Radiation Risk Assessment of Leukemia in Children of Belarus

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Abstracts. Results of an analysis of the incidence in the acute childhood leukemia in Belarus in 1980-2004 carried out on the basis of ecological model are discussed in the report. Published data of the Belarusian Republican Registry of Childhood Hemoblastoses and Hemopoiesis Depressions as well as the Belarusian Cancer Registry were used in the analysis. Only mixed childhood subgroup was considered without separating boys and girls. It was found that a short-time increase in the incidence of leukemia in children of Belarus (0 – 14 years at the time of diagnose) occurred in Belarus soon after the Chernobyl accident. The increase is statistically significant. After 1992 a decline in the childhood leukemia incidence began. As a result, the incidence in the childhood leukemia of Belarus after the period 1986-1992 became less than it was before the Chernobyl accident. 708 cases of acute leukemia were registered in Belarus in the period 1986-1992.

The number of expected leukemia in this period was assessed to be approximately 625 cases. These data give the standardized incidence ratio for the period 1986-1992 equal to 1.13 with 95% CI from 1.02 to 1.26. Radiation risks and attributive risk of leukemia incidence were assessed on the basis of an assumption that observed short-time increase in the childhood leukemia in Belarus had radiation origin. They are for the period 1986-1992: ERR = 7.8% per 1 mSv (95% confidential interval is from 1.0 to 15.4% per 1 mSv), EAR = 30.1 cases per 10^4 PYSv (95% confidential interval is from 3.9 to 59.2 cases per 10^4 PYSv), AR = 11.7% (95%CI is from 1.5 to 23%).

Introduction.

It is well known that hematopoietic tissues and organs are very sensitive to carcinogenic impact of ionizing radiation. This was established in epidemiological studies that have shown an increase of leukemia in different irradiated groups. It was found that infants and children have the highest radiation risks of leukemia [1-3]. This makes leukemia in infants and children a qualitative indicator of irradiation.

A number of epidemiological studies [4-15] were performed after the accident at the Chernobyl NPP in order to study the possible increase in the leukemia incidence in countries that were affected as a result of this accident. Results of these studies are quite controversial.

Petridou et al [4] found an elevated increase in leukemia in infants (from 0 to 11 months after birth) born in Greece in the period from 1 July 1986 to 31 December 1987. The incidence in leukemia in this cohort was by factor 2.6 (95% confidence interval, 1.4 to 5.1: p(2-tailed) ≈ 0.003: 12 cases in the 'exposed' and 31 cases in the control group) higher than in infants born in the periods 1/1/1980 to 31/12/1985 and 1/1/1988 to 31/12/1990 (control group). It was also found that the incidence in leukemia in infants born in contaminated areas in the period from 1 July 1986 to 31 December 1987 correlated with a level of a radioactive contamination. These results were established for areas with low contamination (less than 100 Bq/kg of soil), intermediate (999-1000 Bq/kg) and high contamination (> 1000 Bq/kg) with ^{137}Cs. According to our assessment, such contamination of soil corresponds with levels of the surface contamination in this isotop less than 5 kBq/m^2, 5 to 50 kBq/m^2 and higher than 50 kBq/m^2. Petridou et al [4] explained their findings as a result of an *in utero* irradiation.

The authors [4] established also some small and statistically insignificant increase in the leukemia incidence in children at the age 12-47 months at the time of diagnoses exposed in utero to Chernobyl radiation. The ratio of the incidence in leukemia of such children to the incidence of children born in the period 1/1/1980-31/12/1985 and 1/1/1980-31/12/1990 was equal to 1.1 (95% confidence interval, 0.8 to 1.5: p(2-tailed) ≈ 0.56: 43 cases in the 'exposed' and 266 cases in the control group).

