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INCIDENCE OF CHILDHOOD LEUKEMIA IN SWEDEN 1975–1980

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ABSTRACT. Gustafsson, G. and Kreuger, A. (Department of Paediatrics, University Hospital, Uppsala, Sweden). Incidence of childhood leukemia in Sweden 1975–1980. Acta Paediatr Scand, 71: 887, 1982.—During the six-year period 1975–1980, leukemia was diagnosed in 466 children in Sweden, giving an estimated incidence of 4.4/100 000 children per year (0–15 years at diagnosis). The incidence of acute lymphoblastic leukemia (ALL) was 3.7, of acute non-lymphocytic leukemia (ANLL) 0.6 and of chronic myelocytic leukemia (CML) 0.1/100 000 children per year. The over all incidence among boys was 4.5/100 000 per year and among girls 4.2. The male : female ratio was 1.13. This ratio was 1.22 in ALL and 0.71 in ANLL. Fifty per cent of the children were below 5 years of age at diagnosis, with a pronounced peak between 2–3 years, which was explained by the ALL distribution. In children with acute leukemia 13 % had WBC values of $>100\times10^9$/l, 4 % had CNS leukemia and 10 % had a mediastinal mass at diagnosis. The geographical distribution of leukemia in Sweden was analysed in a search for clusters of cases.

KEY WORDS: Childhood leukemia, leukemia epidemiology, leukemia incidence

In the literature there are many reports concerning incidence of leukemia in children. The aim of the present investigation is to present actual figures of incidence of the various types of leukemia in children, in a national uniform and complete material.

MATERIAL AND METHOD

All Swedish children in whom leukemia was diagnosed in the 6-year period from January 1975 to December 1980, and who were 0–15 years (<16 years) of age at diagnosis, were included in the material. The total number of children thus qualifying for the investigation was 466.

Information concerning the children was obtained by an inventory of all the 45 Departments of Paediatrics in Sweden, carried out in January 1981. The patient material was checked with the Swedish Cancer Registry, but no additional case was found in the Registry.

From the medical records data concerning date of birth and diagnosis, place of residence, sex, type of leukemia, clinical characteristics and hematological data were extracted. The diagnoses were based on representative bone marrow smears examined by members of the Swedish Child Leukemia Group (SCLG) and/or by experienced pathologists at the Regional Hospitals in Sweden.

The leukemias were classified as acute lymphoblastic or stem cell leukemia (ALL), acute promyelocytic or myelocytic leukemia (AML), acute myelomonocytic or monocytic leukemia (AMMoL) and chronic myelocytic leukemia (CML). AML and AMMoL as one group are defined as acute non-lymphocytic leukemia (ANLL).

RESULTS

A survey of the material is given in Table 1. Among the 466 children the estimated incidence of leukemia (all types) during the period in question was 4.4/100 000 children per year aged 0–15 years at diagnosis, with a male : female ratio of 1.13. This ratio was 1.22 for ALL and 0.71 for ANLL. The incidence among boys was 4.5 and among girls 4.2. ALL constituted 84 % of the material, ANLL 14 % and CML 2 %, see Table 1. No case of CLL was diagnosed.

For comparison with other materials, the incidence of leukemia in children aged 0–14 years at diagnosis has been estimated. This incidence was 4.5/100 000 children per year, see Table 2.

The geographical distribution of the whole material is given in Fig. 1, where it is seen that the incidence figures of the Swedish counties

Table 1. *Sex distribution in and incidence of childhood leukemia in Sweden (1975–1980)*
Incidence = annual cases per 100 000 children 0–15 years of age. For abbreviations, see text

Type of leukemia	Number of patients			%	Male : female ratio	Incidence	
	Males	Females	Sum			Total	Male : female
ALL	214	176	390	84	1.22	3.7	3.9/3.4
AML	24	31	55	12	0.77	0.5	
AMMoL	3	7	10	2	0.4	0.1	
CML	6	5	11	2	1.2	0.1	
All types	247	219	466	100	1.13	4.4	4.5/4.2

varied between 2.0 and 7.6.The highest incidence was recorded in the county of Värmland. Here neither a temporal nor a geographical cluster was found, but the proportion of ANLL was 30 % in this county as compared to 14 % for the whole of Sweden. In the county of Kristianstad in southern Sweden the incidence was 7.1. Here in a small community, a cluster of cases was identified which was statistically significantly too large. A thorough analysis has been made with regard to explanatory factors among the families or the environment (1). A comparatively low incidence was found in the districts between the great lakes in Sweden, but this was not significantly lower than expected.

