

## TREND OF CHILHOOD LEUKAEMIA IN EASTERN ROMANIA

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**Abstract.** Descriptive epidemiologic analyses were performed in five districts of eastern Romania. The annual incidence rates and the cumulative incidence rates for two equal ten years periods were calculated. Trend was evaluated in linear regression analysis. All childhood leukaemia cases diagnosed between 1992-2001 comparatively with those of 1980-1989 (the control group) in 0-14 years age group have been analyzed. The trend of incidence rates during 1992-2001 was upward. The cumulative incidence rates were significantly increased in 0-4 y. age group (30.8 vs. 18.5;  $p=0.002$ ) and rural area (25.4 vs. 18.6;  $p=0.02$ ). The most affected districts were Botoșani (43.1 vs. 14.3;  $p=0.02$ ) and Vaslui (33.1 vs. 7.98;  $p=0.02$ ). The majority of cases were acute lymphoblastic leukaemias (69-81%).

**Key words:** leukaemia, trend, incidence rate, epidemiological study, children

**Rezumat.** S-a efectuat un studiu epidemiologic descriptiv în cinci județe din Moldova. S-au calculat ratele anuale ale incidenței și ratele cumulative ale incidenței pentru două perioade egale a câte zece ani (1992-2001 și 1980-1989). Tendința a fost calculată folosind metoda regresiei lineare. Analiza s-a efectuat pe toate cazurile de leucemie diagnosticate la copiii 0-14 ani în perioada 1992-2001 (lotul studiat) și cele diagnosticate în perioada 1980-1989 (lotul martor). Tendința ratelor de incidență a fost net crescătoare în întreg teritoriul investigat. Ratele incidenței cumulative au fost semnificativ crescute pentru grupul 0-4 ani (30,8 vs. 18,5;  $p=0,002$ ) și pentru copiii rezidenți în mediul rural (25,4 vs. 18,6;  $p=0.02$ ). Cele mai afectate județe au fost Botoșani (43,1 vs. 14,3;  $p=0.02$ ) și Vaslui (33,1 vs. 7,98;  $p=0,02$ ). Majoritatea cazurilor au fost leucemii acute limfoblastice (69-81%).

**Cuvinte cheie:** leucemie, tendință, rata incidenței, studiu epidemiologic, copii

### INTRODUCTION

Reports on pattern of childhood incidence are rare in Eastern Europe (1). Leukaemia is the major malignancy in developed countries, accounting for around a third of all childhood cancers. Its incidence has a distinctive shape, with a marked peak at ages 2-3y

followed by a steady decline. For most cases, the cause of disease is uncertain. Recent scientific work has given rise to several hypotheses (2-10). Factors involved in the development of leukaemia are poorly known or their possible role has proven difficult to quantify. In part, this reflects the range

of condition included within the term of "leukaemia". The effect of relatively low doses of radiation is controversial and not clearly established. Other known risk factors include exposure to a number of chemicals, including certain chemo-therapeutic agents and the benzene. Exposure to pesticides may be an important risk factor too. Exposure to electromagnetic fields has been implicated on the basis of circumstantial evidence, but not clearly demonstrated as a risk factor. The role of infectious agents is receiving increasing attention but, apart from the involvement of human T-cell leukaemia/ lymphoma virus-I (HTLV-I) in certain rare leukaemia, a scarce specific information is available. Wider involvement of infectious agents in the development of leukaemia than currently established could, nevertheless, prove to be the case. A pre-natal genetic defect may be involved in acute lymphoblastic leukaemia in children, but it has been suggested that a further event, possibly infection, may be required to trigger full-blown leukaemia. This paper presents a 22 y retrospective survey of childhood leukaemia incidence in eastern Romania.

#### SUBJECTS AND METHODS

During 1980-2001, 442 cases of leukaemia have been diagnosed in Emergency Children's Hospital "Sf. Maria" of Iași. The hospital catchment area being extended to the whole eastern territory, five districts following the

patient's residence have been included in this study: Bacău (Bc), Botoșani (Bt), Iași (Is), Neamț (Nt) and Suceava (Sv). The population of the beginning follow-up period was 1, 131, 329 children.

Diagnosis was established by laboratory findings: complete blood count which included Hb, Hct, WBC count, WBC differential count, platelet count and cellular morphology on peripheral blood smears followed by bone marrow examinations (needle biopsy).

Annual data on 0-14 y age population in each district by age and sex have been obtained from Districtual Offices of Population Census.