Studies of the infant leukemia were performed also in Germany and Belarus [5-7] by using similar temporal cohorts as in the report [4]. Michaelis et al [5,6] compared incidence rates of infants born in the former FRG in areas with the ground contamination with the ^{137}Cs < 6 kBq/m^2, 6 –10 kBq/m^2, > 10 kBq/m^2 with the incidence of "unnexposed in utero" infants. They have found also an increase in the incidence in infant leukemia in West Germany, although smaller than in Greece (rate ratio: 1.48 with 95% CI: 1.02 to 2.15; 35 cases in the 'exposed' and 143 in the control group). However, no correlation between rate ratios and level of contamination was found in the German studies. Therefore authors [5,6] concluded that excess in the leukemia incidence occurred in infants in West Germany after the Chernobyl accident was not related to radiation.

An increase in the infant leukemia was observed after the accident in Belarus [7]. The rate ratio for entire Belarus including Gomel and Mogilev regions was found equal to 1.26 (95% CI: 0.76 to 2.10: 17 cases in the 'exposed' and 89 in the control group). In case of Gomel and Mogilev regions combined together the rate ratio was equal to 1.51 (95% CI: 0.63 to 3.61: 6 cases in the 'exposed' and 27 in the control group). These findings indicate the existence of qualitative correlation between the level of increase and level of contamination of Belarus. In this respect the Belarusian data agree well with data established by Petridou et al [4]. However, excess in the infant leukemia observed in 'exposed' cohorts of Gomel and Mogilev regions was lesser than in Greece despite the fact that average contamination of these regions is higher than the maximal contamination in Greece. This and the absence of statistical significance of rate ratios in case of the Gomel and Mogilev as well as entire Belarus was considered by authors [7] as an evidence that increase in the infant leukemia in Belarus had no link to *in utero* irradiation caused by the Chernobyl accident.

Controversial results were established also in epidemiological studies of the incidence in leukemia in children. Auvinen et al [8] compared incidence rates in leukemia in children in Finland observed in 1986-1988 and 1989-1992 with incidence rate registered in 1976-1985. According them a relative risk assessed for the period 1986-1988 was equal to 0.95 (95%CI from 0.80 to 1.35) and for 1989-1992 – 1.01 (95%CI from 0.87 to 1.17). An excess relative risk equal to approximately 7% per mSv (95%CI from –27% to 41%) have been estimated in this study for the period 1989-1992.

An analysis of childhood leukemia observed in 1986-1992 in areas with different surface contamination was undertaken in Sweden [9]. For all cases diagnosed after May 1986 in highly contaminated areas (> 10 kBq/m^2) compared with areas of low contamination (< 10 kBq/m^2) authors estimated the odds ratio equal to 0.9 (95%CI from 0.7 to 1.3). For acute lymphoblastic leukemia in children aged under 5 years at diagnoses the odds ratio in highly contaminated areas compared with areas of low contamination was 1.2 (95%CI from 0.8 to 1.9). Dose-response analysis undertaken by authors [9] showed no correlation between the degree of contamination and the incidence of childhood leukemia.

A slight increase in the incidence in childhood leukemia in Belarus was observed soon after the accident at the Chernobyl NPP in Belarus [10,11]. 655 cases of leukemia in children aged from 0 to 15 years were observed in Belarus in 1979-1985 and 708 in 1986-1992. The rate ratio assessed for these periods is 1.034 (90% CI from 0.946 to 1.131). The statistical power of the rate ratio was very low

(χ^2=0.383, p = 0.268). The observed increase in the childhood leukemia in Belarus after the Chernobyl accident, as can be seen from these data, was statistically not significant. No statistical significant change in the incidence in leukemia in the Belarusian children was found also in the report [12].

The importance of the incidence in the childhood leukemia that is a qualitative indicator of irradiation requires a careful analysis of different aspects of the childhood leukemia in Belarus before and after the accident. And this is the main aim of the present report.

Materials and Methods.

