for both genders. For NHL there were two peaks for ASIR: 11.1/million (1–4 years of age) and 13.2/million (15–19 years of age). The median ASIR for BL was highest among children aged 1–4 years (4.7/million) and in males. Higher SEI correlated with higher incidence of HL ($P = 0.06$), whereas rates of NHL and BL did not correlate with SEI. Borderline different incidence rates were observed in HL correlated with cities with higher SEIs.
Conclusion: Incidence rates of lymphomas in Brazil do not differ compared to rates reported worldwide, although SES differences deserve further investigation.

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1. Introduction

Lymphoma in children and adolescents comprises a heterogeneous group of malignant diseases of lymphoid tissues. The various lymphoma diagnoses present with distinctive biological and epidemiological features; it is therefore recommended that they are investigated separately. There are substantial variations worldwide in the incidence of childhood malignancies, among which lymphomas are a dominant type [1].

In developed countries, lymphoma is the third most common pediatric malignancy after leukemia and brain tumors. There is a 1.5–2.0-fold male predominance in all ages for non-Hodgkin lymphoma (NHL). Both Hodgkin lymphoma (HL) and NHL are rarely diagnosed in children younger than 5 years. Among NHLs, age-specific incidence varies according to histological subtype. Burkitt's lymphoma (BL) occurs in children between the ages of 5 and 15 years, whereas NHL, mainly lymphoblastic, occurs more commonly in older children and adolescents. HL is more common in children older than 10 years, making the incidence almost twice that of NHL in children between the ages of 15 and 19 years [2].

Data on the incidence of childhood NHL need to be explored, particularly in less developed countries [3]. Temporal studies from the United States and the Manchester Children's Tumour Registry in the United Kingdom report that the childhood incidence rate of NHL has been relatively stable [1,4,5].

Data regarding the incidence of lymphoma in less developed nations are scarce. In Africa, lymphomas account for almost one half of childhood cancers, with the majority being BL [6]. In Brazil, a recent population-based study demonstrated that lymphoma

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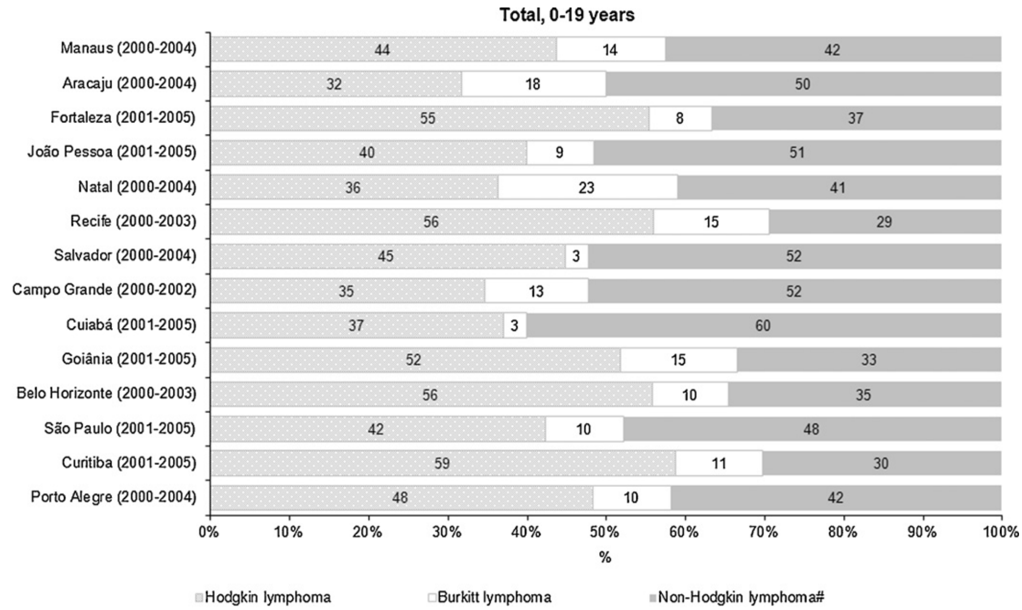

Non-Hodgkin lymphoma (II.b, 79%), that includes Miscellaneous lymphoreticular neoplasms (II.d, 4%), Unspecified lymphomas (II.e, 17%), but Burkitt lymphoma.

