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**PATTERNS IN THE INCIDENCE OF PEDIATRIC CANCER IN  
ALEXANDRIA, EGYPT, FROM 1972 to 2001**

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## ABSTRACT

Cancer among children is a substantial public concern. The epidemiology of childhood cancer is not fully understood. The descriptive epidemiology for cancer incidence has been a subject of considerable debate in order to identify and clarify the role of etiological factors and environmental exposure in cancer. An up-to-date perspective systematically collected data on the incidence of childhood cancer in Alexandria was used. Statistical analysis revealed that the over all cancer incidence rate increased from 1972 to 2001. The incidence of lymphatic and haemopoietic cancers increased dramatically over the specified period. The lymphatic and haemopoietic cancer incidence in 2001 have increased ~11 times cancer incidence in 1972. The incidence of leukemia among infant less than 5 years increased exponentially with a higher incidence among boys. Little increase was observed in the cancers of oral cavity, digestive organs and respiratory system over the specified period. Incidence of genito-urinary cancers have increased 3.7 times cancer incidence in 1973. Brain and central nervous system cancers showed an increase of 4.5 fold during the 30 years studied period. The trends in some cancer types suggest the need of a closer examination of the underlying factors and environmental contaminants leading to the disease in children.

**Key words:** Pediatric cancer, Childhood cancer, Cancer incidence.

## INTRODUCTION

Childhood cancer is a disease of special public concern. Cancer in a child younger than 20 years is rare. Despite its relative rarity, cancer ranked second to accidents as the most common cause of death in children (NIH, 1999; Statistics Canada, 1994). Each year in the United States approximately 12,400 children and adolescents younger than 20 years of age are diagnosed

with cancer (NIH, 1999). Approximately 2,300 children and adolescents die of cancer each year, which makes cancer the most common cause of disease-related mortality for children 1-19 years (NIH, 1999). Analysis of reliable and comparable data on childhood cancer incidence from around the world has revealed geographical and ethnic differences in risk of childhood cancers (IARC, 2000).

Cancer is characterized by the uncontrolled growth of cells. The transformation of a normal cell into a cancerous one requires a series of alterations often involving mutations in DNA, the genetic code (Weinberg, 1994). Little is known about the etiology of cancer in children. Both genetic and environmental factors working separately or together can cause cancer (NSCEHC, 1998). Genetic changes can be either inherited or sporadic. Hereditary changes occur in a parent's germ cells and pass on to the child. While sporadic genetic change is a chance event that occurs in an individual cell (Weinstein, 1988). Familial occurrence of cancer probably result from heredity but may be aggravated by environmental factors to which the family is exposed (Weinstein, 1988).

Exposure to certain carcinogens in the environment through many routes, including air, water, food, drugs, surface contact and tobacco use may be associated with some human cancers (Weinstein, 1988; Zahm & Devesa, 1995). Children can be exposed in several ways to chemical agents used in their neighborhoods. Infants and children who live in households with smokers involuntarily inhale the toxic substances in tobacco smoke which is a complex mixture of more than 4,000 chemicals and some of them are known to be human carcinogens (Tomatis et al., 1990). Exposure to hazardous wastes that have been released into the environment, such as; heavy metals, organic chemicals, pesticides, strong acids or bases, may present serious health hazards to children (Tomatis et al., 1990). Ionizing radiation is known to increase the risk of cancer (Hempelmann et al., 1975; MacMahon, 1962). Prenatal exposure to diagnostic x-rays increase the risk

of acute lymphoblastic leukemia in children (MacMahon, 1962). Exposure to electromagnetic fields was also related to the occurrence of childhood cancers (Hocking et al., 1996; Washburn et al., 1994; Theriault, 1990). Overexposure to the sun's harmful ultraviolet light by children increase the chance of developing malignant melanoma by three folds (ACS, 1996). Research into the causes of childhood cancers is ongoing but the progress is slow because of the relative rarity of childhood cancer and difficulties in defining subgroups of cancers that have same etiology (Li, 1988).