Data of the Belarusian Republican Registry of Childhood Hemoblastoses and Hemopoiesis Depressions (number of registered cases of leukemia) that were published previously [10-12, 15-17] were used in the report. The work on creation of the Registry has been begun in 1988. In course of it specialists of the Institute of Hematology and Transfusion of the Ministry of Health Care of the Republic of Belarus assessed under the scientific supervision of Prof. E.P.Ivanov all information on childhood hemoblastoses and hemopoieses. This information came to the Institute of Hematology and Transfusion from oncological dispensaries, clinics and polyclinics as well as from hematological consultative establishments. It includes the following data: the name and address of the patient, age, date, place of diagnosis, ICD number of diagnosis, and the diagnostic method (e.g. biopsy, autopsy, myelogram, immunohistochemical method used, etc.) [10-12]. These data are available for each oblast (region) of Belarus, the city Minsk (capital of Belarus) and for the entire country. There are 6 oblasts in Belarus: Brest, Gomel, Grodno, Minsk, Mogilev and Vitebsk.

Data of the Belarusian Cancer Registry for the period 2001-2004 [18-20] were also used in the present report. Numbers of children used in the analysis were determined on the basis of population census of the Republic of Belarus [21] and statistical handbooks [22-24]. The analysis was carried out for combined children's population without separate consideration of boys and girls. Using data on the leukemia incidence as well as other data time-averaged radiation risks of the incidence in childhood leukemia in Belarus were assessed.

The excess absolute risk was assessed on the basis of the following simplified expression:

$$EAR_j = \frac{O_j - E_j}{N^j_{PYSv}} \quad . \qquad (1)$$

Here EAR_j - excessive absolute risk in *jth* period of time, O_j and E_j - numbers of observed and expected leukemias in this period respectively, N^j_{PYSv} - number of person-years-sievert in the *jth* period.

The value of N^j_{PYSv} is determined by the expression:

$$N^j_{PYSv} = \sum_{i=1}^{n} H^{Coll}_{i,j} \quad . \qquad (2)$$

Here $H^{Coll}_{i,j}$ collective equivalent dose of the whole body irradiation accumulated from the beginning of irradiation to the end of the *ith* year in the *jth* period.

The excess relative risk was assessed by using the formula:

$$ERR_j = \frac{(O_j / E_j) - 1}{N^j_{PYSv} / N^j_{PY}}, \qquad (3)$$

where N_{PY}^{j} - number of person-years in the *jth* period of time.

The attributive risk , AR_j , was assessed on the basis of the expression:

$$AR_j = 100\% \cdot \frac{O_j - E_j}{O_j} \quad (4)$$

Results and discussion.

Doses of irradiation

Table 1 presents cumulative doses of the whole body irradiation of the total Belarusian childhood population as a result of the Chernobyl accident. Data given in this table were taken from Table 3 of the report [25].

As can be seen from this table, collective and mean individual doses of the whole body irradiation to children of Belarus increased rapidly up to 1989 and then decreased slowly after achieving some maximal values. This temporal pattern of irradiation doses appears in case of children because the childhood subpopulation is an open system. Its composition is determined through two continuous flows. One flow is directed from outside to inside. This is the flow a newborn children. It adds irradiation doses to already accumulated doses. The second flow is directed from inside to outside. This is a flow of persons that achieved the age of 15 years. They leave the subpopulation of children carrying a fraction of accumulated irradiation doss to the subgroup of adolescents and adults.

Table 1. Cumulative collective and mean individual doses of the whole body irradiation of the childhood population of Belarus as a result of the Chernobyl accident.

Year	Collective	Individual	Year	Collective	Individual
	10^4 PSv	mSv		10^4 PSv	mSv
1986	0.25691	1.12204	1996	0.25159	1.17229
1987	0.3722	1.61069	1997	0.21916	1.0531
1988	0.42971	1.84569	1998	0.18428	0.91972
1989	0.45005	1.92296	1999	0.14706	0.7631
1990	0.43956	1.87717	2000	0.10972	0.58983
1991	0.42278	1.81315	2001	0.07712	0.43181
1992	0.38629	1.66962	2002	0.05883	0.3445
1993	0.34885	1.52541	2003	0.04834	0.29606
1994	0.31089	1.38177	2004	0.03834	0.24613
1995	0.28207	1.28037			

It was demonstrated in the report [25] that the main contribution to irradiation doses in Belarus gave irradiation in 1986-1989. After 1989 a significant decrease in irradiation doses occurred in Belarus. All those persons that were members of the children's subpopulation in 1986-1989 left this subgroup in 2004 because achieving of the age 15 years. And this caused significant decrease of irradiation doses of the children's subgroup.