Fig. 1. The percentage ratio distribution of lymphoma subtypes in Brazil, 2000–2005.

corresponded to the second most common childhood cancer [7]. These data led us to analyze the lymphoma incidence rates (HD, NHL, and BL) in children and adolescents (<19 years) and to evaluate their correlation with socioeconomic status (SES) in Brazil.

2. Materials and methods

2.1. Study population

Cases were extracted from the databases of 14 population-based cancer registries (PBCRs) located in 14 major Brazilian cities (Fig. 1, supplementary). Databases contain the period and population coverage for each PBCR, as well as the social exclusion index (SEI). The incidence rates of lymphoma in children and adolescents <19 years of age were collected for the period 2000–2005. 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 gender, 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 occurred), date of birth, and date of diagnosis. To avoid mismatches between cases and population at risk, a double check was performed by automated record linkage, comparing case ascertainment according to home address (included only in the covered area), mothers' names and children's date of birth, gender, and disease characteristics. Then a second data check was performed manually [7]. Case definitions with confirmed diagnosis of cancer were assigned a morphology and topography code as per the International Classifications of Disease for Oncology 2nd edition (ICD-O2) [2] 2000–2004 and ICD-O3 [8] 2005. The different types of lymphoma were then grouped according to the International Classification of Childhood Cancer (ICCC) [9]. Lymphoma was subdivided into three major groups for the analysis: HL, NHL and BL. In the NHL group the following categories were included: NHL (II.b), the miscellaneous lymphoreticular neoplasms (II.d), and unspecified lymphoma (II.e) according to the ICCC. The underlying population at risk for each region was obtained from the Instituto Brasileiro de Geografia e Estatística (http://www.datasus.gov.br).

2.2. Statistical analysis

Analyses included examination of the number of new cases, age-adjusted incidence rates (AAIRs), and age-specific incidence rates (ASIRs) by each PBCR. AAIRs according to lymphoma subtype (HL, NHL, and BL), gender, and time period were calculated with a direct method using the proposed world population by age groups of less than 19 years. For ASIRs according to lymphoma subtypes, gender and time period were calculated by age and age group: <1, 1–4, 5–9, 10–14, and 15–19 years. In the 14 Brazilian PBCRs coverage was limited to the capital city, so it was not possible to obtain an arithmetic average for the entire country. The distribution of lymphoma incidence rates by PBCR was used to obtain the median parameter. Thus, the incidence rates were orderly. The median represented the value referent to 50% of the accumulated distribution. The median was used to measure central tendency in order to obtain an overall assessment of incidence rates (AAIR and ASIR). Median ASIR was calculated by lymphoma subtype, gender, and age group.

The social exclusion index (SEI) was built on the basis of three dimensions: suitable life conditions, knowledge, and youth vulnerability. The first dimension includes a poverty indicator (percentage of family heads with insufficient income in each city), an employment indicator (percentage of individuals aged >10 years working legally), and an inequality indicator (percentage of family heads with a monthly income in US dollars >$1000 and ≤1000. The second comprises two indicators: literacy (percentage of the population aged ≥5 years that is able to read and to write) and years of study (mean number of years of study for family head), and the last dimension includes a youth indicator (percentage of the population aged ≤19 years) and a violence indicator (homicides rate per 100,000 habitants). The SEI – which is a synthesis of all three dimensions of social exclusion – was obtained through the sum of the seven partial scores, which were weighted as follows: poverty (17.0), employment (17.0), literacy (5.7), education (11.3), youth (17.0), and violence (15.0) [10].