Data describing and analyzing cancer incidence, mortality and survival are used in a variety of epidemiological studies in order to identify the role of the variable etiological factors in cancer incidence. In our study, we have investigated the change in incidence and the distribution of childhood cancer in the city of Alexandria, Egypt, during the period of 1972 to 2001.

## **MATERIAL AND METHODS**

**Data collection:** Data were collected from the center of Alexandria Cancer Registry, Medical Research Institute, University of Alexandria. The source for cancer incidence registry is hospital-based registry. The Alexandria Cancer Registry includes all cancers notified by the Alexandria University Hospital, other public and private hospitals, physicians, surgeons and pathology laboratories in the area. Notification of cases is supplemented and checked by routine search in death registries.

**Statistical analyses:** The variations in the incidence of pediatric cancers from 1972 to 2001 was investigated in a follow-up study in which data were analyzed using the programs of MS-Excel 2000, MiniTab version 12.1 and DataPlore version 2.0-8. Data entry and management was performed by MS-Excel 2000 program. Tumor type, age and sex distribution were included in the analysis.

## RESULTS

The patterns in the incidence of childhood cancer in Alexandria from 1972 to 2001 were studied. The distribution of malignant cases according to topographical diagnosis is shown in Table 1 for males and females. The estimated cancer for both sexes together and for all ages during the selected years in the studied period, showed that the most frequent childhood malignant tumors are those of the lymphatic and haemopoietic tissue followed by unspecified sites. The male predominance in most sites of cancers is evident.

The total estimated cancer cases for each year are presented in the histogram of figure 1. The detailed frequencies for the different site-malignancies are shown in figure 2 which presents a trend analysis of the childhood cancer incidence from 1972 to 2001. During the 30-years studied period, lymphatic and haemopoietic cancers increased significantly. The general trend overview shows increase in the overall cancer incidence by time during the studied period but the rates in the last seven years have been fairly stable. Lymphatic and haemopoietic cancer incidence shows the highest increase followed by unspecified site cancers and then by bone, connective tissue, breast and skin cancers. Cancers of lymphatic and haemopoietic tissue in 2001 showed ~11-fold increase in incidence compared to cancer incidence in 1972. Bone, connective tissue, breast and skin cancers increased ~9-fold, while incidence of cancers of unspecified sites increased 3 times during the studied period.

The primary types of childhood cancers as shown in table 2 are leukemia, brain and central nervous system, lymphomas and bone cancers. The incidence of leukemia among children younger than 20 years of age has shown a significant increase in the last 30 years. Compared to the total estimated cancer cases in 1972, leukemia incidence increased 14-fold, lymphoma incidence increased 8-fold and bone tumor incidence increased

8-fold in 2001 (table 2 & figure 3). The male predominance is evident from table 2 and figure 4. The total male:female ratio is about 1.5:1. The highest ratio is that of leukemias and lymphomas (table 3). Overall, pediatric cancers occur more frequently among boys than girls, germ tissue and soft tissue cancers are exceptions, in that they occur more frequently among girls than boys. It seems clear from table 2 that childhood cancers present a small percentage compared to adult cancers.

The average incidence of cancers in children and teenagers by age group in the last five years is shown in table 3 and figure 5. Among children younger than 20 years of age, the highest incidence of cancer occurs during the first five years of life. The lowest period of risk is between the age of 5 and 14 years, after which incidence rises. The different types of cancer vary in their relative frequency by age. The greatest diversity of cancer types is seen in infants less than five years of age. In this category of age group, three types of cancer; leukemia, brain and central nervous system and lymphomas, account for approximately 72% of cancer incidence. Renal tumors account for 9% of cancer incidence in this age. Epithelial carcinomas and soft tissue tumors become evident in children aged 15-19 years.