Annual incidence rates in whole investigated area as well as cumulative incidence rates of each district have been calculated.

The chi-squared corrected by Pearson and Fisher tests have been used to calculate the level of statistical significance.

Epi Info 6 program was used for data processing.

#### RESULTS AND DISCUSSION

The annual incidence rates (cases/10<sup>5</sup> people) in surveyed territory ranged between 1.73 (1982) and 3.78 (1999) as figure 1 shows. The leukaemia trend was clearly rising ( $\alpha = +0.04$ ) during twenty two years. A higher tendency is more evident, for the last ten years analysis ( $\alpha = +0.08$ ) as illustrated by fig. 2.

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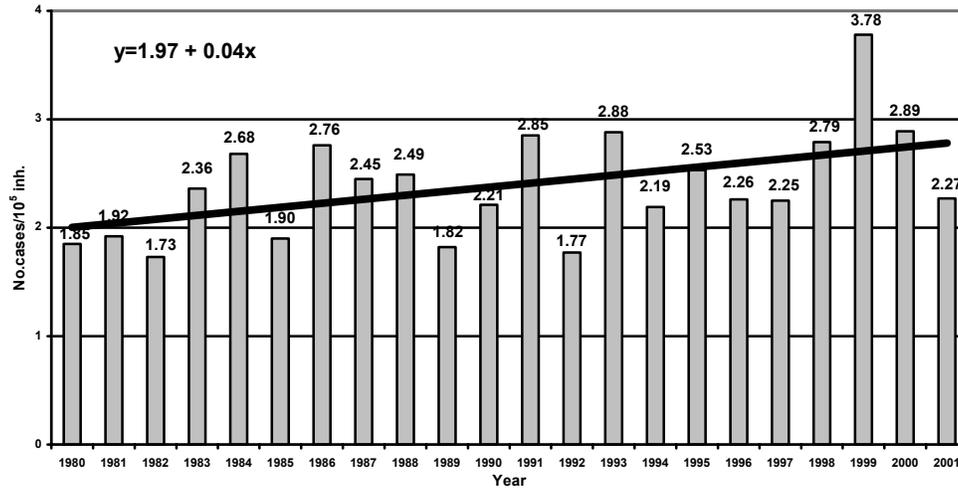


Fig. 1 The tendency of annual rates of leukaemia incidence (1980-2001)

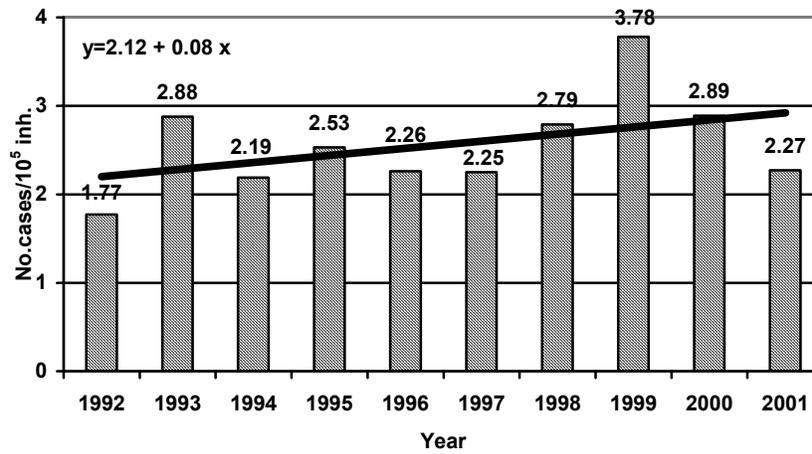


Fig. 2 The tendency of annual rates of leukaemia incidence (1992-2001)

**Table 1. The cumulative incidence rates (cases/10<sup>5</sup> inh.) by districts, age groups, sex and residence area**

District	Period	Age groups (years)			Sex		Residence area	
		0-4	5-9	10-14	Male	Female	Urban	Rural
Bc.	I	21.6	26.5	11.9	23.2	15.7	23.2	17.4
	II	27.8	28.0	25.2	25.8	23.4	27.4	21.3
Bt	I	14.3	14.8	27.7	21.3	16.8	25.1	17.1
	II	43.1**	40.7*	9.9	34.2	16.8	34.4	25.8
Is	I	20.1	25.5	19.2	22.0	21.1	35.3	14.1
	II	24.0	26.5	19.5	26.4	19.8	20.0	25.5
Nt	I	19.2	23.9	21.9	27.5	15.6	24.6	20.5
	II	30.5	18.0	15.2	18.3	23.4	17.2	23.7
Sv	I	23.6	26.0	19.1	26.3	19.3	19.2	24.4
	II	31.2	35.0	21.6	36.1	21.5	13.1	27.1
Vs	I	7.98	38.2	16.6	26.7	14.4	23.0	18.4
	II	33.1**	20.0	9.8	19.0	21.5	10.3	30.4
Total	I	18.5	25.8	18.8	24.4	17.4	25.6	18.6
	II	30.8***	23.7	16.3	24.0	21.9	27.0	25.4**