Cities were classified according to SEI with scores ranging from 0 (minimum) to 1 (maximum), where a higher SEI score indicates better socioeconomic status. Correlations between SEI and incidence rates were investigated using Spearman's test. Wilcoxon's test was

Table 1
Age-adjusted incidence rates for lymphomas in Brazilian PBCR, by gender according to lymphomas subtype.

Regions	PBCR (period)	*n*	Ratio M/F			HL[a]			NHL#[b]			BL[c]			Total lymphomas[d]
			M	F	Total	M	F	Total	M	F	Total	M	F	Total	
North	Manaus (2000–2004)	73	1.61	11.04	7.62	9.29	13.70	4.73	9.15	1.94	4.11	3.05	26.69	16.46	21.49
Northeast	Aracaju (2000–2004)	22	1.75	5.35	7.18	6.28	15.39	8.33	11.85	9.43	0.00	4.77	30.17	15.51	22.90
	Fortaleza (2001–2005)	101	1.35	11.73	11.36	11.51	10.76	5.48	8.13	3.17	1.12	2.16	25.66	17.96	21.80
	Natal (2000–2004)	22	1.75	8.07	2.59	5.32	4.41	8.37	6.42	7.99	0.00	4.06	20.46	10.96	15.80
	Recife (2000–2003)	41	1.05	7.97	11.06	9.58	7.43	4.63	6.02	3.32	2.56	2.90	18.72	18.25	18.50
	Salvador (2000–2004)	69	1.65	6.59	4.89	5.72	9.10	4.51	6.79	0.46	0.48	0.47	16.15	9.88	12.98
	João Pessoa (2001–2005)	35	1.92	11.53	8.73	10.14	24.27	9.26	16.83	3.08	1.44	2.25	38.87	19.43	29.21
Middle-West	Campo Grande (2000–2002)	23	4.75	14.38	4.18	9.37	26.63	3.33	15.09	5.34	3.33	4.33	46.35	10.85	28.79
	Cuiabá (2001–2005)	35	2.18	10.98	4.92	7.97	17.92	9.75	13.82	1.69	0.00	0.86	30.59	14.67	22.66
	Goiânia (2001–2005)	54	2.00	17.49	6.83	12.26	10.37	6.22	8.30	6.21	1.75	4.03	34.08	14.81	24.59
Southeast	Belo Horizonte (2000–2003)	84	2.11	17.64	8.27	12.97	12.73	4.55	8.64	3.30	2.26	2.78	33.67	15.08	24.39
	São Paulo (2001–2005)	668	1.73	17.00	10.76	13.89	21.40	11.97	16.69	5.62	2.18	3.92	44.02	24.91	34.50
South	Curitiba (2001–2005)	73	1.52	16.56	9.20	12.92	6.52	7.21	6.84	4.08	1.37	2.75	27.16	17.79	22.51
	Porto Alegre (2000–2004)	60	1.50	14.83	7.76	11.32	12.32	9.26	10.79	2.06	4.28	3.15	29.22	21.30	25.27
Median		57	1.74	11.63	7.69	9.86	12.52	6.71	8.89	3.31	1.59	2.97	29.69	15.98	22.78

Abbreviations: PBCR, population-based cancer registry; HL, Hodgkin lymphomas; NHL, non-Hodgkin lymphomas#; BL, Burkitt lymphoma; *n*, total number of cases include HL, NHL#, BL; M, male; F, female; # non-Hodgkin lymphomas (II.b, 79%), that includes miscellaneous lymphoreticular neoplasms (II.d, 4%), unspecified lymphomas (II.e, 17%), but Burkitt lymphoma; differences between gender.
[a] HL, $p = 0.0035$ (Wilcoxon test).
[b] NHL, $p = 0.0024$.
[c] BL, $p = 0.0067$.
[d] Total lymphomas, $p = 0.0000$ (*t*-test).

applied to test the differences between gender/age and lymphoma subtypes; 95% confidence intervals (CIs) were calculated using the Poisson approximation, or exactly when less than 30 cases were observed.