## DISCUSSION

The relative frequency of different topographical sites of pediatric cancer in Alexandria, Egypt, during the period of 1972 to 2001 was investigated. The estimated cancer cases, as reported by Alexandria cancer registry, were all cases presented for treatment to Alexandria University hospital and other public and private hospitals in the area. Age and sex distribution were involved in the study according to the sorting of the hospital-based cancer registry. The aim of this study is to describe and address the patterns in the incidence of pediatric cancers over time with the evolving daily environmental carcinogenic factors. The results revealed that the main childhood cancers are most often those of the blood cells, brain and central

nervous system and lymphatic system. Those three sites account for 70-80% of childhood cancers. The incidence of cancers in bone, kidney, eye, skin, breast, connective tissue, liver, gastrointestinal organs, oral cavity and respiratory system account for the remaining percentage. In general, lymphatic and haemopoietic cancers increased significantly during the 30 years studied period. In 2001 compared to 1972, the incidence of leukemias increased ~14-fold and of lymphomas increased 8-fold with predominance of occurrence among boys. Brain and central nervous system increased ~4-fold. Bone tumors increased ~8-fold. The general overview of the time series analysis revealed a moderate increase in the incidence of cancers of oral cavity, digestive system, respiratory system and genito-urinary organs.

Cancer among children is of important public concern. The exact etiology of pediatric cancer is not clearly evident till now. Results from all over the world indicates that cancer among children younger than 20 years of age is increasing equally among girls and boys (IARC, 2000; Bleyer, 1993). Relating the cancer incidence to patients age revealed that children in the 0-5 years age-group represent a unique subgroup. When analyzed by 5-year age intervals, cancer incidence was increasing with age except for the youngest group who have a higher incidence than children 5-9 and 10-14 years of age. In boys, the incidence rate during the first 5 years of life is higher than the rate between 5-20 years of age. It was reported that on the average, a child is more likely to have cancer developed during the first 5 years of life than during the rest of childhood (Bleyer, 1993). This observation must have certain biologic clues that lead to the etiology of cancer early in life and yet undiscovered (Linnet et al., 1999).

From different epidemiological studies, there is clear evidence that cancer in children is due to a different set of factors than those responsible for the development of cancer later in life (IARC, 2000; NIH, 1999; Doll, 1976). The occurrence of childhood cancer varies fourfold world wide with the geographic and ethnic differences (IARC, 2000; Parkin et al., 1988). This

variation results from the distribution of genetic and environmental factors that influence the development of cancer (Parkin et al., 1988). These factors can exert their effects at different periods in development before conception, during pregnancy and after birth. The association between exposure to drugs in utero and neonatal occurrence of tumors was reviewed and some associations were reported such as; antibiotics with leukemia, hormonal treatment with vascular tumors and phenytoin with neuroblastoma (Satge et al., 1998). Some other childhood cancers are associated with specific birth defects or malformation syndromes (IARC, 2000; Li, 1988; Miller, 1966). Unusual exposure to infectious agents have been suggested as explanations for some clusters of childhood leukemias (Grufferman, 1998). Prenatal exposure to x-rays increases the risk of acute lymphoblastic leukemia in the child (MacMahon, 1962).

Despite the fact that several possible risk factors related to the development of cancer in young people have been investigated (including physical, chemical and infectious agents and genetic and immunologic factors), only a few risk factors have been identified and these account for only a small proportion of cases (IARC, 2000; Linet et al., 1999; Doll, 1976). The greatest success of the past two to three decades with respect to childhood cancer has been the development of more effective treatment. Treatment for childhood cancers has become more complex and intensive which has declined dramatically the mortality rate from childhood cancer in recent years (IARC, 2000; NIH, 1999; Linet et al., 1999). Despite improvements in treatment, prevention remains an important goal. To prevent cancer, factors contributing to its development should be identified so that exposures can be reduced. Thus, research into the causes of cancer in young people is urgently needed.



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Table 1: Reported incidence for childhood cancer cases by gender from 1972 to 2001<sup>a</sup>

Tumor site	1972		1977		1982		1987		1992		1997		2001	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F
.Oral cavity & pharynx	0	1	6	0	2	3	2	3	2	3	10	8	6	3
.Digestive organs	6	4	8	2	7	3	1	1	8	1	16	6	9	0
.Respiratory organs	2	1	1	0	7	2	2	0	9	2	10	5	5	4
.Lymphatic & Haemopoietic	15	4	30	18	28	22	49	28	87	51	155	88	132	80
.Bone, skin, breast & connective tissue	4	3	5	4	6	7	11	13	25	23	52	48	37	34
.Genito-urinary organs	0	0	9	6	6	4	11	12	5	12	32	17	12	10
.Other unspecified sites	20	17	23	11	21	21	35	26	51	46	64	41	63	35
Male : Female ratio	1.6:1		2:1		1.2:1		1.3:1		1.4:1		1.6:1		1.6:1	
Percentage of occurrence in males to females	61:39%		67:33%		55:45%		57:43%		58:42%		61:39%		61:39%	

<sup>a</sup> Data were collected from the center of Alexandria Cancer Registry, using the ICD-9 code.

