

Original Article

Descriptive epidemiology of childhood cancer in Cali, Colombia 1977-2011

Epidemiología descriptiva de cáncer infantil en Cali, Colombia 1977-2011

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Bravo LE, García LS, Collazos P, Aristizabal P, Ramirez O. Descriptive epidemiology of childhood cancer in Cali, Colombia 1977-2011. *Colomb.Med.*2013;44 (3):155-64

Article history:

Received Dec 21 2012

Received in revised form

Feb 24 2013

Accepted : Sep 15 2013

Keywords:

Child; neoplasms; epidemiology; incidence; leukemia; lymphoma; mortality; survival;

Palabras Clave:

Cáncer infantil, supervivencia, incidencia, mortalidad, epidemiología

Abstract

Objective: To describe the occurrence and survival patterns of childhood cancer patients over the last 20 years in Cali.

Methods: Information was obtained from the Cancer Population Registry in Cali and the Municipal Department of Health. The International Classification for childhood Cancer (ICCC) was used. Vital status data was obtained from MDH death certificates and hospital databases. Additionally, clinical records were reviewed and, in some cases, telephone contact was made to gather data. Follow-up was completed until December 31, 2011. Incident (IR) and mortality rates (MR) were estimated and adjusted for age. Life-tables were made to estimate overall survival.

Results: Between 1977-2011 there were 2,311 cases of cancer identified in children less than 15 years of age. The IR and MR for Cali were found to be 141.2 and 55.6 per million of people per year. Leukemias, lymphomas, Central nervous system (CNS) tumors and soft tissue sarcomas showed IR's of 60.1, 20.5, 25.7 and 9.4, respectively. 5-years OS was 48%, and showed an improvement from 24.9%±4.3 to 51.8%±4.6, compared 1992-96 vs 2002-06 periods.

Conclusion: The IR found is comparable with those from affluent countries. Taking into account that pediatric cancer is curable in about 75-80% of the cases, an enormous challenge is presented to the Colombian health system: to improve current clinical results.

Resumen

Objetivo: Describir los patrones de ocurrencia y supervivencia por cáncer infantil en los últimos 40 años en Cali, Colombia.

Métodos: La información fue obtenida del Registro Poblacional de Cáncer de Cali y el estado vital de las bases de datos de mortalidad de la Secretaría de Salud Pública Municipal (SSPM) y de los egresos hospitalarios. Se utilizó la clasificación internacional de cáncer infantil versión-3. El seguimiento se hizo hasta el 31/12/2011. Se estimaron las tasas de incidencia (TI), mortalidad (TM), se ajustaron por edad y se realizó un análisis de período para la sobrevida global (SG).

Resultados: Se identificaron 2,311 casos en <15 años entre 1977-2011. Las TI y TM fueron de 141.2 y 55.6 por millón de personas-año. Leucemias, linfomas, tumores del SNC y sarcomas de tejidos blandos mostraron TI de 60.1, 20.5, 25.7 y 9.4 por millón de personas-año, respectivamente. La SG a 5 años fue 48%, al discriminar por quinquenio mostró una mejoría de 24.9%±4.3 al 51.8%±4.6, al comparar los periodos 1992-96 vs 2002-2006.

Conclusión: La TI encontrada es comparable con las descritas en EEUU y Europa, sin embargo, la supervivencia es menor. Como el cáncer infantil es curable en alrededor del 75-80% de los casos, se plantea un gran reto para el sistema de salud Colombiano, mejorar los resultados actuales.

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Introduction

Childhood cancer is an uncommon group of diseases in the population with an age standardized incident rates (ASR) (per million of persons <15 years old per year) that fluctuates from 106 to 203¹⁻³. On the American continent, most cases of childhood cancer (CC) (65%) occur in Latin America and the Caribbean, where 17,500 new cases are diagnosed each year and more than 8,000 deaths are registered due to these illnesses^{3,4}.

In developed countries, the CC long-term survival proportion is close to 80%^{5,6}. Unfortunately, this proportion decreases to 10-20% among the poorest countries of the world in which information, opportune diagnosis, and access to treatment are often difficult⁷. The number of children with these illnesses is greater than in most affluent countries due to the their demographic compositions. The combination of these two factors impacts the population with these illnesses, making them relevant from the public health point of view in countries with low and medium resources⁷. With the exception of the city of Cali where a cancer population-based registry exists, knowledge of the risk of CC in Colombia is limited. A population estimate for the survival of these patients is unknown. Nevertheless, national statistics from 2008 show that CC occupied 2nd place as the most frequent cause of death in children and teenagers from 2 to 19 years of age.

In children, the cell origin of cancers is diverse. Compared to adults, in whom around 80% are epithelial, most of them are not in children⁸. Due to this finding, a histological classification is considered more appropriate than the topographical one, commonly used with adults⁸. Therefore, this was a prerequisite for the development of a classification system for childhood cancer. The first one developed that was internationally accepted was published in 1987⁹. At present, the one most commonly used is the International childhood cancer classification (ICCC), third version, developed by the International agency for cancer research (IACR)^{10,11}.

This classification system includes 12 main tumoral groups and 47 subgroups. It is noteworthy that this only includes tumors considered malignant, with the exception of group III where intracranial or intra-spinal tumors of benign histology are also included. The 12 main groups are: I leukemias, II lymphomas and reticular neoplasms, III central nervous system tumors, IV neuroblastoma and other peripheral nervous cell tumors, V retinoblastoma, VI renal tumors, VII liver tumors, VIII malignant bone tumors, IX soft tissue sarcomas, X germinal tumors, trophoblastic, and other gonadal tumors, XI other epithelial neoplasm and melanoma, and XII other specified neoplasms and malignant non-specified neoplasm¹¹.

It is not possible to carry out CC community control with primary prevention activities. Neither is it possible to conduct early intervention screening strategies as they are not suitable at the current time (with the exception of retinoblastoma). Therefore, the responsibility for its control depends directly upon the capacity to achieve a proper diagnostic classification, highly complex medical treatment, and a strong family and social engagement.

The determination of the burden of cancer on the population is only possible through the availability of information about

the incidence of the disease, mortality, and survival for sick individuals. This knowledge provides a framework for contributing to the control of these illnesses. This is a report on estimates of pediatric cancer incidence, mortality and survival in Cali for the last 40 years.

Materials and Methods

Study population

Information on cancer incidence and mortality for all the tumor types in subjects less than 15 years of age was obtained from the Cancer population registry of Cali (RPCC) databases and the Municipal department of health (MDH)¹². Briefly, RPCC is a cancer population-based database established in 1962 that obtains continuous information on the incidence of all cancer types for the urban population of Cali. RPCC actively collects information for the different types of cancers using both private and public health services and death certificates as data sources^{12,13}.