The number of children with different types of leukemia and the incidence rates in relation to age at diagnosis are shown in Table 2 and Fig. 2. The incidence was highest for ALL in children below 5 years of age at diagnosis. Here a peak incidence of 10.6 was found for children between 2 to 3 years of age and an incidence of 9.7 for children between 3 to 4 years of age at diagnosis. No age-related peaks were found in the other forms of childhood leukemia in this material.

In the 6-year period in question there was an even yearly distribution of diagnosed cases of leukemia (84, 82, 71, 66, 75 and 88 children respectively). Fig. 3 shows the month of diagnosis, with only small seasonal variations and slight though not significant peaks in April and November for ALL.

Concerning the month of birth, there was a distinct though not statistically significant incidence peak in February for ALL, Fig. 4.

Table 3 gives the distribution of WBC at diagnosis in the whole material and in the various types of leukemia. WBC counts $>100\times10^9$/l were recorded in 43/390 children with ALL (11 %) and in 9/65 children with ANLL (14 %).

CNS leukemia was found at diagnosis in

Table 2. *Incidence of childhood leukemia in Sweden (1975–1980) with respect to age at diagnosis*
Incidence = annual cases per 100 000 children 0–15 years of age. For abbreviations, see text

Age at diagnosis (years)	ALL		AML		AMMoL		CML		All types	
	N	Incidence	*N*	Incidence	*N*	Incidence	*N*	Incidence	*N*	Incidence
0–4	198	6.2	22	0.7	5		2		227	7.1
5–9	122	3.6	16	0.5	1		4		143	4.2
10–15	70	1.7	17	0.4	4		5		96	2.4
0–15	390	3.7	55	0.5	10	0.1	11	0.1	466	4.4
(0–14	379	3.8	47	0.5	9	0.1	10	0.1	445	4.5)

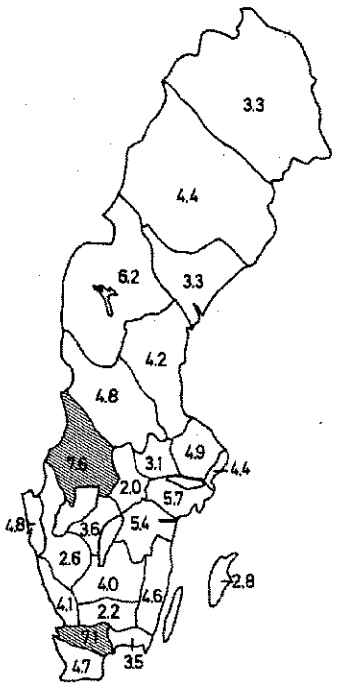

Fig. 1. Annual incidence rates of childhood leukemia per 100 000 children aged 0–15 years diagnosed 1975–1980 by the 24 counties in Sweden.

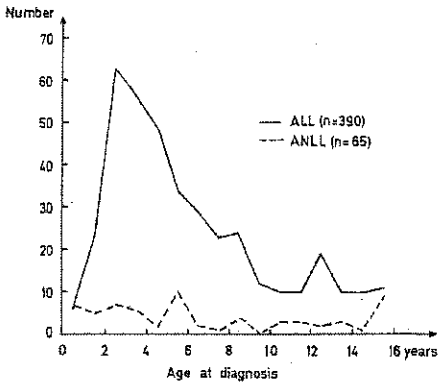

Fig. 2. Age at diagnosis in 455 children with acute leukemia diagnosed in Sweden 1975–1980. ALL = acute lymphoblastic leukemia, ANLL = acute non-lymphocytic leukemia.