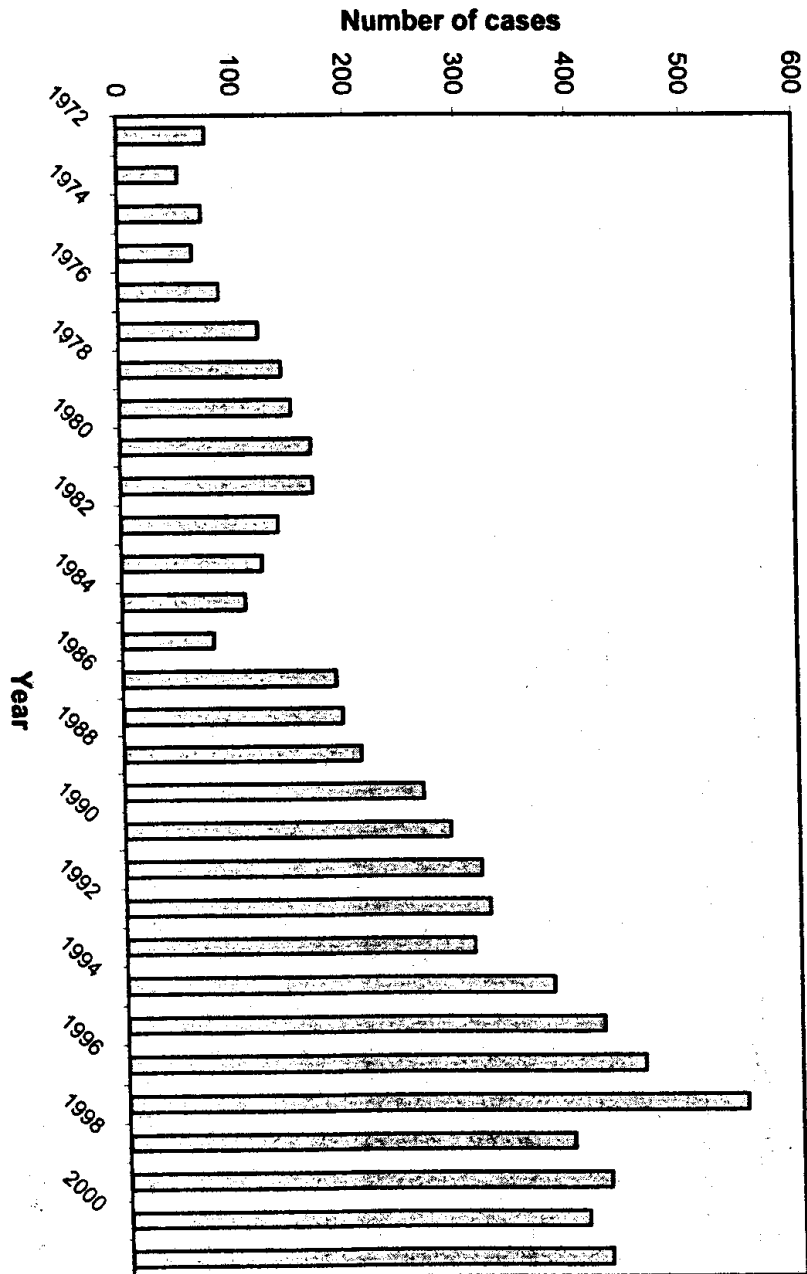
Table 2: Percentage of incidence for different types of childhood cancers from 1972 to 2001.