We selected as incident cases all children living in Cali from 1977 to 2011 with the first malignant neoplasms diagnosed in each subject, with the exception of benign tumors of the CNS that were also included. We used the ICCC-3 classification system for grouping¹¹.

The RPCC complies with international standards for good practice; it is an accredited member of the World Cancer Registration Association and has demonstrated exceptional quality with its information^{14,15}. Cancer population registry of Cali (RPCC) shows a proportion of cancer cases with morphological verification of 94.4%, with 0.5% of cases using only a death certificate as evidence of cancer, and a mortality incident ratio of 0.36.

Vital status determination

We determined the vital status of children by matching: 1) the MDH mortality database (290,357 registries from 1984 to 2011), 2) the System of Identification of Potential Social Program Beneficiaries (SISBEN) survey database, and 3) the hospital/clinics records database. We included hospitals/clinics in Cali that serve as referral centers for complex pediatric pathologies, such as the Hospital Universitario del Valle, the Fundación Valle del Lili, Centro Médico Imbanaco and the Rafael Uribe Clinic. We could estimate mortality rates since 1984, but for survival analyses we only had data on patients diagnosed since 1992. We excluded from survival analysis those cases with tumors detected during autopsy or detected only by means of a death certificate.

We used the ID card number as an initial step for key identification of the paired registrations. To solve the problem of cases without an ID card, we selected the following attributes for matching: first name, middle name, first surname, second surname, date of birth, address and telephone number. The process started with an exact chains comparison. This was followed by a truncated chains comparison (three first characters), a comparison by approximation of chains, and finally, by comparisons by means of phonetic codes. To match ages and dates it was necessary to consider the absolute and daily tolerance percentages. For matching information, we used a probability approximation based on the hidden Markov chain models as well as a deterministic

approach with rules defined by RPCC based on frequency charts, dictionaries and correction lists for the names, surnames, dates, places and localities. When a couple of records were compared, the tolerance percentages and the comparison functions provided a vector of weight for each field compared. This allowed for the classification of the pairs into one of three possible groups: matching, not matching and possible matching.

We verified reliability by manually reviewing the medical records, the cancer morbidity surveys, and the subject mortality chart records for the all residents of Cali. By doing this verification we could establish the coincidence of each pair of cases.

We included an active follow-up by using a survey of registered cases, checking with various sources of information, and by following RPCC standardized procedures^{12,16}. When we had no information about a case, RPCC workers assisted by making contacts through home visits or phone calls.

Outcome

The outcome variable was the death of the child. To do the analyses of survival, it was necessary to determine the time elapsed for the subject of each study. For this estimate, we used the date of diagnosis and the date of death. If we identified a subject as still being alive at the end of the study period, we used that date to determine survival time. When the vital status of the subject was unknown at the end of the study period, we used the last contact date with vital status data. We decided to use an initial observation date of January 1, 1992, and to use June 30, 2012 as the completion date. Survival for each childhood cancer group was described in terms of 1-year, 3-years, 5-years and 10-years of observed survival. The observed survival and corresponding standard errors were computed via the life tables method in SEER*Stat¹⁷. Five-year observed survival was estimated for four quinquennial periods: 1992-1996; 1997-2001; 2002-2006, 2007-2011. The patients who were alive at the end of the study or were lost during study follow-up were excluded.

We estimated the annual average incidence and mortality rates per million persons per year. We also determined the age-specific rates according to the following groups: 0-4, 5-9, and 10-14 years. For the estimation of the global rate, we did an adjustment by age taking into account the world population structure as followed by Segi. The population denominators used for calculation of the incidence rate were estimated from the Colombian national population censuses (National statistical office, DANE)¹⁸. Rate trends were evaluated by the annual percentage change (APC), using the weighted least squares method that is incorporated in the US National Cancer Institute's publicly accessible SEER*Stat software¹⁷. The APC represents the average percentage of annual increase or decrease in cancer rates adjusted by age that assumes a constant rate of change for the incidence or mortality rates over the evaluation period. For this, we assumed a constant rate of change for the incidence or mortality rate during the interval of time evaluated. We examined this tendency in cancer incidence using the Poisson regression. This models the natural logarithm annual rates for age groups as a function of the year of diagnosis. From the corresponding regression coefficient of these models, we derived the APC and its 95% confidence interval¹⁷.

We defined as censored observations those children who remained alive at the end of the study period or who were lost during follow-up. We used the life-table method to determine survival probabilities. We estimated the standard error using the Greenwood method. For all the analyses, we considered a two tailed *p-value* <0.05 as significant. We carried out the data analyses by using the Stata 10.0 statistical program.

Results

During the period of study, 2,311 incidence cases were registered. Of these, 54.5% were males and 40.2% were younger than 5-years-old. If these percentages are analyzed by five-year periods, there were no substantial changes in the frequency of cases occurring according to age or gender.

The diagnostic method was morphological in 95.0% of the cases (histological 63.9%, hematology 29.3% and cytology 1.7%), and 4.5% were from clinical diagnoses (including different imaging methods). For the survival analysis, 8 (0.5%) cases were excluded due to the death certificate being the only available evidence.

The distribution of neoplasms, according to the ICCC-3, is presented in Tables 1 and 2. Most of the cases (69.6%) were from the first three main diagnostic groups: leukemias (group I, 37.3%), lymphomas (group II, 15.4%) and CNS tumors (group III, 16.3%). It should be noted that Neuroblastoma represented 2.8% of cases and Retinoblastoma represented 3.7%. The IR was 141.2 for all the diagnostic groups. The IR values varied according to 5-year periods and gender varied from 130.1 to 185.3 in boys and 107.9 to 157.3 in girls. The age-specific rates (ASR) per group and diagnostic subgroup, as well as sex and five-year period rates are presented in Tables 1 and 2.

During the first period, the MR from CC for a million persons per year was 66.2, and it was 52.9 during the years 2007-2011 (Table 3). There was a significant increase in CC incidence in Cali between 1977 and 2011 with an annual percentage change (APC) of 0.9 (95% CI: 0.4, 1.5). It is remarkable to note a significant increase for leukemia with an APC of 1.0 (95% CI: 0.2, 1.8). A mortality standardized rate decrease was observed during this period in approximately 1.1 cases per year on average (Table 4).

The 5-year overall survival (OS) rate for the different periods was: $31.6 \pm 3.2\%$, $48.3 \pm 2.7\%$, and $54.9 \pm 2.8\%$. The OS was not possible to determine for the last five-year period; however, the OS at 2 and 3 years are remarkably similar to the prior five-year period (Table 5). The survival for CC that was observed in the main diagnostic categories is shown in Figure 1. Hematological and lymphoid neoplasms (groups I and II) showed evident improvements in survival for the recent 5-year periods. In children with leukemia, the 5-year OS was 24.9% from 1992-96 as compared to 51.8% for the period of 2002-06.