Incidence in acute leukemia in children of Belarus

Figure 1 and Table 2 present time-averaged incidences in the acute childhood leukemia in different regions of Belarus. Three time periods are shown here. They are 1980-1985, 1986-1992 and 1993-2000. The time after the Chernobyl accident was divided in two periods: 1986-1992 and 1993-2000.

As can be seen from Fig.1 and Table 2, a short-time increase in the childhood leukemia occurred immediately after the Chernobyl accident in all regions of Belarus except the Mogilev oblast. In case of the Mogilev region a permanent decrease in the incidence in the childhood leukemia was observed in the period 1980-2000. The most plausible reason of this temporal pattern of the incidence in the childhood leukemia in case of the Mogilev region could be an incorrectness of the empirical data established for this region before the Chernobyl accident.

Data presented in Fig.1 and Table 2 demonstrate that time-averaged incidence rates in practically all regions of Belarus as well as in the entire Belarus in 1993-2000 were lower than in 1980-1985. This is an

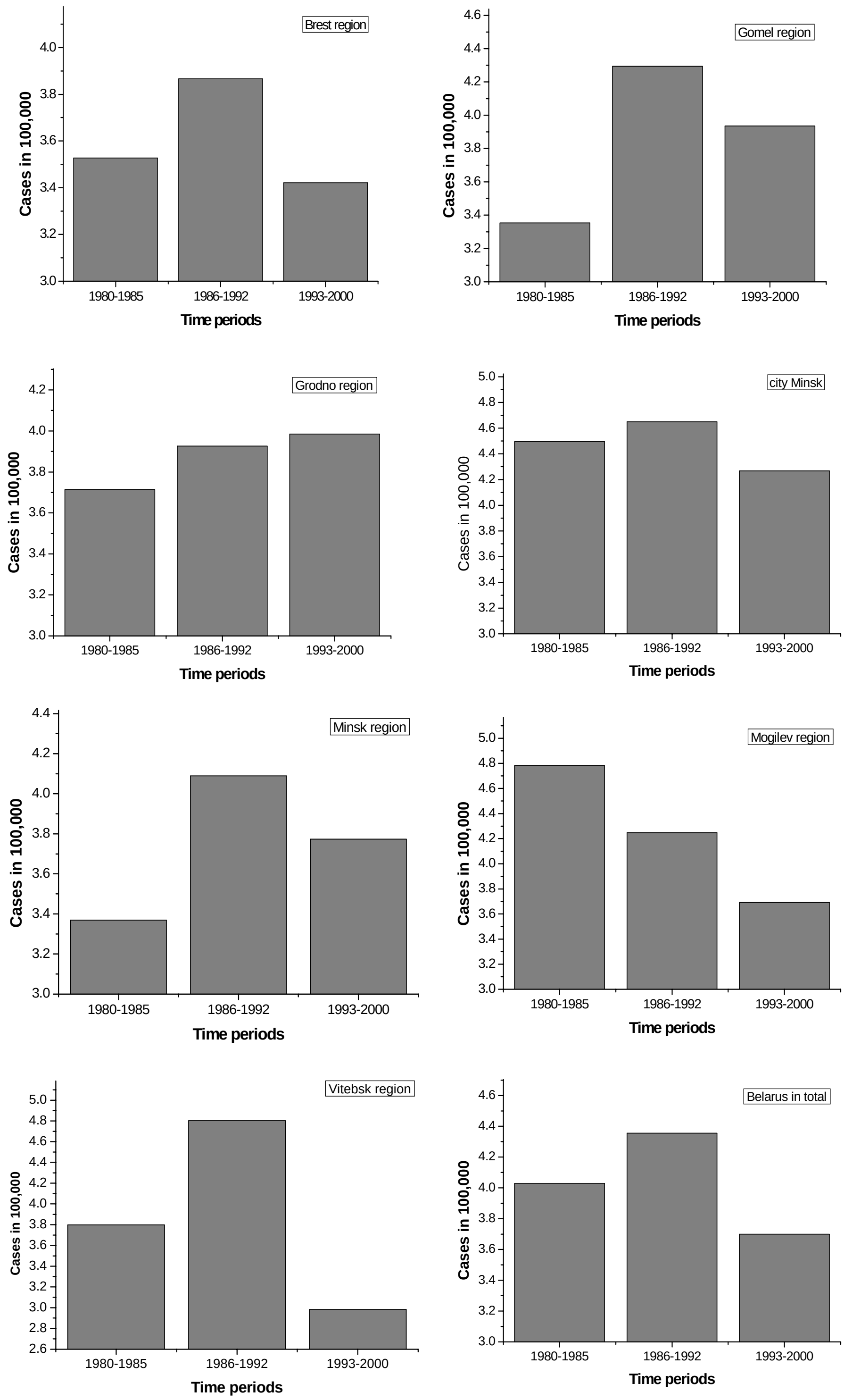

Fig. 1. Time-averaged incidences in the acute childhood leukemia in different regions of Belarus.

Table 2. Incidence in the acute childhood leukemia in regions of Belarus in 1980-1985, 1986-1992 and 1993-2000.

Region	Cases	Person·years	$IR \cdot 10^5$, a	$SE \cdot 10^5$, a
