Patterns and trends of childhood malignancy in Sri Lanka.

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Abstract

Objective: To determine the pattern and trends in morbidity and mortality from childhood malignancy in Sri Lanka

Methodology: Data on morbidity from 3633 malignancies in children 0-15 years of age for the period 1982 –1994 were collected from the three cancer hospitals in Sri Lanka. The death register maintained at the Office of the Registrar General was utilized to obtain information on deaths from malignancy in the same age group from 1980 to1990. Age standardization of rates was achieved by using the mid-year population of children in the age group for the year 1988.

Results: An increase in incidence of childhood malignancy from 2.6 in 1982 to 6.2 in 1994 from all causes was observed. Leukaemia (42%) was the commonest malignancy of which 82.7% of cases were acute lymphoblastic leukaemia, followed by lymphomas (12.6%) and malignant tumours of CNS (9.7%). The highest rate of increase was observed for CNS malignancies. Of 40.4% solid tumours, 27.2% were localized to the site at diagnosis while 47.2% had spread by direct extension and 10% to distant sites.

4.2% of all deaths during the study period were from childhood malignancies and of these 52% were of lymphatic and heamopoietic origin. Leukaemias accounted for 82% of deaths.

Conclusion: Childhood malignancy shows an increase in the rate of admission during the period. The pattern is that of a developing country undergoing a change towards that of a developed country.

Key words: Childhood malignancy, morbidity, mortality, patterns, trends

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Introduction:

Non-communicable diseases are increasing worldwide and are expected to account for 54% of all diseases in the year 2015 while infectious and parasitic diseases are expected to decline to 16% from the 1985 level of 35% (1). Cancer is one of the non-communicable diseases that is gaining recognition as a major public health problem and an emerging one, especially in developing countries. In Sri Lanka (excluding the North and East provinces), hospital morbidity and mortality rates from cancer in 1990 were, 142 and 10.2 per 100,000 population respectively (2). Of a total of 5,000 new cases of malignancy diagnosed annually, 5-6% were observed to occur in children under 15 years of age (3).

The trends of disease show the extent of the problem the country will have to face in the years to come and reflect the effectiveness of existing control activities. The prevailing pattern of disease and the changes observed can be used to identify specific interventions that are necessary and to assess the usefulness of such interventions prevention and control that are already in operation.

This study was undertaken with the objective of determining the trends and patterns of morbidity and mortality from malignancy in children 0-15 years of age.

Methodology

Morbidity

A descriptive retrospective study of records of children 0-15 years of age admitted to the three cancer hospitals in Maharagama, Kandy and Galle, with a diagnosis of malignancy was carried out. The period of study was from 1st

January 1982 through 31st December 1994. The three cancer hospitals account for approximately 95% of cancer patients treated at government hospitals (3). Cases transferred from other hospitals were excluded to avoid duplication.

Every patient referred to or admitted for the first time is issued a clinic record. This record is used at every re-admission along with a Bed Head Ticket (BHT) and information with regard to each admission is entered in the clinic record from the BHT. Hence, the record contains an up to date account of the progress and current situation of the patient's condition.

Mortality

Mortality data were collected from the Office of the Registrar General for the period 1st January 1980 to 31st December 1989. The data collectors were medical officers.

Results

Morbidity

The registers showed that 3,959 children had been admitted during the study period and 3,633 records (91.8%) were complete and fulfilled criteria for inclusion.

From 1982 to 1994, malignancy in children of 15 years and less accounted for 2.2- 6.8% (mean 4.8%) of admissions per year to the three cancer hospitals. Eighty six percent of the subjects were Sinhalese, 7.4% Moslem , and 6.4% Tamil (Table 1). The male female ratio was 1.4:1. Thirty eight percent of malignancies were observed in preschool children, of which 3.4% were in infants. One-third occurred among children between 10-15 years and 30% among the 5-9 year olds. The Western Province recorded the highest percentage (38.3) of cases and a rate of 6.4 per 100,000 children.