3. Results

The catchment area covered and time-points of data collection for all 14 PBCRs represented 14% of the total Brazilian population restricted to the main metropolitan areas; it was not possible to obtain an arithmetic average for the entire country because these PBCRs cover only the capital city. The period analyzed was from 2000 to 2005, and collected data were obtained consecutively for at least 3 years in the five different geographical regions. AAIRs in both genders of all cases of lymphoma in the 14 PBCRs varied from 12.9 to 34.5 per million, being lower in Salvador (12.9, CI 95% 9.86–16.10) and higher in São Paulo (34.5, CI 95% 31.85–37.14), João Pessoa (29.2 CI 95% 19.31–39.12), Campo Grande (28.8, CI 95% 16.81–40.76), and Porto Alegre (25.3, CI 95% 18.77–31.77). The AAIR was higher in males (M:F ratio of 1.35:4.75) with the exception of one city, where gender was equally distributed. Median AAIR was 22.7 per million for all lymphomas, 9.8 per million for HL, 8.8 per million for NHL, and 2.9 per million for BL (Table 1 and Supplementary Table 1). The percentage ratio distribution of the main lymphoma subtypes is shown in Fig. 1. HL was the most common subtype in seven PBCRs (43–59%), whereas NHL was the most common in seven PBCRs including Natal (41%) to Cuiabá (60%). BL represented 3% in Salvador and Cuiabá and 23% in Natal.

The AAIRs observed for HL ranged from 2.5 to 11.3 per million for females and 5.3 to 17.6 per million for males; for females, the highest AAIR was present in Fortaleza (11.36, CI 95% 7.10–15.61) and the lowest was found in Natal (2.5, CI 95% 1.05–6.22). For males the highest AAIR was found in Belo Horizonte (17.6, CI 95% 11.38–23.90) and the lowest in Aracaju (5.3, CI 95% 0.71–11.4). The AAIRs observed for NHL in females ranged from 3.3 per million (CI 95% 3.20–9.86) in Campo Grande to 11.9 per million (CI 95% 9.74–14.20) in São Paulo, and for males from 4.4 per million in Natal to 26.6 per million in Campo Grande (Table 1).

HL had the highest median ASIR in both genders in the age group 15–19 years (18.5 per million, Table 2). NHL show the highest ASIR at two peaks: 11.1 per million (1–4 years of age) and 13.2 per million (15–19 years of age). For BL the ASIR decreased with age, being 4.7 per million at 1–4 years of age and 3.6 per million at 5–9 years of age. Higher median ASIRs were observed for males with HL in age groups 1–14 years; ASIR was similar between genders for the age group 15–19 years. Median ASIR for NHL was higher for males in all age groups. Median ASIR for BL was higher among age group 1–4 years (4.7/million) and in males (5.3/million) (Table 2).

The SEIs measured from different Brazilian regions varied from 0.52 to 0.76. The lowest SEI was observed in the city of Fortaleza and Manaus located in the north region (0.52) and the highest SEI was observed in Porto Alegre (0.76) in South Brazil (Supplementary Figs. 1 and 2). The correlation between SEI and lymphoma subtypes was of borderline significance for HL ($P = 0.06$) but not for NHL ($P = 0.53$) or BL ($P = 0.60$) (Fig. 2A, B, and C, respectively). The differences in the incidence rates of HL correlating borderline with SEI were observed in different geographic regions (Fig. 2A). HL incidence was higher in the south, south-east, and middle-west, where the SEI varied from 0.59 to 0.76; the opposite was observed in the North and North-east regions (SEI 0.52–0.59).

4. Discussion

As a whole, the NHL age-specific patterns found in Brazil are similar to those described in developed countries. For instance, in the surveillance, epidemiology, and end results database 2003–2007, the National Cancer Institute in the USA reported an NHL AAIR of 8.5 per million [11]. The demographic characteristics of developed countries were similar to those we observed in Brazil, with males more prevalent among observed cases of NHL. Data from the International Agency for Research on Cancer showed that lymphoid malignancies are generally more common in males than females, with differences tending to be slightly more pronounced in less developed regions of the world. Regarding ages for NHL, the greatest ASIR was found at two peaks: at 1–4 years of age and at 15–19 years of age. For HL, ASIR rates increase with increasing age;

Table 2
Age-specific incidence rates for lymphomas in Brazilian PBCR, by gender according to lymphomas subtype.