Cancer	1972	1976	1980	1984	1988	1992	1996	2000
.Leukemia	9%	9%	10%	50%	18%	19%	17%	24%
.Brain & CNS	44%	16%	17%	14%	30%	23%	23%	21%
.Lymphoma & other reticuloendothelial	16%	24%	30%	18%	25%	23%	24%	24%
.Carcinomas & other epithelial	18%	16%	10%	4%	6%	8%	8%	5%
.Germ cells & gonadal	0%	2%	1%	1%	1%	2%	1%	2%
.Soft tissue	5%	13%	11%	5%	4%	4%	8%	10%
.Bone	4%	4%	4%	0%	6%	10%	6%	6%
.Endocrine & other unspecified	1%	6%	6%	2%	3%	6%	3%	1%
.Renal	0%	7%	8%	5%	6%	3%	7%	5%
.Retinoblastoma	2%	2%	1%	0%	0%	2%	1%	1%
.Hepatic	1%	1%	2%	1%	1%	0%	2%	1%
Total estimated cancer cases for each year	77	88	169	109	210	325	462	410
Male : Female ratio	1.6:1	1.8:1	1.5:1	1.3:1	1.7:1	1.4:1	1.2:1	1.3:1
Percentage of cancer in children to total estimated adult cancer <sup>a</sup>	10%	7%	8%	5%	9%	10%	11%	9%

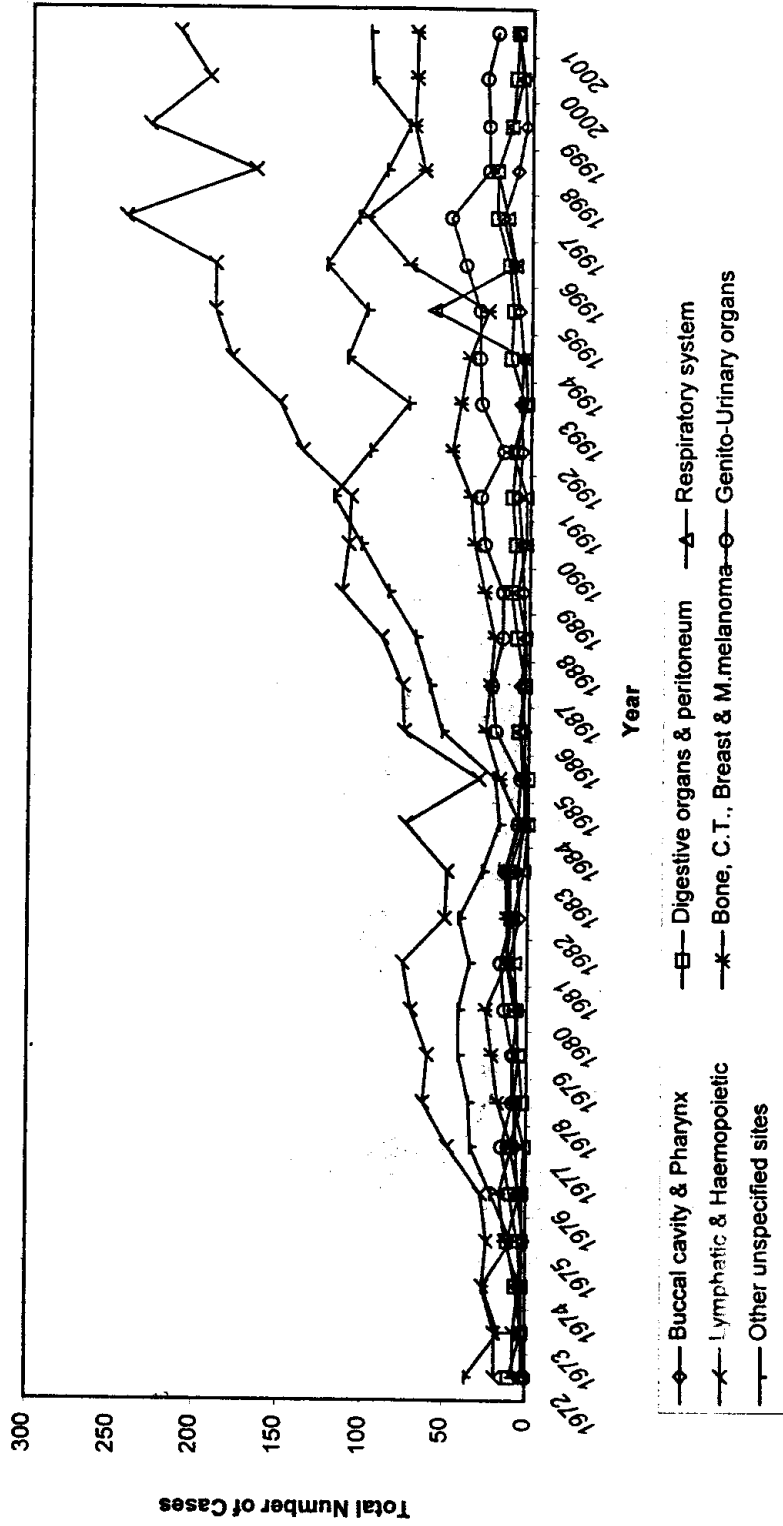
<sup>a</sup> Data were collected from the center of Alexandria Cancer Registry.