Table 1: Summary table showing the sociodemographic characteristics of the study population

	N=3633	
1. Ethnicity		
	No.	%
Sinhala	3107	85.5
Tamil	231	6.4
Moslems	267	7.4
Others	26	1.0
No information	2	0.1
2. Age in years		
<1	123	3.4
1-4	1271	35.0
5-9	059	29.9
10-15	1180	32.5

3. Province	No.	Rate*	%
Western	1391	6.4	38.3
Southern	509	4.7	14.0
Central	444	4.1	12.2
N. Western	385	3.9	10.6
Sabaragamuwa	281	3.4	7.8
N.Central	221	4.4	6.1
Uva	163	3.1	4.5
Eastern	134	2.1	3.7
Northern	91	1.4	2.5
Unknown	14	-	-

Rate - per 100,000 children <15 years of age, mid year population of 1998

The Colombo district accounted for one fifth (22.5%) of admissions followed by Gampaha (11%) and Kandy (8.4%). Incidence rates

calculated by district using hospital data may not reflect the true distribution of malignancy by district since it is based on the address given by patients. The Southern Province ranked second with a rate of 4.7 cases per 100,000 population and accounted for 14% of the admissions.

Ninety four percent of the diagnoses had been based on histological or morphological criteria (Table 2). In 4%, the diagnosis was based on clinical criteria only or on clinical criteria and the results of non- specific investigation such as white cell counts and erythrocyte sedimentation rate.

Of the 3,633 malignancies studied, 1,469 (40.4%) were solid tumours. Clinical staging at time of diagnosis of the solid tumours showed 399 (27.2%) to be localized to the site. Nearly half (47.2%) had spread by direct extension to regional lymph nodes (3.7%) or by both methods (1.1%). Distant metastases had already occurred in 10%.

Table 2: Distribution of cases by criteria of diagnosis and clinical stage at diagnosis

1.Criteria for diagnosis	No.	N=3633 %
Clinical only	7	0.2
Clinical/investigation	134	3.7
Cytology	3411	93.9
Unknown	81	2.2
2. Clinical stage at diagnosis		
Tumour in situ	19	1.3
Localized	399	27.2
Direct extension (DE)	694	47.2
RLN*	54	3.7
DE &RLN	17	1.1
Distant metastasis	151	10.3
Unknown	135	9.2

*Regional Lymph Nodes

Pattern of distribution

The majority of childhood malignancies were leukaemias (41.9%) followed by lymphomas (12.5%, Table 3). One-tenth were malignancies of the central nervous system.

Table 3: Distribution by type of malignancy

Type of malignancy	No.	%
Leukaemia	1522	41.9
Lymphoma	456	12.5
Central nervous system	354	9.7
Bone	222	6.1
Eye	191	5.3
Kidney	155	4.3
Soft tissue	151	4.2
Sympathetic Nervous system	119	3.3
Gonadal	114	3.1
Liver	30	0.8
Skin	11	0.3
Other	308	8.5
All cases	3633	100

Of the 1,522 cases of leukaemias 1,437 (94%) were acute leukaemias (Table 4). Only 2.6% cases were chronic leukaemias. Among the acute leukaemias, 1,259 (82.7%) cases were histologically diagnosed as Acute Lymphoblastic Leukaemia (ALL).

The mean incidence rate per year over the period of study for ALL using the mid-year population of children in 1988 as the denominator was 1.66 per 100,000 children.

Table 4: Distribution of Leukaemia cases by histological type

Type	No	%
Acute Lymphoblastic	1259	82.7
Acute myeloid	178	11.7
Chronic myeloid	39	2.5
Chronic lymphoid	1	0.1
Other	45	3.0
All cases	1,522	100

Table 5 :Distribution of different malignancies by age group

Type	Age group <1		1-4		5-9		10-15		Total
	No.	%	No.	%	No.	%	No.	%	No.
Leukaemia	36	2.4	589	38.7	494	32.5	403	26.5	1522
Lymphoma	5	1.1	96	21.1	183	37.9	183	39.9	456
CNS	1	0.3	61	17.2	144	40.7	148	41.8	354
Bone	0	0	16	7.2	56	25.2	150	67.6	222
Eye	21	11.0	150	78.5	15	7.8	5	2.6	191
Kidney	21	13.6	96	61.9	30	19.4	8	5.2	155
Soft tissue	14	9.3	57	37.8	41	27.2	39	25.8	151
SNS	2	1.7	77	64.7	26	21.9	14	11.8	119
Gonadal	4	3.5	32	28.1	12	10.5	66	57.9	114
Other	19	5.4	97	27.8	68	19.5	165	47.3	349
Total	123	3.4	1271	35.0	1059	29.2	1180	32.5	3633

Out of 456 cases of lymphomas, 45% were Non-Hodgkins's in type. Thirty three percent were Hodgkin's lymphomas. Of the Non-Hodgkin's, 3.3% were Burkitt's lymhomas

Nearly 60% of brain tumours were histologically diagnosed as gliomas (36.4%) and medulloblastomas (21.2%). Astrocytomas accounted for 16.9% and craniopharyngiomas for 11.6%.