Regions	PBCR (period)	Gender	1–4			5–9			10–14			15–19		
			HL	NHL#	BL	HL	NHL#	BL	HL	NHL#	BL	HL	NHL#	BL
North	Manaus (2000–2004)	M	2.80	19.57	5.59	14.45	7.23	2.41	15.66	10.44	0.00	14.37	21.56	0.00
		F	0.00	0.00	2.87	12.30	12.30	2.46	17.96	5.13	10.27	2.22	2.22	2.22
		T	1.42	9.91	4.25	13.39	9.74	2.43	16.82	7.76	5.18	8.06	11.52	1.15
Northeast	Aracaju (2000–2004)	M	0.00	34.67	11.56	0.00	0.00	19.00	8.50	8.50	8.50	15.28	22.91	0.00
		F	0.00	0.00	0.00	9.68	19.36	0.00	0.00	8.45	0.00	21.16	7.05	0.00
		T	0.00	17.70	5.90	4.79	9.59	9.59	4.24	8.47	4.24	18.34	14.67	0.00
	Fortaleza (2001–2005)	M	11.34	15.87	11.34	5.42	7.23	1.81	13.84	8.65	0.00	20.17	11.77	0.00
		F	4.67	4.67	4.67	13.05	7.46	0.00	17.20	3.44	0.00	13.79	7.66	0.00
		T	8.05	10.35	8.05	9.17	7.34	0.92	15.53	6.04	0.00	16.84	9.62	0.00
	Natal (2000–2004)	M	7.45	0.00	14.90	5.88	17.64	17.64	16.29	0.00	0.00	5.09	0.00	0.00
		F	0.00	15.43	0.00	6.05	0.00	0.00	0.00	15.98	0.00	4.78	4.78	0.00
		T	3.79	7.58	7.58	5.96	8.95	8.95	8.07	8.07	0.00	4.93	2.46	0.00
	Recife (2000–2003)	M	0.00	5.11	0.00	15.94	11.96	3.99	7.38	7.38	0.00	10.33	6.89	0.00
		F	0.00	10.67	10.67	4.14	8.28	0.00	11.21	0.00	0.00	33.35	0.00	0.00
		T	0.00	7.83	5.22	10.15	10.15	2.03	9.29	3.71	0.00	22.03	3.39	5.08
	Salvador (2000–2004)	M	0.00	4.56	0.00	7.41	9.26	1.85	6.91	6.91	0.00	14.14	18.38	10.33
		F	0.00	2.38	0.00	7.63	1.91	1.91	5.22	8.70	0.00	8.04	6.70	0.00
		T	0.00	3.49	0.00	7.52	5.64	1.88	6.07	7.80	0.00	11.01	12.38	0.00
	João Pessoa (2001–2005)	M	0.00	53.60	0.00	6.92	20.76	6.92	25.54	0.00	0.00	18.00	18.00	6.00
		F	9.27	0.00	0.00	0.00	14.17	0.00	6.41	0.00	6.41	22.49	5.62	0.00
		T	4.55	27.29	0.00	3.50	17.51	3.50	15.99	0.00	3.20	20.32	11.61	2.90
Middle-West	Campo Grande (2000–2002)	M	13.39	26.78	13.39	10.12	20.24	0.00	19.45	38.91	0.00	18.93	28.39	9.46
		F	0.00	13.88	13.88	0.00	0.00	0.00	0.00	0.00	0.00	18.60	0.00	0.00
		T	6.81	20.44	13.63	5.13	10.26	0.00	9.90	19.80	0.00	18.76	14.07	4.69
	Cuiabá (2001–2005)	M	7.06	21.17	7.06	10.76	16.14	0.00	9.98	14.97	0.00	19.32	24.15	0.00
		F	7.29	14.59	0.00	0.00	0.00	0.00	0.00	10.18	0.00	14.09	9.39	0.00
		T	7.17	17.93	3.59	5.46	8.19	0.00	5.04	12.60	0.00	16.67	16.67	0.00
	Goiânia (2001–2005)	M	5.13	15.40	5.13	28.82	8.23	16.47	26.91	3.84	3.84	13.35	16.69	0.00
		F	0.00	10.62	0.00	4.22	0.00	4.22	3.89	3.89	0.00	21.78	12.45	3.11
		T	2.61	13.05	2.61	16.67	4.17	10.42	15.46	3.86	1.93	17.71	14.49	1.61
Southeast	Belo Horizonte (2000–2003)	M	0.00	13.59	3.40	16.72	5.57	5.57	25.80	15.48	2.58	34.02	20.41	2.27
		F	3.50	0.00	3.50	0.00	5.68	5.68	2.60	5.21	0.00	30.43	8.70	0.00
		T	1.72	6.90	3.45	8.44	5.63	5.63	14.26	10.37	1.30	32.19	14.43	1.11
	São Paulo (2001–2005)	M	3.28	14.20	11.47	18.63	23.28	5.59	18.45	18.88	3.95	32.90	32.90	2.01
		F	2.26	12.97	5.07	7.17	10.52	1.91	9.28	8.40	1.77	28.15	19.28	0.39
		T	2.77	13.59	8.32	12.98	16.99	3.77	13.88	13.66	2.86	30.48	25.96	1.18
South	Curitiba (2001–2005)	M	3.59	0.00	0.00	17.04	0.00	11.36	11.02	16.53	5.51	39.81	12.44	0.00
		F	0.00	3.75	0.00	0.00	8.88	2.96	14.05	8.43	2.81	26.86	9.77	0.00
		T	1.83	1.83	0.00	8.69	4.35	7.25	12.52	12.52	4.17	33.28	11.09	0.00
	Porto Alegre (2000–2004)	M	4.66	9.31	4.66	11.34	11.34	3.78	10.79	7.19	0.00	37.57	25.05	0.00
		F	0.00	14.52	9.68	0.00	7.83	7.83	18.69	7.48	0.00	15.79	9.47	0.00
		T	2.37	11.86	7.12	5.77	9.62	5.77	14.67	7.33	0.00	26.72	17.29	0.00
Median	M	3.44	14.80	5.36	11.05	10.30	4,78	14.75	8.58	0.00	18.47	19.40	0.00	
	F	0.00	7.65	1.44	4.18	7.65	0.96	5.82	6.35	0.00	19.88	7.36	0.00	
	T	2.49	11.11	4.74	7.98	9.27	3.64	13.20	7.64	0.65	18.55	13.23	0.56	