For lymphomas, the findings were similar, and the OS rate rose from 57.4% to 70.8%. Although, it was not possible to determine this proportion for the last 5-year period, survival at 2 and 3 years is very similar to that of the prior 5-year period. The CNS neoplasms continued showing a poor prognosis with 5-year OS rate of less than 50%.

Table 1. Cali, Colombia. Childhood Cancer Incidence rates per million by ICCC groups in boys from 1977 to 2011.

International Classification of Childhood Cancer (ICCC) Group	1977-1981		1982-1991		1992-1996		1997-2001		2002-2006		2007-2011	
	n	ASR	n	ASR	n	ASR	n	ASR	n	ASR	n	ASR
I Leukemias, myeloproliferative & myelodysplastic diseases	55	53.0	85	40.9	70	62.7	94	75.8	71	52.6	72	52.5
I(a) Lymphoid leukemias	41	40.0	57	27.4	56	50.4	78	63.6	56	42.6	56	40.6
I(b) Acute myeloid leukemias	3	2.5	16	7.7	11	9.6	13	9.7	10	6.7	10	7.9
I(c) Chronic myeloproliferative diseases	2	1.9	1	0.4	1	0.7	1	0.8	1	0.6	4	2.5
I(d) Myelodysplastic syndrome and other myeloproliferative	0	-	2	0.8	0	0.0	0	0.0	0	0.0	1	0.9
I(e) Unspecified and other specified leukemias	9	8.6	9	4.6	2	1.9	2	1.8	4	2.7	1	0.6
II Lymphomas and reticuloendothelial neoplasms	29	26.8	72	33.5	28	23.4	38	30.0	42	29.8	45	27.2
II(a) Hodgkin lymphomas	9	7.8	29	13.2	11	8.5	9	7.2	13	8.9	13	7.5
II(b) Non-Hodgkin lymphomas (except Burkitt lymphoma)	12	11.9	16	7.4	4	3.3	13	9.9	11	7.4	12	7.1
II(c) Burkitt lymphoma	4	3.7	16	7.7	7	6.2	16	12.9	15	10.8	17	10.5
II(d) Miscellaneous lymphoreticular neoplasms	0	-	4	1.8	1	1.0	0	0.0	0	0.0	2	1.5
II(e) Unspecified lymphomas			7	3.4	5	4.4	0	0.0	3	2.7	1	0.6
III CNS and misc intracranial and intraspinal neoplasms	19	16.8	38	17.1	22	18.7	40	32.2	28	20.0	39	28.0
III(a) Ependymomas and choroid plexus tumor	0	-	3	1.4	2	1.6	5	4.2	3	2.1	4	3.0
III(b) Astrocytomas	8	7.0	9	4.1	8	6.9	16	12.8	8	5.6	15	11.1
III(c) Intracranial and intraspinal embryonal tumors	2	1.7	11	4.8	6	5.0	5	3.8	6	4.6	10	7.6
III(d) Other gliomas	1	0.9	1	0.4	2	1.7	7	5.7	6	4.0	5	3.2
III(e) Other specified intracranial/intraspinal neoplasms	8	7.3	0	-	1	0.7	0	0.0	1	0.6	3	1.9
III(f) Unspecified intracranial and intraspinal neoplasms	0	-	14	6.3	3	2.8	7	5.7	4	3.1	2	1.3
IV Neuroblastoma and other peripheral nervous cell tumors	5	5.7	7	3.6	5	5.0	6	5.6	5	4.0	6	4.7
IV(a) Neuroblastoma and ganglioneuroblastoma	5	5.7	7	3.6	5	5.0	6	5.6	5	4.0	6	4.7
IV(b) Other peripheral nervous cell tumors	0	-	0	-	0	0.0	0	0.0	0	0.0	0	0.0
V Retinoblastoma	4	4.5	8	4.3	6	5.5	13	12.4	5	4.5	7	6.1
VI Renal tumors	4	4.0	19	9.6	2	1.8	8	7.0	8	7.1	8	6.8
VI(a) Nephroblastoma and other nonepithelial renal tumors	4	4.0	18	9.2	2	1.8	8	7.0	8	7.1	8	6.8
VI(c) Unspecified malignant renal tumors	0	-	1	0.4	0	0.0	0	0.0	0	0.0	0	0.0
VII Hepatic tumors	1	0.8	6	3.0	1	0.8	0	0.0	3	2.5	2	1.5
VII(a) Hepatoblastoma	0	-	4	2.0	1	0.8	0	0.0	2	1.8	2	1.5
VII(b) Hepatic carcinomas	1	0.8	1	0.5	0	0.0	0	0.0	1	0.7	0	0.0
VII(c) Unspecified malignant hepatic tumors	0	-	1	0.4	0	0.0	0	0.0	0	0.0	0	0.0
VIII Malignant bone tumors	4	3.1	14	6.0	5	3.6	8	5.5	16	10.3	8	4.5
VIII(a) Osteosarcomas	3	2.4	9	3.8	3	2.2	5	3.6	11	6.9	4	2.2
VIII(b) Chondrosarcomas	0	-	0	-	1	0.7	0	0.0	0	0.0	0	0.0
VIII(c) Ewing tumor and related sarcomas of bone	1	0.8	5	2.1	1	0.7	3	2.0	1	0.7	3	1.7
VIII(d) Other specified malignant bone tumors	0	-	0	-	0	0.0	0	0.0	0	0.0	1	0.6
VIII(e) Unspecified malignant bone tumors	0	-	0	-	0	0.0	0	0.0	4	2.7	0	0.0
IX Soft tissue and other extraosseous sarcomas	6	6.2	11	5.2	12	10.0	12	9.4	10	6.4	15	10.7
IX(a) Rhabdomyosarcomas	2	2.3	7	3.5	9	7.8	5	4.1	2	1.2	7	5.4
IX(b) Fibrosarcomas, peripheral nerve & other fibrous	1	1.1	0	-	1	0.8	1	0.7	1	0.7	1	0.6
IX(d) Other specified soft tissue sarcomas	0	-	2	0.8	0	0.0	5	3.7	5	3.2	4	2.4
IX(e) Unspecified soft tissue sarcomas	0	-	2	0.9	2	1.4	1	1.0	2	1.3	3	2.3
X Germ cell & trophoblastic tumors & neoplasms of gonads	0	-	10	4.8	5	4.6	4	3.8	4	3.6	7	4.8
XI Other malignant epithelial neoplasms and melanomas	7	6.1	8	3.5	8	6.8	4	2.6	8	5.4	7	4.4
XII Other and unspecified malignant neoplasms	3	3.0	3	1.5	1	0.8	1	0.9	3	2.2	6	4.4
All	137	130.1	281	133.1	165	143.7	228	185.3	203	148.4	222	155.6

ASR=Age-Standardised Rates (World) per million

Group I (Leukemias)