The distribution of different malignancies by age is shown in Table 5. The malignancies of bone observed were Ewing's sarcoma(47.3%) and osteogenic sarcoma (46.8%) Retinoblastoma(97.4%) andnephroblastoma(93.5%) were the commonest tumours of the eye and the kidney respectively.

In all age groups leukaemia was the commonest malignancy observed and 39% of cases had occurred between 1 to 4 years of age. Other malignancies common in this age group were those of the eye (78.5%), sympathetic nervous system (64.7%) and the kidney (62%).

Table 6: Distribution of different cases of malignancy by sex

Type	Males	Females	Total	Sex Ratio
Leukaemia	938	584	1522	1.6
Lymphoma	324	132	456	2.5
CNS	211	143	354	1.5
Bone	104	118	222	0.9
Eye	85	106	191	0.8
Kidney	87	68	155	1.3
Soft tissue	91	60	151	1.5
SNS	76	43	119	1.8
Gonadal	30	84	114	0.4
Other	187	162	349	1.2
Total	2133	1500	3633	1.5

The highest prevalence of lymphomas (77.8%) and tumours of the central nervous system (82.5%) were seen after 5 years of age. Those of bone (67.6%) and gonads (57.9%) were higher in the older children between 10 and 15 years. In infancy leukaemia ranked number one followed by malignancies of the eye and kidney.

Table 6 shows the distribution of malignancies by sex. Although there was an overall male preponderance, tumours of the bone, eye and gonads were commoner among the females.

Trends

A slow and gradual increase in the incidence, from 2.65 cases per 100,000 in 1982 to 6.2 cases per 100,000 in 1994, with a mean rate of 4.75 cases per 100,000 children 15 years and less (SD=1.0) was observed (Table 7).

Table 7: Age specific incidence rates of childhood malignancy : 1982-84

Year	Frequency	Population < 15 years~ '000	Rate*
1982	142	5356	2.65
1983	225	5437	4.14
1984	238	5502	4.33
1985	228	5588	4.08
1986	224	5675	3.95
1987	258	5765	4.48
1988	277	5843	4.74
1989	272	5917	4.60
1990	316	5983	5.28
1991	335	6070	5.52
1992	342	6126	5.58
1993	387	6203	6.24
1994	389	6276	6.20

~Source -Department of Census and Statistics 1989
*per 100,000 children < 15 years
Mean rate = 4.75 SD=1.0 .Range 2.65-6.24

The overall trend in childhood malignancy, indicating the general trend of the progress of the series was calculated by fitting a regression line to the data. The equation for the fitted line was: $y = a+bx$ where y= rate, x= year, $R^2=0.8896$. Thus the predicted rate = $3.058+0.244*x$.

The mean incidence rate for males (5.5 cases per 100,000) was significantly higher than for females (4.0 cases per 100,000 children per year, $t=9.2$, $df=24$, $p<0.01$). The incidence rates for Sinhalese, Moslem and Tamil were 5.1, 4.0 and 3.7 cases per 100,000 children respectively. The mean incidence rate (per 100,000 children per year) in the different age group were: infants – 2.57 (range 1.28-4.52, SD=1.04); 1-4 years – 5.66 (range 1.42-8.24, SD=1.41); 5-9 years- 4.3 (range 2.08 – 5.41, SD=0.98); 10-14 years – 4.79 (range 2.78-6.44, SD=0.93).

The mean incidence rate per year per 100,000 children for the districts of Colombo, Gampaha, Kandy, Galle and Kurunegala in order were, 8.5 (SD=0.5) , 5.1 (SD=0.6), 4.9 (SD=0.4), 5.1 (SD=0.8) and 3.3 (SD=0.4) respectively.

Table 8 shows the change in the incidence rates for different disease categories during the period of study.
A fivefold increase is observed for malignant tumours of the brain. The incidence of leaukaemia, lymphoma, bone and soft tissue tumours show a two to threefold increase.