1980-1985				
Brest	80	2,268,213	3.527	0.394
Gomel	80	2,385,799	3.353	0.375
Grodno	59	1,588,899	3.713	0.483
City Minsk	90	2,002,278	4.495	0.474
Region Minsk	75	2,226,026	3.369	0.381
Mogilev	84	1,756,243	4.783	0.522
Vitebsk	70	1,843,033	3.798	0.454
Belarus	538	13,349,317	4.030	0.174
1986-1992				
Brest	108	2,793,433	3.866	0.372
Gomel	117	2,724,858	4.294	0.397
Grodno	71	1,808,251	3.926	0.466
City Minsk	122	2,623,805	4.650	0.421
Region Minsk	103	2,518,720	4.089	0.403
Mogilev	86	2,024,855	4.247	0.458
Vitebsk	101	2,103,497	4.802	0.478
Belarus	708	16,256,056	4.355	0.164
1993-2000				
Brest	92	2,718,244	3.385	0.353
Gomel	104	2,642,182	3.936	0.386
Grodno	77	1,932,447	3.985	0.454
City Minsk	113	2,647,839	4.268	0.401
Region Minsk	96	2,544,115	3.773	0.385
Mogilev	74	2,003,962	3.693	0.429
Vitebsk	64	2,145,307	2.983	0.373
Belarus	620	16,758,117	3.700	0.149

indication of a decreasing trend of spontaneous incidence in the childhood leukemia in Belarus

The slight decline in the leukemia incidence in Belarus began already before the accident at the Chernobyl NPP. This can be seen in Fig.2 that shows annual incidence rates in Belarus in the period 1980-1985 (left panel). The right panel of the Fig.2 displays annual incidence rates in the periods 1980-1985 and 1993-2004 combined together.

In case of data presented in the left panel of Fig. 2 only data of the Belarusian Republican Registry