For group I the average annual IR varied from 87.9 in children <5 years old to 35.4 in the group of 10 to 14 year-olds. Among all neoplasms of this group, (ALL) was the most frequent (82.5%). It showed a higher IR in children younger than 5 years of age for a rate of 73.5 when compared to other age groups. In ALL, the group of males from 5 to 9 years old presented a greater IR than females (65.9 vs 41.0), and this is not the same for the other age groups. The ALL standardized age IR was 6.8 times greater than that of the non-acute lymphoid leukemias (AML). Non-acute lymphoid leukemias also showed a greater rate in the group less than 5 years of age. Upon examining the rates of the 5-year period for this group, there is an apparent decrease in the rates after the year 2002. This decreasing trend was more evident for

ALL and the non-specified leukemia subgroup. The APC for this group was -1.0 (95% CI: -2.5, 0.6). The MR standardized by age for this group was of 2.5 (x 100,000 /year); 2.9 for males and 2.2 for females, resulting in a male/female ratio of 1.3. The lowest MR (2.0) was seen in children under <5 years of age. The 5 and 10-year OS of children with leukemia was of $40.1 \pm 3.1\%$ and $30.8 \pm 3.7\%$, respectively. Five-year OS rate by period (1992-1996, 1997-2001, and 2002-2006), showed the following values: $24.9\% \pm 4.3$, $37.9\% \pm 4.0$ and $51.8\% \pm 4.6$, respectively (Table 5).

Group II (Lymphomas)

The IR for group II was greater by 20.5 in males than in females (27.6 vs. 13.2). In this group, Burkitt's lymphoma showed the highest IR (7.2). This lymphoma showed its highest IR in the 5

Table 2. Cali, Colombia. Childhood Cancer Incidence rates per million by ICCC groups in girls from 1977 to 2011.

International Classification of Childhood Cancer (ICCC) Group	1977-1981		1982-1991		1992-1996		1997-2001		2002-2006		2007-2011	
	n	ASR	n	ASR	n	ASR	n	ASR	n	ASR	n	ASR
I Leukemias, myeloproliferative & myelodysplastic diseases	38	35.1	91	44.7	69	61.7	64	51.9	79	64.2	75	55.7
I(a) Lymphoid leukemias	25	23.2	73	35.8	51	45.4	55	44.7	63	51.1	61	45.4
I(b) Acute myeloid leukemias	0	-	10	5.0	12	10.6	7	5.8	12	9.9	9	6.7
I(c) Chronic myeloproliferative diseases	8	7.2	2	0.8	0	0.0	0	0.0	1	0.6	2	1.5
I(d) Myelodysplastic syndrome and other myeloproliferative	1	1.1	0	-	0	0.0	0	0.0	0	0.0	1	0.9
I(e) Unspecified and other specified leukemias	4	3.5	6	3.2	6	5.7	2	1.3	3	2.6	2	1.2
II Lymphomas and reticuloendothelial neoplasms	14	13.2	27	12.9	18	15.9	12	10.1	22	15.2	16	11.2
II(a) Hodgkin lymphomas	5	4.3	5	2.2	6	4.6	3	2.5	2	1.2	5	3.2
II(b) Non-Hodgkin lymphomas (except Burkitt lymphoma)	6	5.5	8	3.6	4	3.5	1	0.8	12	7.9	6	4.3
II(c) Burkitt lymphoma	0	-	9	4.6	4	4.0	5	4.4	6	4.7	4	3.2
II(d) Miscellaneous lymphoreticular neoplasms	0	-	1	0.6	1	1.0	0	0.0	1	0.7	1	0.6
II(e) Unspecified lymphomas	3	3.4	4	2.0	3	2.8	3	2.4	1	0.6	0	0.0
III CNS and misc intracranial and intraspinal neoplasms	18	16.9	34	16.6	25	22.1	31	24.0	44	32.4	33	23.1
III(a) Ependymomas and choroid plexus tumor	2	2.0	2	1.1	3	2.8	1	0.8	5	4.0	5	3.1
III(b) Astrocytomas	5	4.4	11	5.3	8	7.3	17	13.6	22	15.5	9	6.4
III(c) Intracranial and intraspinal embryonal tumors	4	3.8	3	1.4	4	3.2	2	1.6	9	6.9	10	7.8
III(d) Other gliomas	0	-	4	1.9	5	4.4	2	1.4	1	0.7	5	3.2
III(e) Other specified intracranial/intraspinal neoplasms	7	6.7	0	-	2	1.4	2	1.3	3	2.0	1	0.6
III(f) Unspecified intracranial and intraspinal neoplasms	0	-	14	6.8	3	3.0	7	5.3	4	3.2	3	2.1
IV Neuroblastoma and other peripheral nervous cell tumors	6	6.3	9	4.7	4	3.5	5	4.5	3	2.3	7	6.1
IV(a) Neuroblastoma and ganglioneuroblastoma	5	5.2	9	4.7	4	3.5	5	4.5	1	0.9	7	6.1
IV(b) Other peripheral nervous cell tumors	1	1.1	0	-	0	0.0	0	0.0	2	1.3	0	0.0
V Retinoblastoma	8	8.9	12	6.5	5	5.2	8	7.9	5	4.7	7	6.1
VI Renal tumors	7	8.0	12	6.5	8	7.0	12	11.0	9	8.0	9	6.9
VI(a) Nephroblastoma and other nonepithelial renal tumors	7	8.0	11	6.1	8	7.0	11	10.1	9	8.0	8	6.3
VI(c) Unspecified malignant renal tumors	0	-	1	0.5	0	0.0	1	1.0	0	0.0	1	0.6
VII Hepatic tumors	1	1.1	1	0.6	4	4.2	0	0.0	3	2.5	3	2.3
VII(a) Hepatoblastoma	1	1.1	1	0.6	1	1.2	0	0.0	2	1.9	2	1.8
VII(b) Hepatic carcinomas	0	-	0	-	1	0.7	0	0.0	0	0.0	1	0.6
VII(c) Unspecified malignant hepatic tumors	0	-	0	-	2	2.3	0	0.0	1	0.6	0	0.0
VIII Malignant bone tumors	4	3.0	6	2.7	6	4.6	6	4.4	11	6.9	10	6.6
VIII(a) Osteosarcomas	4	3.0	3	1.3	5	3.9	4	2.7	6	3.8	4	3.0
VIII(b) Chondrosarcomas	0	-	0	-	0	0.0	0	0.0	0	0.0	0	0.0
VIII(c) Ewing tumor and related sarcomas of bone	0	-	1	0.6	1	0.7	2	1.6	3	1.9	5	3.0
VIII(d) Other specified malignant bone tumors	0	-	0	-	0	0.0	0	0.0	0	0.0	0	0.0
VIII(e) Unspecified malignant bone tumors	0	-	2	0.9	0	0.0	0	0.0	2	1.2	1	0.6
IX Soft tissue and other extraosseous sarcomas	5	4.5	15	7.2	13	11.2	11	9.5	8	5.1	14	10.0
IX(a) Rhabdomyosarcomas	3	2.5	5	2.6	7	5.9	8	7.2	4	2.6	7	5.4
IX(b) Fibrosarcomas, peripheral nerve & other fibrous	2	2.0	4	2.0	1	0.8	1	0.7	2	1.2	2	1.1
IX(d) Other specified soft tissue sarcomas	0	-			3	2.7	1	1.0	2	1.2	3	2.2
IX(e) Unspecified soft tissue sarcomas	0	-	3	1.3	2	1.8	1	0.7	0	0.0	2	1.2
X Germ cell & trophoblastic tumors & neoplasms of gonads	4	3.8	8	3.4	5	3.5	5	3.6	8	5.6	10	7.2
XI Other malignant epithelial neoplasms and melanomas	5	4.8	9	3.8	6	4.3	5	3.7	12	7.4	8	5.1
XII Other and unspecified malignant neoplasms	2	2.0	4	1.9	1	1.0	2	1.7	3	2.8	6	4.6
All	112	107.9	233	133.1	164	144.3	161	132.3	207	157.3	198	144.9