The outcome of disease was assessed using the data from the clinic records. It was found that 2,082 (57.3%) had not been reviewed for a year or more and the outcome could not be decided as they were lost to follow up (Table 9). The case fatality rate was 20.2% for the period under study though it could be different depending on the underlying reasons for loss to follow up. The status of disease could be considered as satisfactory only in 17.4%, where 9.6% had been recorded as not showing evidence of

Table 8: Incidence rate (per 100,000 children per year) by selected disease categories : 1982-1994

	Disease categories							
Year	Leukaemia	Lymphoma	CNS	Bone	Eye	Kidney	Soft tissue	Gonads
1982	1.2	0.3	0.2	0.1	0.3	0.1	0.2	0.0
1983	1.6	0.7	0.4	0.3	0.2	0.2	0.2	0.1
1984	2.0	0.6	0.3	0.3	0.3	0.2	0.1	0.1
1985	1.9	0.5	0.3	0.3	0.2	0.2	0.4	0.1
1986	1,7	0.5	0.3	0.2	0.3	0.3	0.3	0.2
1987	2.0	0.5	0.5	0.3	0.2	0.2	0.4	0.1
1988	1.9	0.8	0.3	0.2	0.3	0.2	0.3	0.1
1989	1.9	0.6	0.4	0.4	0.2	0.2	0.3	0.3
1990	2.1	0.5	0.5	0.4	0.4	0.3	0.3	0.2
1991	2.3	0.7	0.4	0.4	0.3	0.2	0.5	0.2
1992	2.2	0.6	0.6	0.4	0.3	0.2	0.6	0.2
1993	2.6	0.8	0.8	0.3	0.2	0.1	0.4	0.2
1994	2.4	0.6	1.1	0.3	0.2	0 3	0.4	0.2

malignancy and 7.8% were in remission. Those lost to follow up could not be studied further due to time and resource constraints.

Table 9: Distribution by outcome

Outcome	Frequency	%
Died	733	20.2
No evidence of cancer	347	9.6
Cancer unchanged	5	0.1
Cancer in progress	183	5.0
Cancer in remission	283	7.8
Not known	2082	57.3
Total	3633	100

Mortality

Information on deaths by malignancy in children 15 years and less was obtained from the death register of the Office of the Registrar General in Colombo for the period 1980 to 1989. There were 1,795 such deaths and these deaths as a percentage of all deaths ranged form 3.3% to 4.8% with an average of 4.2% per year. Forty six percent of deaths were seen in under 5 year old children and of them 31% were seen in the 1 to 4 year age group. The percentage of deaths in the 5– 9 and 10- 15 year olds were 28.6 % and 25.6% respectively. The sex ratio was 1.3:1.

Age specific death rate for 0-15 years ranged from 2.6-3.7 per 100,000 (mean 3.2, SD= 0.3). The highest rate was seen in infants (6.76, SD=2.4) with a gradual decline in the other age group (1-4 years: 3.47, SD=0.6, 5-9 years: 2.79, SD=0.4 and 10-14 years: 2.51, SD=0.4). During the period under study the mean age specific death rates for males (3.5) was higher than for females (2.8).

Table 10: Distribution of deaths by broad disease categories

ICD No.	Disease category	No.	%
08	Neoplasms of lip oral cavity & pharynx	31	1.7
09	Neoplasms of digestive organs	130	7.2
10	Neoplasms of respiratory organs	38	2.1
11	Neoplasms of bone connective tissue etc.	51	2.8
12	Neoplasms of genito-urinary organs	38	2.1
13	Neoplasms of other and unspecified sites	588	32.8
14	Neoplasms of lymphatic & haemopoietic system	912	50.8
15-18	Others	7	0.3
Total	All diseases	1795	100

The distribution of deaths by broad categories is shows in Table 10. In 51% of deaths the cause had been neoplasms of lymphatic and haemopoeitic tissue (ICD No.14). Of these 82% were attributed to leukaemias and 6% to lymphomas. One third classified as malignant neoplasms of other and non specific sites included neoplasms of eye, brain and endocrine glands. Brain tumours accounted for 86 deaths (14.6%) of this group.