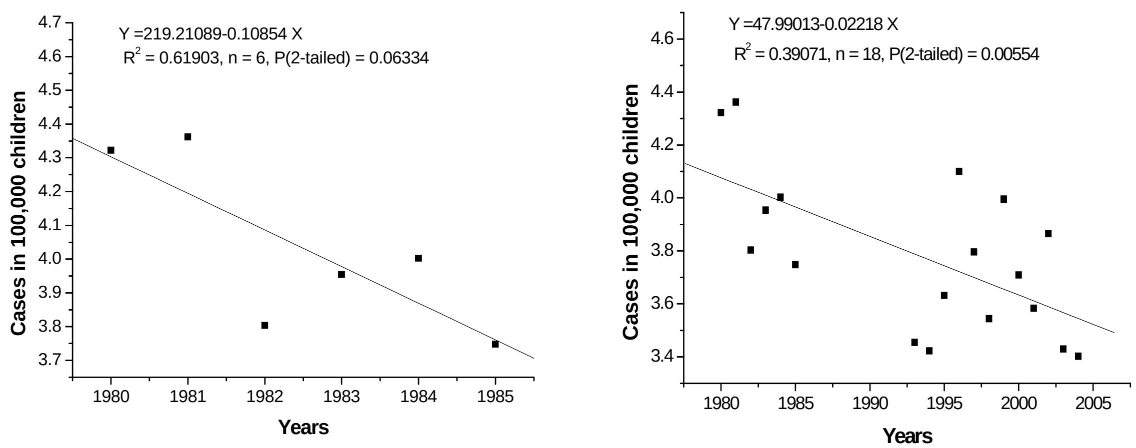

Fig.2. Incidence in the childhood leukemia in Belarus in 1980-1985 (left panel) and in 1980-1985, 1993 –1994 (right panel).

of Childhood Hemoblastoses and Hemopoiesis Depressions were used. The data presented in the right panel of this figure were constructed by using data of the Belarusian Republican Registry of Childhood Hemoblastoses and Hemopoiesis Depressions for the periods 1980-1985, 1993-2000 and data of the Belarusian Cancer Registry for the period 2001-2004 [18-20].

The decreasing trend in the childhood leukemia observed in Belarus before the Chernobyl accident indicates the necessity to analyze the increase of the childhood leukemia in Belarus after the Chernobyl accident on the basis of comparison of observed and expected incidences in this period of time. Three different simplified methods can be used for assessment of expected incidence rates in the period 1986-1992. At first, expected incidence rates in the period 1986-1992 can be determined as arithmetic means of empirical incidence rates estimated in periods 1980-1985 and 1993-2000. This method gives for the entire Belarus the value $3.865 \cdot 10^{-5}$ a^{-1} as the expected incidence rate for the period 1986-1992.

The second method of assessment is based on combining numbers of leukemia cases and person-years established in different periods of time. Assessment on the basis of Table 2 determines the total number of leukemias in registered in children of Belarus in periods 1980-1985 and 1993-2000 equal to 1,158 cases. The combined number of person-years in these periods is 30,107,434 person-years. Dividing of the first number by the second gives the value $3.846 \cdot 10^{-5}$ a^{-1}. It differs only by 0.5% from the value assessed with the first method.

The third method in case of the entire Belarus is based on using the fitting expression shown in the right panel of Fig.2. It gives the value $3.877 \cdot 10^{-5}$ a^{-1} that is practically the same as values assessed by using two first methods. This means that any described methods can be used for estimation of expected time-averaged incidence rates of the childhood leukemia in the entire Belarus.

The analogous methods can be used also by estimation of expected incidence rates in the period 1986-1992 for separate regions of Belarus.

Table 3 presents standardized incidence ratios (SIRs) of the childhood leukemia in the period 1986-1992 estimated as ratios of observed incidence rates in the childhood leukemia in the period 1986-1992 to expected incidence rates in the same period 1986-1992 for separate regions of Belarus and for the entire country. The second method for estimation of the expected incidences was used by assessment of SIRs shown in this table.

As can be seen from Table 3, analysis on the basis of standardized incidence ratios demonstrates an increase in the incidence in the childhood leukemia in the period 1986-1992 in all regions of Belarus including the Mogilev region. The highest increase occurred in the Vitebsk region. It was statistically significant only in this region. The lowest increase occurred in the Mogilev and Grodno regions.

The use of standardized incidence ratios instead of rate rates demonstrates the existence of statistical significance of the increase in the incidence of the childhood leukemia in the entire Belarus.

Table 3. Standardized incidence ratios of the childhood leukemia in Belarus in 1986-1992.