4.4% and a mediastinal mass was found in 10% of the children with acute leukemia, the ALLs as well as the ANLLs, Table 4.

DISCUSSION

This investigation includes all known cases of childhood leukemia diagnosed in Sweden during the period 1975–1980.

Sweden is a country with a well developed health and welfare service (2), especially for children of all ages, which strengthens the probability that every case of leukemia in the country is discovered and diagnosed. The material thus comprises all cases of childhood leukemia diagnosed in this country, with 8.3 million inhabitants, of whom 1.77 million are children aged 0–15 years. The population is comparatively homogeneous with 90% of the people originating from the Scandinavian countries, 5% from Finland, 3% from other European countries and 2% from non-European countries (3). These figures are important, since differences in incidence related to racial factors have been reported (4).

Table 3. *White blood cell (WBC) count at diagnosis in relation to types of childhood leukemia in Sweden (1975–1980)*
For abbreviations, see text

Type of leukemia	WBC×10⁹/l <10 N	(%)	10–20 N	(%)	20–50 N	(%)	50–100 N	(%)	>100 N	(%)	Total
ALL	212	(54)	46	(12)	59	(15)	30	(8)	43	(11)	390
AML	20	(36)	11	(20)	11	(20)	7	(13)	6	(11)	55
AMMoL	3	(30)	2	(20)	1	(10)	1	(10)	3	(30)	10
CML	1	(9)	–		1	(9)	–		9	(82)	11
All types	236	(51)	59	(13)	72	(15)	38	(8)	61	(13)	466

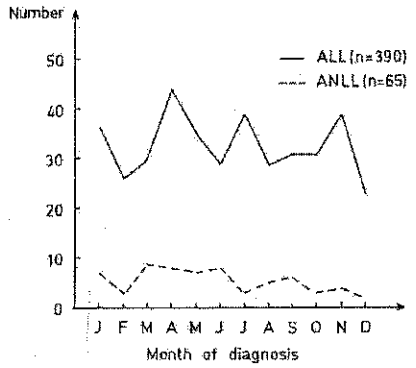

Fig. 3. Month of diagnosis in 455 children with acute leukemia diagnosed in Sweden 1975–1980.

Table 4. *Number of patients with CNS-leukemia and a mediastinal mass at diagnosis in childhood acute leukemia in Sweden (1975–1980)*

For abbreviations, see text

Type of leukemia	CNS-leukemia *N* (%)	Mediastinal mass *N* (%)	No. of cases with acute leukemia
ALL	17	42	390
AML	3	2	55
AMMoL	–	2	10
All types	20 (4.4)	46 (10)	455

The annual incidence rate in other countries vary considerably. Table 5 illustrates these incidence variations in different materials since the 1940's, and even the sex distribution in some of the materials. Most of these studies concerned children 0–14 years of age at diagnosis. The present study revealed an even distribution throughout the period, with a mean annual incidence among children 0–14 years at diagnosis of 4.5/100 000 children (see Table 2). This rate was higher than found in any of the materials in the literature, even the earlier Swedish material, see Table 5. The reason to this may reflect variations in diagnosing and reporting leukemia earlier, or may imply a real increase in the incidence of leukemia. Improvement in diagnostic possibilities, especially laboratory methods, may partly explain the increased number of diagnosed cases and the rise in incidence rate in recent years.

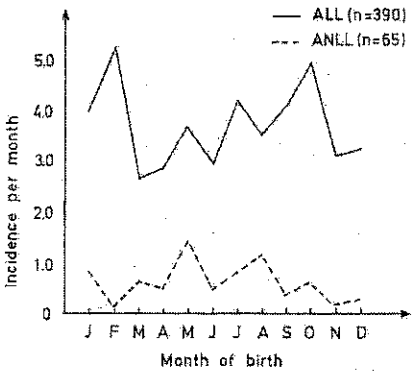

Fig. 4. Monthly incidence rate (per 100 000 children) in 455 children with acute leukemia diagnosed in Sweden 1975–1980.