Abbreviations: PBCR, population-based cancer registry; HL, Hodgkin lymphomas; NHL#, non-Hodgkin lymphomas#; BL, Burkitt lymphoma; *n*, total number of cases include HL, NHL#, BL; M, male; F, female; T: total.
#Non-Hodgkin lymphomas (II.b, 79%), that includes miscellaneous lymphoreticular neoplasms (II.d, 4%), unspecified lymphomas (II.e, 17%), but Burkitt lymphoma.

the highest median ASIR in both genders was found in the group aged 15–19 years of age [12].

The interpretation of the highest AAIRs for NHL found in São Paulo and João Pessoa compared with the lowest observed. Recife and Natal may reflect the better opportunities for diagnosis in some regions and, in contrast, greater rates of misdiagnosis and under-diagnosis in resource-poor regions of the country. It is well known that the broad anatomy-based categories of NHL require modern laboratory facilities to classify lymphoid malignancies appropriately. Even considering these pitfalls, the median AAIR for total lymphomas was 22.6 per million, similar to the SEER data of 23.8 per million in the United States [1].

It has been demonstrated that childhood HL displays characteristic epidemiological, clinical, and pathological features according to various geographic areas, particularly according to the socioeconomic level of a given country [13]. HL incidence distribution has two peaks – one in adolescents/young adults and one in the elderly – which comprise distinct disease entities [14–19]. Recently, three Brazilian studies suggested that the epidemiological patterns are not strictly segregated, and that overlap may exist among the described forms of the disease. Gualco et al. reported on 476 cases of classical HL ascertained from all Brazilian geographic regions. NS was found to be the most frequent subtype (76.9%) in all age groups [20]. Similarly, Barros et al. reported data from a single center located in the Brazilian south-east region where the authors did not observe an early childhood peak of HL. The majority of cases occurred in children over 10 years of age and were of the NS subtype; Epstein–Barr virus (EBV) was identified in 44.8% of cases, without preferential association with age ($<$10 years versus $>$10 years); EBV positivity was more prevalent in MC cases [21]. The third study was performed in the north-east region, and in contrast to previously reported data found EBV-associated HL disease to be the most common (87%) with a high frequency of the MC subtype [22].

In agreement with these data, our analyses of 14 PBCRs showed increasing median ASIR with age, most notable in south-east and south PBCRs. Higher SEI was borderline correlated with higher incidences of HL ($P = 0.06$) occurring in more developed Brazilian