ASR=Age-Standardised Rates (World) per million

to 9 year-olds group (11.9). Most of the cases (94%) occurred in children <10 years old. In general, the rates did not show differences in the group of <5 years of age, but in the group from 5 to 9 years of age the male/female ratio was of 2.9. Other non-Hodgkin lymphomas (excluded Burkitt's) presented an IR of 5.2, with the highest IR among children in the 10 to 14 year-old group (7.4).

Hodgkin lymphoma showed an IR of 6.6, with an IR in the group from 10 to 14 years of 13.0. The male/female ratio for this tumor was of 2.6 and 3.7 in the group from 10 to 14 years of age. In the last 5-year period, a decrease in the group of non-specified lymphoma

was encountered. The MR for lymphomas was 0.5 and by gender was 0.7 for males and 0.4 for females. Lymphomas for 5-year OS rate were $65.4 \pm 5.2\%$ reaching a plateau about 48 months after diagnosis. Five-year OS, by period, found the following values: $57.4\% \pm 10.6$, $63.1\% \pm 7.6$, and $70.8\% \pm 6.5$, respectively (Table 5).

Group III (CNS tumors)

The IR for group III was 25.7. Astrocytoma presented the highest IR in all age groups (11.2). In males, Astrocytoma IRs were greater in children <10 years of age than they were in the older group. This contrasts with females who showed relatively stable rates by age

Table 3. Cali, Colombia. Trends in Childhood Cancer Incidence and Mortality from 1977 to 2011

International Childhood Cancer Classification Group	Sex	Incidence			Mortality		
		A.P.C	C.I. 95%		A.P.C	C.I. 95%	
Leukemias	Male	0.6	-0.5	1.7	-0.6	-2.7	1.5
	Female	1.4*	0.5	2.4	-1.5	-3.4	0.4
	Both	1.0*	0.2	1.8	-1.2	-2.6	0.3
Lymphomas	Male	-0.2	-1.4	1	~	~	~
	Female	~	~	~	~	~	~
	Both	-0.2	-1.2	0.9	-6.4*	-9.3	-3.3
CNS	Male	~	~	~	~	~	~
	Female	1.5	-0.2	3.2	~	~	~
	Both	1.3*	0.3	2.4	1.8	-0.4	4
Other	Male	1	-0.1	2.2	-2	-4.1	0.2
	Female	0.6	-0.5	1.8	~	~	~
	Both	0.9*	0	1.7	-1.5*	-3	-0.1
All	Male	0.8*	0.2	1.4	-1.3	-2.6	0
	Female	1.0*	0.2	1.8	-1.1	-2.3	0.1
	Both	0.9*	0.4	1.5	-1.1*	-2	-0.3

APC= Annual Percent Change

*APC is significantly different from zero ($p < 0.05$)

group. The primitive neuroectodermal tumor subgroup, in which Medulloblastoma is included, showed a relatively stable rate in all the age groups, with an IR of 2.8.

The IR was greater for males than for females (3.9 vs 2.8). The IR for non-specified intracranial/intraspinal tumor group was 4.0. MR of this group was 7.0, i.e. 6.6 for males and 7.3 for females. OS was 41.9 ± 5.0 and 33.6 ± 6.4 for 5 and 10 years, respectively. Five year OS by period were found to be $29.6\% \pm 8.6$, $44.3\% \pm 6.3$, and $38.3\% \pm 7.0$, respectively (Table 5).

Other groups

In group IV, Neuroblastoma presented an IR of 3.8, with a greater incidence (8.8) in <5 year-old group and without substantial gender differences. OS reached a plateau at 48 months in 35.4% of cases. Retinoblastoma presented an overall IR of 5.8. It was 18.2 in

children less than 5 years of age, and was higher in males than in females (6.7 vs 4.8). OS from this tumor showed notable progress when noted by five-year period.

Group VI, including Wilms tumor, Clear cell sarcoma and Rhabdoid tumor presented an overall IR of 6.2. The risk for the occurrence of these tumors was higher among females than males (8.4 vs 3.9). The age group under 5 years showed a higher incidence for this group of tumors (11.9), and MR was of 0.2. It was found that the five and ten-year OS rates were 69.9 ± 9 and 61.9 ± 10.8 , respectively. There was improvement shown in the 5-year OS rate when comparing the 1997-2001 period with the previous one (78.6 vs 42.9). This trend was not maintained in the subsequent period as shown in Table 5. In group VII, Hepatoblastoma presented an IR of 0.2; all cases occurred in children less than 5 years old.

Tumors in group VIII showed an IR of 6.2, with a higher IR in the oldest group. They showed a higher IR in males as compared to females (7.5 vs 4.8). Of this group, the highest IR was for Osteosarcoma (4.2). It was also found to be higher in males than in females (5.1 vs 3.1). Ewing sarcoma presented an IR of 1.4. Overall MR for this group was 2.0, and by gender 2.1 for males and 1.8 for females. The OS rate from these tumors stabilized at 29.1 ± 10.1 at 48 months from diagnosis.

Group IX comprised soft tissue sarcomas and presented an IR of 9.4 and showed a similar distribution by gender. In this group, the most frequent tumor was the Rhabdomyosarcoma with an IR of 5.0. This IR showed two peaks: one in children younger than 5 years of age (6.3) and the other among 10 to 14 year-olds (7.0).

This tumor showed a greater incidence in females than in males (6.0 vs 3.9). Five and 10-year OS rates for this group were 64.1 ± 8.7 and 45.6 ± 13.1 .