The studied period: I=1980-1989; II=1992-2001

\* p=0.04; \*\* p=0.02; \*\*\* p=0.002

These findings were subsequently analyzed by cumulative incidence rates of two periods: 1980-1989 and 1992-2001.

As table 1 data indicate, significant increases have been found in 0-4 y children (30.8 vs. 18.5; p = 0.002).

In this territory, two districts (Vaslui and Botoşani) clearly detached with high peaks in second period, respectively 33.1 and 43.1.

The cumulative incidence rates in the other age subgroups (5-9 y and 10-14 y) were insignificantly changed, excepting Botoşani district. The highest number of leukaemia cases has been recorded in subgroup 5-9 y, during 1992-2001 in this district.

More cases has come from rural localities so, for the whole rural area, the cumulative incidence rate of leukaemia was significantly higher during 1992-2001 (25.4 vs. 18.6; p = 0.02).

Sex distribution of cases shows no significant differences between them.

Three morphological types of leukaemia have been diagnosed: acute lymphoblastic (ALL); myeloid (AML) and chronic myeloid (CML) as shows fig. 3. A small percentage of cases (0.49-3.3) don't belong these types. The most frequently type of leukaemia was the acute lymphoblastic one, as the other authors found (3,7,8). Its frequency rised during the last ten years, comparatively with

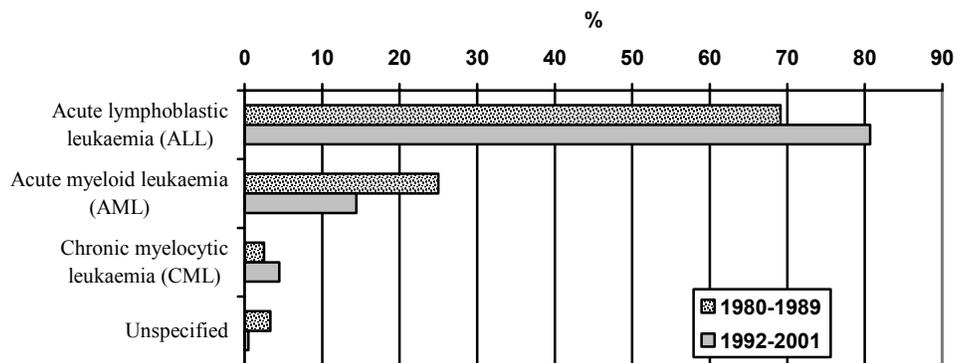
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that of the first period (80.7 vs. 60.1;  $p = 0.006$ ).

The frequency of AML had a reverse order decreasing in the last period up to 14.4 from 25.0 during 1980-1989 ( $p = 0.005$ ). Unsignificantly changes have been observed in the frequencies of chronic myelocytic leukaemia in both periods: 2.50 (1980-1989) vs. 4.43 (1992-2001).

A previous study on leukaemia incidence at children aged 0-14 years

pointed out a statistical significant increase in the 1989-1994 period against that of 1980-1985 in the group 0-4 years (11). A detailed reanalysis of cases by cohort ages of Chernobyl accident and effective dose levels during the first year following the nuclear accident showed no influence of Chernobyl on incidence rate in early childhood (0-6 years) and a small increase of disease in the cohort of children exposed *in utero* (12).



**Fig. 3 The distribution of cases by morphological type (%)**

### CONCLUSION

1. The leukaemia incidence had an upward trend in eastern territory of Romania during 1980-2001. The increased trend was more evident in the last ten years ( $a = +0.08$  vs.  $a = +0.04$ ).
2. The cumulative incidence rate risen significantly between 1992 and 2001 in the 0-4 years group and the rural area.
3. The most affected districts were Botoşani and Vaslui.
4. The most cases of acute lymphoblastic leukaemias, appeared during 1992-2001 whereas acute myeloid leukaemia decreased significantly.
5. A small increase of chronic myeloid leukaemia cases was noted in the last ten years.

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