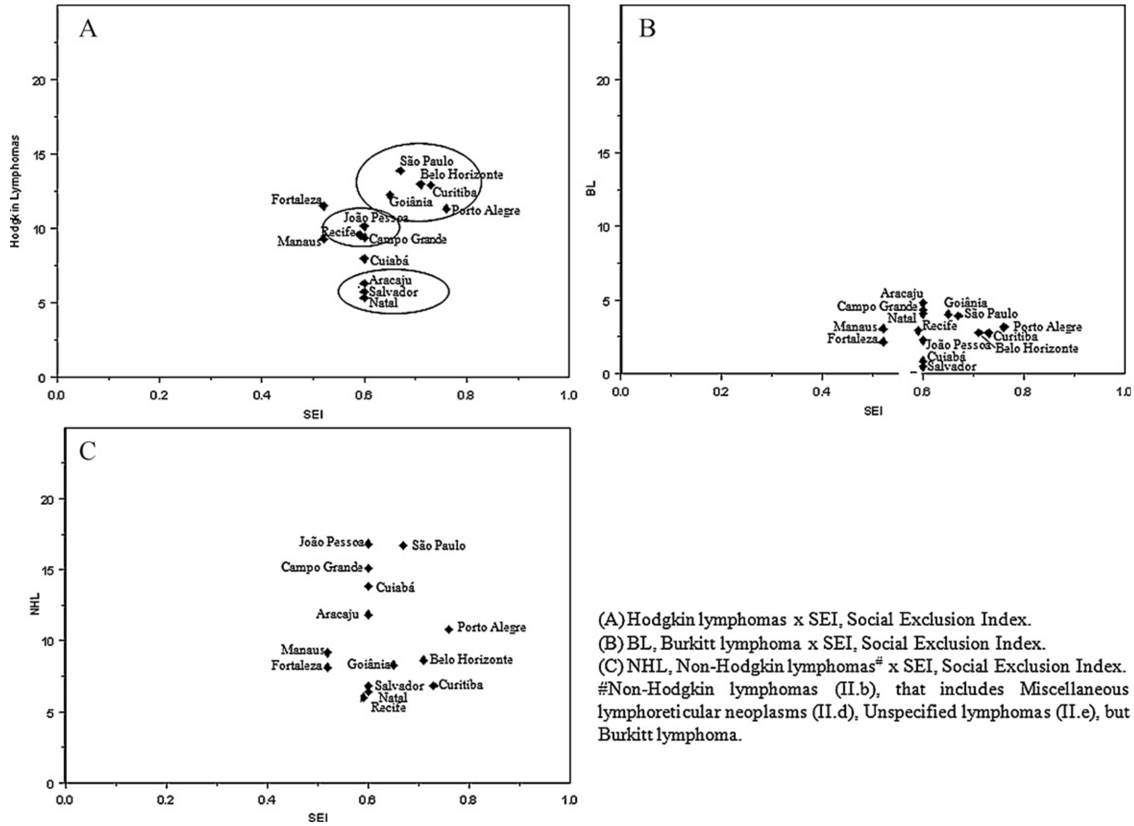

Fig. 2. The incidence rates of lymphoma subtypes and correlation with social exclusion index in different Brazilian regions.

regions. On the other hand, Smith et al. recently failed to uncover evidence of any significant trends for lymphoma subtypes, or for Hodgkin lymphoma at younger ages [23]. In addition, a Canadian study explored the relationship between socioeconomic status, neighborhood income, and the incidence of childhood solid tumors and lymphomas. In this study no consistent relationship between socioeconomic status and lymphoma was found, suggesting an overall pattern compatible with random variability [24].

BL is a highly proliferative B-cell tumor first described in African children more than five decades ago by Dennis Burkitt as being EBV associated [25]. Within the cancer registries available in Africa, the incidence of endemic BL (eBL) is highest in the cancer registry from the Kyadondo County, Uganda, with an AAIR of 4.7 per 100,000 for boys and 3.0 per 100,000 for girls [6]. In recent years the incidence of BL has increased in the endemic areas of Africa, overlapping with the epidemic of HIV and malaria in the region. In Uganda, BL incidence rates have reportedly increased from 9.5 per 106 in 1960–1971 to 34.3 per 106 for the period 1991–1997 [26]. Sporadic BL (sBL) is the form described outside of African endemic regions and is the third most common lymphoid malignancy among children less than 15 years old in the United States, after acute lymphoblastic leukemia (ALL) and HL [1].

Whereas eBL is linked to EBV and malaria, this factor appears to be less important in sBL where EBV DNA is integrated or clonally detected in only 20–30% of tumors [27,28]. Previous studies on BL in Brazil demonstrated intermediate features between endemic and sporadic cases regarding EBV–tumor association and clinical disease presentation [29–32]. However, the incidence rates of BL in different regions of Brazil have been unknown until