Germinal tumors in group X presented an IR of 4.4 with two peaks in occurrence; one in children younger than 5 years old

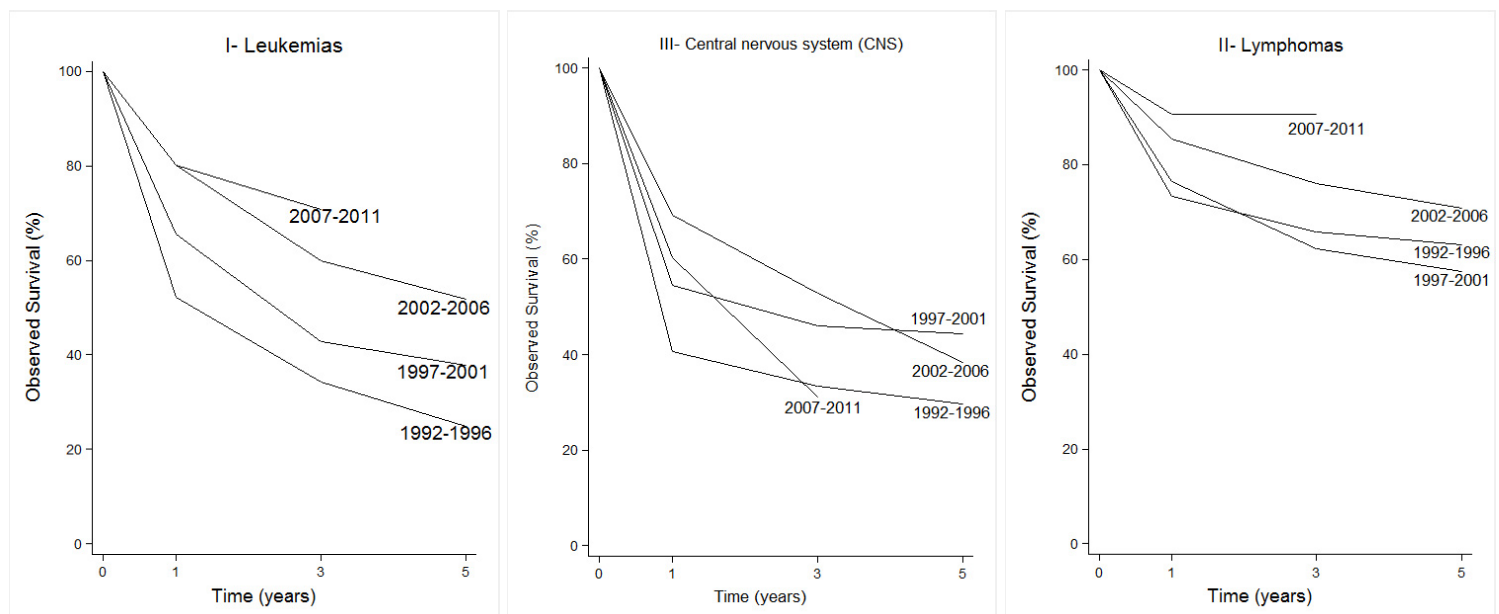
Figure 1. Cali, Colombia. Observed Survival estimates at 1, 3 and 5 years for Childhood Cancer trough 1992-2011 with follow-up to June, 2012.

Table 4. Cali, Colombia. Childhood Cancer Mortality Rates per million by diagnostic category and sex from 1977 to 2011.

Sex	Categorías diagnósticas	1984-1988		1989-1993		1994-1998		1999-2003		2004-2008		2009-2011	
		n	TEE	n	TEE	n	TEE	n	TEE	n	TEE	n	TEE
Boys and Girls	Leukemias, myeloproliferative & myelodysplastic diseases	55	26.6	73	32.8	85	36	85	33.1	72	25.5	35	19.0
	Lymphomas and reticuloendothelial neoplasms	16	7.8	21	9	22	9.3	14	5.1	6	1.9	4	1.9
	CNS and misc intracranial and intraspinal neoplasms	19	8.9	16	7.3	20	7.9	26	10	29	10	27	16.1
	Retinoblastoma	3	1.6	7	3.5	4	1.9	4	1.9	1	0.5	2	1.3
	Renal tumors	7	3.2	5	2.3	6	2.2	6	2.7	6	2.1	2	1.1
	Hepatic tumors	7	3.6	4	2	2	1.1	1	0.5	5	2.1	1	0.8
	Malignant bone tumors	6	2.7	4	1.6	5	1.8	8	2.7	7	2.1	3	1.4
	Soft tissue and other extraosseous sarcomas	4	1.9	5	2.5	9	4	2	0.7	4	1.4	1	0.5
	Germ cell & trophoblastic tumors & neoplasms of gonads	-	-	2	1	2	0.8	1	0.3	-	-	-	-
	Other malignant epithelial neoplasms and melanomas	12	6.2	12	5.5	19	8.8	11	4.7	12	4.9	12	7.2
	Other and unspecified malignant neoplasms	8	3.7	12	5.5	18	7.7	22	9.3	12	4.6	7	3.8
	All	137	66.2	161	73	192	81.8	180	71	154	55.1	94	52.9
Boys	Leukemias, myeloproliferative & myelodysplastic diseases	27	26	34	30	45	38.7	52	40	36	24.2	15	17
	Lymphomas and reticuloendothelial neoplasms	11	10.3	15	13.1	14	11.1	10	7	3	1.8	2	1.8
	CNS and misc intracranial and intraspinal neoplasms	12	10.9	7	6.4	11	8.6	11	8.8	13	9.2	18	21
	Retinoblastoma	2	2.1	3	2.8	1	1	2	1.9	-	-	-	-
	Renal tumors	5	4.5	4	3.7	2	1.5	2	1.7	2	1.6	1	1
	Hepatic tumors	4	4.2	-	-	1	1.1	-	-	2	1.8	1	1.5
	Malignant bone tumors	4	3.4	1	0.8	4	3	3	2.2	4	2.5	-	-
	Soft tissue and other extraosseous sarcomas	1	0.9	3	2.9	3	2.8	1	0.7	2	1.5	1	1
	Germ cell & trophoblastic tumors & neoplasms of gonads	-	-	-	-	-	-	-	-	-	-	-	-
	Other malignant epithelial neoplasms and melanomas	6	5.8	7	6.9	8	7.6	4	3.5	8	6.5	6	7.3
	Other and unspecified malignant neoplasms	5	4.6	7	6.6	8	6.4	14	11.3	5	3.8	3	3.4
	All	77	72.8	81	73	97	81.7	99	77.1	75	52.8	47	54.1
Girls	Leukemias, myeloproliferative & myelodysplastic diseases	28	27.1	39	35.7	40	33.3	33	25.9	36	26.9	20	21.0
	Lymphomas and reticuloendothelial neoplasms	5	5.3	6	4.8	8	7.5	4	3.2	3	2	2	2.0
	CNS and misc intracranial and intraspinal neoplasms	7	6.9	9	8.2	9	7.2	15	11.1	16	10.9	9	10.9
	Retinoblastoma	1	1.1	4	4.3	3	2.9	2	1.9	1	0.9	2	2.6
	Renal tumors	2	2	1	0.9	4	3	4	3.8	4	2.6	1	1.1
	Hepatic tumors	3	2.9	4	4	1	1.1	1	1	3	2.5	-	-
	Malignant bone tumors	2	2.1	3	2.5	1	0.7	5	3.2	3	1.8	3	2.8
	Soft tissue and other extraosseous sarcomas	3	2.9	2	2.1	6	5.3	1	0.6	2	1.3	-	-
	Germ cell & trophoblastic tumors & neoplasms of gonads	-	-	2	2.1	2	1.7	1	0.6	-	-	-	-
	Other malignant epithelial neoplasms and melanomas	6	6.6	5	4.1	11	10.1	7	6	4	3.2	6	7.0
	Other and unspecified malignant neoplasms	3	2.7	5	4.4	10	9.2	8	7.3	7	5.5	4	4.2
	All	60	59.6	80	72.9	95	81.9	81	64.8	79	57.5	47	51.6