Region	SIR	95%CI of SIR	χ^2 (1df)	P(1-tailed)
Brest	1.121	0.881 - 1.426	0.864	0.184
Gomel	1.173	0.931 - 1.479	1.831	0.091
Grodno	1.017	0.763 - 1.355	0.013	0.456
City Minsk	1.065	0.851 - 1.333	0.303	0.299
Region Minsk	1.141	0.893 - 1.457	1.116	0.146
Mogilev	1.011	0.777 - 1.314	0.0064	0.464
Vitebsk	1.429	1.104 - 1.850	7.420	0.00326
Belarus	1.133	1.017 - 1.261	5.168	0.0123

Radiation risks

It is clear, that any increase of the incidence in some cancer in population with the stabile age distribution (for example, in population of children) could be caused by two different reasons. At first, it can be a result of an improved screening of this cancer. At second, it can arise due to appearance of new carcinogen/carcinogens in the environment as well as a result of an increase in amounts of carcinogen/carcinogens that was/were in the environment before the increase in the incidence in this cancer. In the first case the incidence rate has to reach some increased value that remains constant later. In the second case, a decrease of the incidence will occur after some short-time increase in the incidence in cancer. Data given in the present report show a short-time increase in the incidence in the childhood leukemia in all regions of Belarus after the Chernobyl accident and the following decline. Such temporal pattern excludes the screening improvement as a main reason of observed increase in the incidence in the childhood leukemia in Belarus after the accident at the Chernobyl NPP. It is clear that appearance of new carcinogen/carcinogens or increasing of their amount is responsible for observed change in the leukemia incidence in Belarus after the Chernobyl accident.

It is remarkable that the observed short-time increase in the childhood leukemia manifested at the same time when a constant decrease in the chemical pollution occurred in Belarus [26,27]. It began in Belarus in seventies of the last century as a result of a transfer from the use of hard fuel to natural gas for electricity and heat production. This caused a significant improvement in the environment of Belarus. Starvation of industry and agriculture at the beginning of eighties contributed also very significantly to the improvement of the environment in Belarus [26,27]. As a result of these processes the discharge of different pollutants into the environment of Belarus decreased by factors 2-3 in the period 1985-2004 [26,27].

The decrease of antropogenic pollution caused by industry, agriculture etc occurred in Belarus simultaneously with an increase of irradiation as a result of the Chernobyl accident. All these facts indicate that radiation is the most probable factor that caused observed changes in the childhood leukemia in Belarus after the Chernobyl accident because this change can not result from the decrease in the amount of chemical pollutants.

There is only one finding that contradicts with the assumption that the increase in the childhood leukemia in Belarus after the accident at the Chernobyl NPP was caused by the impact of ionizing radiation. As can be seen from Table 3 standardized incidence ratio of the childhood leukemia in the Vitebsk region is the highest in Belarus. However this region was practically not affected by the Chernobyl accident [28]. Amount of radioactive substances deposited in this region is lower than in the Gomel region approximately by three orders in magnitude [29]. A question arises. If radiation were the origin of the observed increase in the childhood leukemia in Belarus after the Chernobyl accident why the standardized incidence ratio of the childhood leukemia in the clean Vitebsk region is than in the high-contaminated Gomel region?

There is a plausible answer on this important question. Probable the high value of the standardized incidence ratio of the incidence in the childhood leukemia in the clean Vitebsk region could be a result of the migration of inhabitants of high-contaminated territories of the Gomel and Mogilev regions to this region.

The migration began soon after the accident at the Chernobyl accident. In first 10 years after the Chernobyl accident 842.6 thousand of the Belarusian citizens or 8.4% of the total population changed the places of their living in borders of Belarus [30]. The internal migration (moving in borders of Belarus) was especially high in contaminated territories. According to information [31], approximately one sixth of inhabitants of the high-contaminated Slavhorod district (Mogilev oblast) left their contaminated settlements during three first years after the Chernobyl accident. The similar situation arose in other contaminated districts of this region. The process of migration was even more pronounced in contaminated areas of the Gomel oblast [30].

The total number of people that changed their place of residence in borders of Belarus in 1986-2000 is 1,500,000 or 15% of the averaged population that was approximately 10 Million persons in this period [30].