now. This is the first report of Brazilian childhood BL incidence which includes analysis of all five geographic regions. Despite some discrepant variation in the AAIR found among the 14 PBCRs (0.47 per million in Salvador up to 4.77 per million in Aracaju), the median AAIR was 2.97 per million, which is comparable to the ASIR of sBL in the United States for the period 2003–2007 (2.4 per million person-years, 0–19 years) [11]. One possible explanation for the lower incidence rate of BL observed in Salvador could be related to unreported cases, as previously reported in the same PBCR for ALL [33,34].

Regarding median ASIR of BL in the 14 PBCRs, the incidence rates for both age groups (4.74 per million for 1–4 years and 3.64 per million for 5–9 years) were similar, and then declined with increasing age. Overall, BL predominated among boys in both age groups (1–4 and 5–9 years). Mbulaiteye et al. recently reported an age peak incidence for BL similar to that in the present report [35].

Socioeconomic status has been proposed to modulate EBV infection and the risk of EBV-associated lymphomas [36]. In fact, poverty lowers the age of initial EBV infection, and early exposure to EBV could be a trigger for BL development [31,37,38]. Furthermore, socioeconomic status may also be a surrogate marker for the presence of factors associated with a poor defense response toward environmental exposure to infection and chronic malnutrition [39].

To summarize, we describe for the first time the incidence rates of childhood lymphomas in Brazil. Our findings may be useful for prioritizing cancer registry quality and supporting additional research on risk factors for childhood lymphomas.

Conflict of interest statement

All authors disclose no financial and/or personal relationships with other people or organizations that could inappropriately influence (bias) this work.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.canep.2012.03.006.

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