In this material the male : female ratio was 1.13 for all forms of leukemia, as well as for the acute leukemias only. This is lower than any ratio we found in the literature for white children, Table 5. Compared to the earlier Swedish investigation (12), the present high incidence and the comparatively low male : female ratio may be due to a real increase in incidence in Sweden in recent years, especially for girls. This contrasts with the conclusion drawn by Birch (13), who found the rise of incidence in England to be due to an increase of incidence in boys. Whether the low male: female ratio in Sweden has a racial-geographical explanation, or whether there is a gradual, real shift towards equalization as regards the sex incidence, can only be decided by future follow-up studies or by other complete national surveys. There may be differences between countries with regard to ethnical and environmental factors, though such differences are so far unclear, and can only be of speculative order at present.

The proportion of the various types of leukemia are not the same in all materials. The proportion of ALL varied between 78 and 86% in two large investigations (11, 14). In the actual material ALL constituted 84%. Other authors have reported a considerably lower

Table 5. *Incidence of and male : female ratio of childhood leukemia in different materials in children 0–14 years of age at diagnosis*

Incidence = annual cases per 100 000 children, M = males, F = females

Country	Year of diagnosis	No. of patients	Incidence	Male : female ratio	Reference
USA	–1940	1 500	–	1.45	Cooke (5)
Sweden	1941–1950	490	–	1.26	Vahlquist (6)
Denmark	1946–1957	516	M 4.4 F 3.2	1.46	Iversen (7)
USA	1949	1 492	3.7	–	Cooke (8)
Finland	1953–1970	856	M 4.37 F 3.47	1.31	Teppo (9)
England	1954–1977	809	3.3	1.30	Birch (10)
USA[a]	1957–1964	1 770	–	1.27	Pierce (11)
Sweden	1958–1974	1 180	3.9	1.27	Eriksson (12)
USA[b]	1969–1971	651	4.21	1.38	Young (4)
Present material	1975–1980	445	4.5	1.13	

[a] 0–15 years at diagnosis.
[b] White children.

proportion of ALL and conversely an increased proportion of AML (15, 16). One explanation of these differences might be dissimilarities or advances in diagnostic practice. It is well known, that the May-Grünwald-Giemsa method of staining bone marrow smears (until recent years the most common and sometimes the only technique used in Swedish Departments of Pediatrics), does not offer optimal opportunities for proper classification of the leukemias (17). There is therefore a great need for multiple staining techniques and experienced expertise in cyto- and histochemistry for proper classification of the leukemias. In recent years, improved diagnostic procedures are also being used in diagnosis of childhood leukemia in Sweden. However, there is a possibility that some of the earlier diagnosed ALLs in this material should in fact have been AMLs.

The geographical distribution of cases in the 24 counties in Sweden shows some interesting features. The highest incidence rate was found in the County of Värmland, with 7.6 cases/100 000 per year. The distribution in the county was even and no real clusters, neither geographically nor in time could be identified. In the County of Kristianstad in the southern Sweden, with an incidence figure of 7.1, there was a cluster in a small community, where the incidence was statistically significantly increased. A thorough investigation was made in this community with regard to family constellations, parents' occupations, parental and child exposure to toxic agents, industries and environmental factors, but no definite explanations for the cluster were found (1).

At diagnosis, the distribution of the WBC-counts, the proportion of CNS-involvement and proportion of mediastinal mass enlargement in this material is in agreement with corresponding figures in other materials of leukemic children (7, 19).

Fifty per cent of the children were of ages 0–5 years at diagnosis, which can mostly be attributed to the ALLs, in agreement with other reports (5, 9). ALL showed a peak incidence at age 2–3 years at diagnosis, which is an earlier peak than reported from most other materials (5, 7, 9, 18), but is in agreement with the previous Swedish material (12). Pierce (11) has also reported this early peak in Caucasian children. The reason for this difference is unclear. It is worth to point out, that the leukemias, even the ALLs, constitute a group of diseases, probably with different etiologic factors in different age groups. If the early incidence peak found here is explained by perina-

tal, medical, ethnical, environmental, or other factors, still remain to be proved.

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