Discussion:

The three cancer hospitals are referral institutions and 90 to 95% (2) of cancer patients are referred to them and would therefore yield a representative sample. However, a percentage of cases completely managed in the private sector would have been missed. Use of clinic record cards from the cancer hospitals issued only on the first admission and updated at each subsequent admission, ensured that there was no duplication of cases. All data were transcribed into data sheets and were rechecked for accuracy. Only two data collectors were used after training.

Of children had been admitted during the study period 3,633 (91.8%) records were complete and fulfilled criteria for inclusion. Age standardization of rates was achieved by using 1988 mid-year population of 0-15 year-olds in the calculation.

The percentage of children under 15 years with a diagnosis of malignancy admitted to the premier cancer hospitals in Sri Lanka increased from 2.2% in 1982 to 6.8% in 1992. According to the Surveillance Epidemiology and End Results Survey (SEER), cancer in children accounted for about 1% of all reported malignancies in the U.S.A. (4). An actual increase in number of cases, an increase in the numbers that seek treatment as well as better diagnosis and referral may be some of the reasons for the observed increase. A decrease in the incidence of adult cancer too, needs to be excluded.

Incidence rates show an increase from 2.6 in 1982 to 6.2 cases per 100,000 children in 1994. The underlying trend in the series was studied by fitting a regression line and the incidence rate predicted by the fitted equation ($x = 3.058 + 0.242$*years) for 1998 is 7.17 cases per 100,000 children.

The incidence rate of Sri Lanka appears to be lower than that of developed countries which is about 11.2 per 100,000 children (5). The male preponderance with a male:female sex ratio of 1.4:1 is slightly in excess of the value for

U.S.A. of 1.2 :1 (6). In most developed countries sex ratio is around 1.3:1 (6,7,8). This may be related to differences in the patterns of diseases seen between different countries.

The incidence and the frequency of childhood malignancy vary between different age groups. In this study 38% of all cases were seen in the 0-4 year age group, a pattern observed in most western countries (9). The highest percentage of cases were from leukaemia, lymphoma and malignancy of eye and kidney.

Malignancies of the CNS, bone and gonads were commoner in children >=5 years while the highest percentage of bone tumors (67.6%) and gonadal tumors (57.9%) was seen in 10-15 year olds.

Leukaemia accounted for 42% of all malignancies in children. This is higher than in western countries where it is around 30-40%. The frequency observed in this study is similar to the pattern of childhood malignancy observed in developed countries three decades ago (6). Leukaemia in children is fairly low in most developing countries. Indian studies have found that leukaemias account for only 12% of childhood malignancies (10).

Eighty three percent of all leukaemias were Acute Lymphoblastic Leukaemia (ALL) with a mean incidence rate of 1.7 per 100,000 children. This percentage is higher than in most developed countries where only two thirds of leukaemias are ALL (11). In part two of this study where all incident cases of ALL were identified more accurately over a period of one year, the incidence was found to be 2.5 cases per 100,000 children.

The second commonest malignancy observed in this study were lymphomas (12.5%). A high incidence of lymphomas is seen in most developing countries. In India lymphomas accounted for one third of cases of childhood cancer (10). This pattern is also seen in African countries where 40% of malignancies in children are lymphomas with only 12% being leukaemia (12). In this study 45% were Non Hodgkin's type, 33% Hodgkin's. Most developed countries show Hodgkin's lymphomas to be commoner than others unlike in African countries where 97% of lymphomas are accounted for by Non-Hodgkin's lymphomas (13).

Tumors of the central nervous system which ranks second in developed countries, occupied third rank in the study accounting for 10% of all cases. The highest increase in incidence during the period under study was observed for CNS tumors. A true increase in the incidence as well as availability of advanced techniques in diagnostic technology leading to accurate identification of more cases may be reasons for this.

In developed countries malignant tumors of the bone and eye rare relatively rare in comparison to those of soft tissue (11). In the study bone tumors and retinoblastomas were more common than those affecting soft tissue, kidney and sympathetic nervous system. Tumors of bone, eye and gonads were common among girls. This also has been documented among Black American children (14).

Conclusion:

Childhood malignancy in Sri Lanka showed an increase in the rate of admission over the period of study. The pattern is that of a developing country undergoing a change towards the pattern seen in developed countries. The largest proportion of cases were leukemia, among which ALL accounted for 82%. Lymphomas was the second commonest, and malignancy of the CNS was third. The latter also showed the highest rate of increase during the period under study.

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