Table 3: Average annual estimated cancer cases in children by age and gender in the last five years (1997-2001).

Cancer	>5	5-	10-	15-	M	F
.Leukemia	48	28	32	23	76	55
.Brain & CNS	21	17	20	24	47	35
.Lymphoma & other reticuloendothelial	22	14	20	28	55	29
.Carcinomas & other epithelial	6	2	5	13	17	9
.Germ cells & gonadal	2	0	1	5	2	6
.Soft tissue	7	5	7	23	13	29
.Bone	1	3	10	11	16	9
.Endocrine & other unspecified	1	1	2	3	3	4
.Renal	12	2	1	2	10	7
.Retinoblastoma	6	0	0	0	4	2
.Hepatic	1	0	1	2	3	1
Total estimated cases	127	72	99	134	246	186
Percentage to total number of cases	29.4%	16.7%	22.9%	31%	57%	43%



**Figure 1.** Incidence of different types of cancers, collectively, in children and teenagers in Alexandria from 1972 to 2001. The total estimated cancer cases for each year are presented in each column of the histogram. Note that, overall, cancer incidence is increasing during the specified period.



**Figure 2.** The detailed frequencies for the incidence of the different topographical sites of childhood cancer in Alexandria from 1972 to 2001.

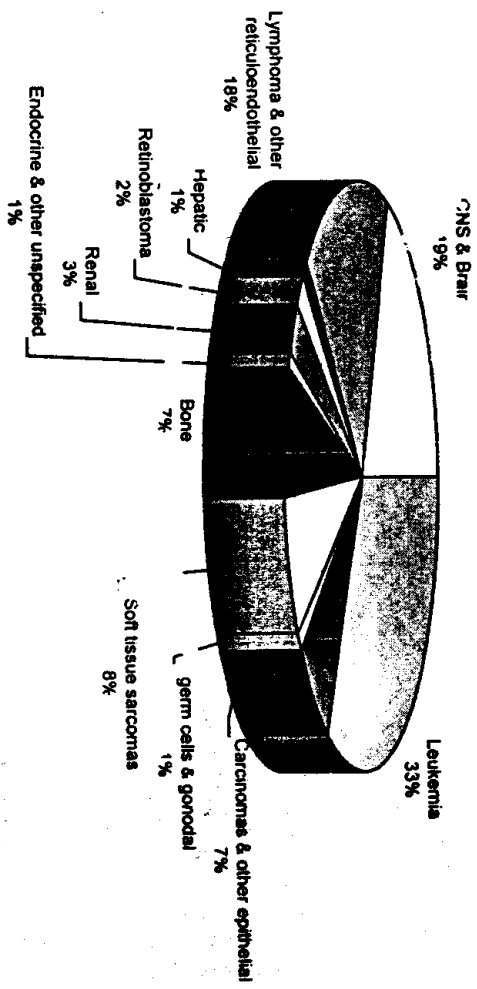


Figure 3: Distribution of different types of childhood cancers (Age 0-19) in Alexandria in 2001.