(6.3), and the other in the 10 to 14 year-old group (11.0). There was no significant difference between genders. OS rates steadied at 36 months from diagnosis in 47.4 ± 13.0 .

The epithelial cancers in group XI presented with only a few number of cases and with an IR of 3.8. The age group with a higher IR was that of the 10 to 14 year olds. The adreno-cortical carcinoma presented an overall IR of 0.2, with 1 female case <5 years old. Thyroid carcinoma showed a global IR of 1.0. It mainly presented in the 10 to 14 year old age group. This was more prominent in females than in males (1.2 vs 0.8). Five-year OS rate for this group was 61.4 ± 12.6 . This last group showed an overall IR of 1.0.

Discussion

We estimated an overall CC IR in Cali during the period of study of 141.2 million children (<15 years old), ranking us in an intermediate position in comparison with other countries. In 1998, IARC reported an IR from 160 Hispanic patients in Los Angeles and 122.1 patients from England and Wales. The most recent information from Europe according to the ACCIS system, reported an overall IR of 138.5. This varied according to region from 131.1 in the United Kingdom to 160.1 in northern countries^{6,19-21}. In the U.S., SEER reported an overall IR of 154.

Brazil reported an IR which varied between 94.7 (Salvador Bahia) and 226.2 (Goiania). This geographical variation is important and suggests the presence of environmental factors that contribute to the cause of these tumors. In order to interpret these changes in the IRs, it is necessary to keep in mind the role that sub-registration problems and classification errors may play.

In general, CC cases in Cali occurred more often in children younger than 5 years of age, and in males. There were exceptions for Wilms tumor, thyroid cancer and rhabdomyosarcoma in which the male/female ratio was 0.46:1, 0.66:1, and 0.65:1. The predominance of the Wilms tumor and thyroid carcinoma in females is consistent with reports from other countries. Nevertheless, the female predominance of rhabdomyosarcoma does not show as much consistency. For example, in the ACCIS and the SEER the ratio between males/females for this tumor was 1.3:1^{6,19-21}.

As was previously mentioned, leukemias were the most frequent group reported, followed by CNS tumors and lymphomas. This pattern of occurrence is similar to that reported in North America and Europe. In other South American countries, a higher frequency of lymphomas over CNS tumors has been reported, especially in

Table 5. Cali, Colombia. Observed Survival estimates at 1, 3 and 5 years for Childhood Cancer trough 1992-2011 with follow-up to June, 2012.

Categorías diagnósticas	1992-1996				1997-2001				2002-2006				2007-2011			
	Interval (years)				Interval (years)				Interval (years)				Interval (years)			
	n	1	3	5	n	1	3	5	n	1	3	5	n	1	3	5
Leukemias, myeloproliferative & myelodysplastic diseases	139	* 52.2	34.3	24.9	158	65.6	42.9	37.9	150	80.1	60	51.8	147	80.2	70.7	!
		• 4.9	4.7	4.3		3.9	4.1	4		3.4	4.3	4.6		3.4	4.3	!
Lymphomas and reticuloendothelial neoplasms	46	* 76.5	62.2	57.4	50	73.4	65.8	63.1	63	85.5	76	70.8	61	90.6	90.6	!
		• 8.9	10.4	10.6		6.9	7.5	7.6		4.8	5.8	6.5		4	4	!
CNS and misc intracranial and intraspinal neoplasms	47	* 40.7	33.3	29.6	71	54.5	46.1	44.3	71	69.3	52.8	38.3	72	60.3	31.1	-
		• 9.2	8.9	8.6		6.2	6.3	6.3		5.8	6.5	7		6.5	9.7	-
Neuroblastoma and other peripheral nervous cell tumors	9	* 19.4	0	0	11	77.8	66.7	55.6	8	58.3	58.3	!	13	43.3	!	!
		• 17.2	0	0		13.9	15.7	16.6		18.6	18.6	!		17.9	!	!
Retinoblastoma	11	* 30.3	30.3	30.3	21	88.2	82.4	82.4	10	90	90	90	14	91.7	!	!
		• 24.9	24.9	24.9		7.8	9.2	9.2		9.5	9.5	9.5		8	!	!
Renal tumors	10	* 100	57.1	42.9	20	92.9	78.6	78.6	17	87.8	75.3	58.1	17	87.5	75	!
		• 0	18.7	18.7		6.9	11	11		8.1	10.7	13.7		8.3	13.6	!
Hepatic tumors	5	* -	-	-	0	!	!	!	6	16.7	16.7	16.7	5	66.7	-	-
		• -	-	-		!	!	!		15.2	15.2	15.2		27.2	-	-
Malignant bone tumors	11	* 90.9	60.6	45.5	14	58.3	33.3	33.3	27	86.5	52.1	45.6	17	90.9	39.8	-
		• 8.7	18.4	19.1		14.2	13.6	13.6		7.2	11.1	11.4		8.7	17.5	-
Soft tissue and other extraosseous sarcomas	25	* 61.7	41.1	41.1	23	61.9	61.9	61.9	18	92.3	69.2	69.2	29	90.1	!	!
		• 12.5	12.8	12.8		11.4	11.4	11.4		7.4	12.8	12.8		7	!	!
Germ cell & trophoblastic tumors & neoplasms of gonads	10	* 60	40	40	9	77.8	55.6	55.6	12	77.1	77.1	64.3	17	93.3	!	!
		• 21.9	21.9	21.9		13.9	16.6	16.6		14.4	14.4	16.8		6.4	!	!
Other malignant epithelial neoplasms and melanomas	14	* 64.3	53.6	42.9	9	75	60	60	20	88.7	81.8	81.8	15	83.6	!	!
		• 14.9	15.8	15.9		15.3	18.2	18.2		7.6	9.6	9.6		10.8	!	!
Other and unspecified malignant neoplasms	2	* -	-	-	2	-	-	-	6	50	50	50	9	50	!	!
		• -	-	-		-	-	-		20.4	20.4	20.4		18.6	!	!
All	329	55.4	38.6	31.6	388	67	51.5	48.3	408	78.9	63	54.9	416	79.1	64.8	-
		3.4	3.4	3.2		2.5	2.7	2.7		2.1	2.6	2.8		2.2	3.1	-

* Observed Survival estimates (%)

• Standard Error

! The statistics could not be calculated

Brazil. In Africa, excluding the southern part of this continent, the tumors with greater IR's were lymphomas, especially Burkitt's. This tumor is considered endemic of this region and is believed to be due to the coexistence of high malaria transmission and early infection by Epstein Barr virus (EBV)^{6,19-22}.