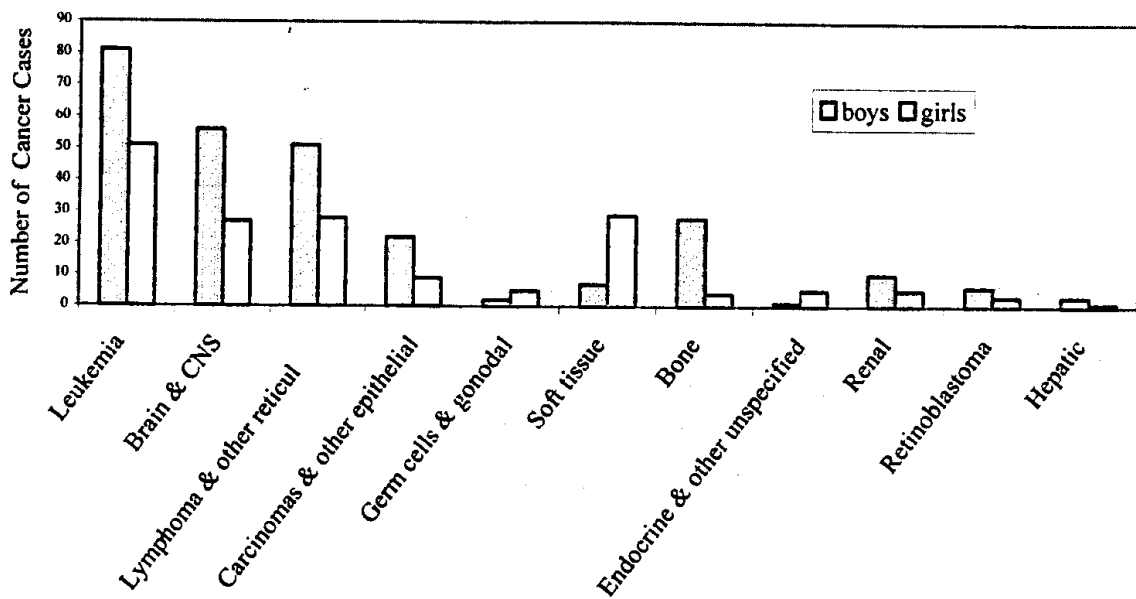


Figure 4: Incidence of pediatric cancers by gender in Alexandria in 2001. Overall cancer occurs more frequently among boys than girls.

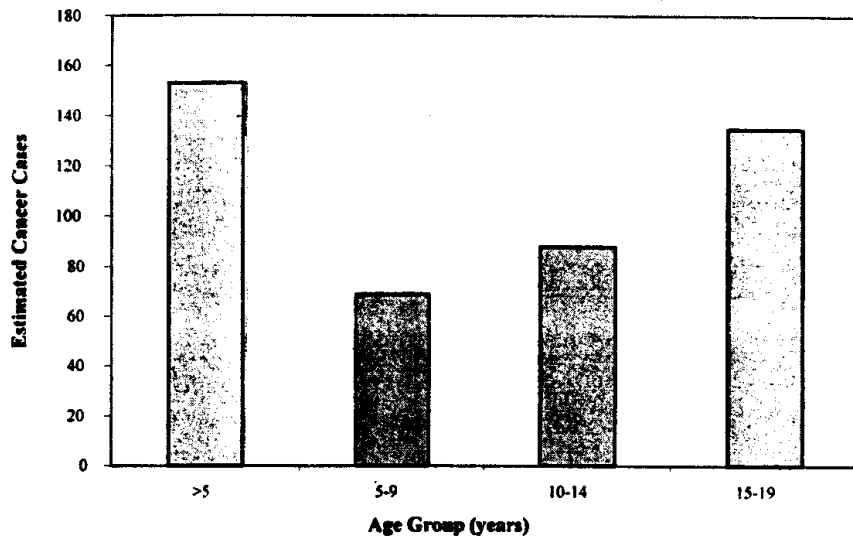


Figure 5: Incidence of all cancers in children by age group in Alexandria in 2001. Among children younger than 20 years of age, the highest cancer incidence occurs during the first five years of life. The lowest period of risk is between the ages of 5 and 14 years, after which incidence rises.

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