All showed its greatest incidence rates in children younger than 5 years old for both genders. Nevertheless, it showed a higher peak of incidence in the group of males from 5 to 9 years old when compared with that of females. This is compatible with what has been described in other countries. This corresponds to a peak incidence of common precursor B-cell cell leukemia, usually with t(12;21), that occurs in males around 5 years of age. Looking at the IRs for Cali during the 1977-1981 period, they are approximately equal for males and females (37.8 vs 37.9), suggesting that the characteristic peak incidence of this illness did not occur before 1981. Upon taking the 5 to 10-year OS rate for this illness, the existence of a great gap with most developed countries is evident. Nevertheless, it is encouraging to find that there is an apparent progressive increase with the 5-year OS rate, which practically doubles between the first and third five-year period as reported in this study.

In the epidemiology of Burkitt's lymphoma, attention is focused on the enormous differences encountered according to geographical area. In equatorial Africa, for example, Burkitt's lymphoma is considered endemic and an IR of 36.1 has been reported (Uganda, Kampala 1992 to 1995). This compares with an IR of 0.6 reported in U.S. Afro-descendants (SEER 1983-1992). South and Central American countries report IRs from 7.2 (Cuba 1986 to 1990) to 0.5 (Costa Rica 1984 to 1992). In Cali from 1982-1991, an IR of

6.2 was accepted and during this recent reporting period the rate of 7.2 was found. This is the only lymphoma that is more frequent in the younger age group (<5 year old), occurring almost 3-times more frequently in males than in females. The other non-Hodgkin lymphomas and Hodgkin lymphoma were more frequently found in the older age group (10 to 14 years old) than in the younger ones. Lymphoma was the tumor group with the best 5 to 10-year OS rate, with a clearly increasing trend when each five-year period is compared. In the last period, more than two-thirds of those patients were reported to be cured^{6,19-21}.

CNS tumor²³ group was second in frequency and first in MR. Although 5 to 10-year OS for all this group was similar to that of the leukemia group, when examining 5-year OS by time periods CNS showed no prominent increases, as were found for the leukemia and lymphoma groups. In Cali, the Neuroblastoma IR (3.8) was comparatively lower than found in other countries and only represents 2.8% of all registered tumors in children. In North America, Europe and Australia, Neuroblastoma represents between 6% and the 10% of all CCs with an IR that varies between 7 and 10. In Central American countries and among the Hispanic population of Los Angeles, the IR was noted as less than 6.0. We found that the majority of cases (74%) occurred in children younger than 5 years old. In Cali, Retinoblastoma represented 3.9% of all the cases. This is similar to reports from North America, Europe and Australia (2% to 4%).

This contrasts with Brazilian reports where the IR was as high as 9.8 reported in Natal city (Rio Grande do Norte State). Although the 5-year OS found for Retinoblastoma is not considered bad, the hope is to find higher OS's given that it is a tumor susceptible to

early detection and has effective therapeutic interventions in place. In spite of the previously noted trends, an important increase of the 5-year OS (from 30% to 90%) was noted between the period of 1992-1996 and 2002-2006. Renal tumors represented 4.3% of the total, and in this group Wilms tumor was the most frequent type noted. We consider that the incidence found for these tumors in Cali, i.e., 6.2, is at the intermediate level (from 6 to 9) when compared to other reports. In Asia, including India and Japan, the incidence of these tumors is 2 to 4. Wilms tumor long-term OS is considered as a paradigm in the treatment of CC. Improvements were quickly obtained from use of a combination of approaches, including surgical, chemotherapy and radiation therapies. We found 5 and 10-year OS rate to be below those reported in other countries^{6,19-21,24}.

The uncommon Hepatoblastoma is mostly an infant cancer that represents only 0.3% of all CC reported for this period in Cali. This frequency is relatively lower when compared with North America and Europe where it represents about 0.8% to 1.3%. In Japan and Thailand, it is higher and represents around 2.5%. The highest IR reported has been in China where an IR of 4 has been reported^{6,15-17}. Bony tumors represented 4.2% of all registered cancers. They are tumors that are usually present in adolescence and rarely present in children less than five years of age. Globally, the IR for Osteosarcoma was 3 times greater than that of Ewing sarcoma. This relationship is similar to data reported by other cancer registries²⁵. In Asian countries Osteosarcoma presents an IR from 1 to 2. In most European countries and in the "whites" group in the United States, the IR reported was 2 and 3.5. Unfortunately, the OS rate for this group of tumors is still low and of relatively short duration. We noted that this was one of the groups that in Cali did not show progress in OS. The soft tissue sarcomas group is extensive, and highly heterogeneous, with Rhabdomyosarcoma being the most frequent. This group represented 6.4% of all the registered tumor cases in this report. The IR in different parts of the world oscillates from 2 to 5. In this group of tumors, an increase in 5-year OS was apparent, from 41.1 ± 12.8 to 69.2 ± 12.6 ,^{15-17,26}. The germinal tumor group also includes a remarkably heterogeneous series of tumors. This group represented 3% of all reported cases. According to various cancer registry reports, the frequency of this group ranges between 2% and 4%. Epithelial cancer is less frequent in children than in adults, and alone represents 2.6% of all pediatric cancer cases. In this group, the unspecified carcinomas were the most frequently found, followed by thyroid carcinoma. We found an increase in 5-year OS of 42.9 ± 15.9 to 81.8 ± 9.6 .^{6,19-22}.

The descriptive epidemiology for cancer is an indispensable source of information. It not only offers knowledge of the causal etiologies of these illnesses, but also contributes as an indicator of the progress of public health policies and the health system.

Conflict of Interest Disclosure:

The authors declare that there is no real or potential conflict of interest regarding the possible publication of this work.

Acknowledgements:

This work was supported by grants from the Universidad del Valle - COLCIENCIAS 106-40820552. RC-302, 2007 (Colombia) and

PPG CA 028842, the National Cancer Institute, and the National Institute of Health (U.S.A.).

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