The internal migration in Belarus from contaminated regions of Belarus was occurring partly as a result of an implementation of the State Program of minimization of the Chernobyl consequences. On this way about 135,000 persons were resettled from contaminated to clean territories [32]. Approximately 200,000 persons migrated from contaminated areas of Belarus without any assistance of the state [33].

Simultaneously with internal migration an intensive external migration began in Belarus after the accident at the Chernobyl NPP. As a result of it only in 1990-2000 the country was left for other states of the world 675.1 thousand of the Belarusian citizens [30]. This is 6.75% of the total population of Belarus.

Significant fraction of people that emigrated from Belarus after the accident at the Chernobyl NPP lived on the territories affected by this accident. For example, approximately 130 thousand of persons of the Jewish nationality immigrated to Israel from contaminated areas of Belarus and the Ukraine [34]. About 50% persons from this number lived before the emigration in high-contaminated territories of Belarus.

It is evident that external and internal migration influences significantly the possible correlation between incidence rates in different disease and levels of a radioactive contamination caused by the Chernobyl accident. This influence had to be very significant in case of rare diseases such as the childhood leukemia. This indicates that more correct analysis of radiation risks of the childhood leukemia caused in Belarus as a result of the Chernobyl accident can be established only on the basis of data established for the total country.

Radiation risks of the childhood leukemia assessed on the basis of an assumption that increase in the incidence in the childhood leukemia observed in Belarus after the Chernobyl accident were assessed in the present report. Results of this assessment are presented in Table 4. They were estimated for two periods: 1986-1992 and 1986-2004. Data estimated by Auvinen et al [8] are shown also in Table 4 (fourth column).

Table 4. Radiation risk of the incidence in the childhood leukemia.

Parameters	This report		Auvinen et al [8]
	1986-1992	1986-2004	1989-1992
Person-years	16,256,056	39,698,347	
Observed cases	708	1,567	
Expected cases	625	1,484	
Observed-expected	83	83	
SIR	1.133	1.056	
95% of SIR	1.017 ~ 1.261	0.984 ~ 1.134	
$N_{PYSv}/10^4$ PYSv	2.758	4.833	
$EAR \cdot 10^4$ PYSv	30.1	17.2	
95% CI of EAR	3.9 ~ 59.2	-5.0 ~ 41.0	
h, mSv	1.694	1.151	0.47
ERR, %/mSv	7.8	4.9	7
95% CI of ERR in %/1mSv	1.0 ~ 15.4	-1.4 ~ 11.6	-27 ~ 41
AR,%	11.7	5.3	
95% CI of AR	1.5 ~ 23.0	-1.6 ~ 12.7	

For the assessment of data presented in Table 4, incidence rates in the childhood leukemia in the entire Belarus given in Table 2 were used. The expected incidence rate in the period 1986-1992 was then assessed by combining noncorrected numbers of leukemia cases established for periods 1980-1985 and 1993-2000 and respective person-years also presented in Table 2. Collective and mean individual doses of the whole body irradiation presented in Table 1 were used for assessment of radiation risks given in the second and third columns of Table 4.

As can be seen from Table 4 the relative excess risk of 7.8% per mSv (95%CI from 1.0% to 15.4% per mSv) was estimated for the period 1986-1992 for the entire Belarus on the basis of observed data. This value agrees very well with estimation of Auvinen et al [8] that found relative risk for Finnish children for the period 1989-1992 equal to 7% per mSv (95%CI from –27% to 41%).

Comparison with other studies

The very good agreement in radiation risks established in the present report and study [8] gives an additional evidence of a radiation origin of the short-time increase in the childhood leukemia manifested after the accident at the Chernobyl NPP in Belarus and Finland.

It is clear that a very good agreement in radiation risks found in this report and by Auvinen et al [8] could not be achieved simply by chance. Two sets of data are used for estimation of radiation risks. One set consists of data of medical statistical account. The second set consists of physical data such as contamination and irradiation levels. All these sets of data are quite different in case of children of Finland and children of Belarus. Therefore the existing agreement in radiation risks established in the present report and by Auvinen et al [8] gives an evidence that increase in the childhood leukemia manifested in Belarus and Finland is a result of irradiation caused by the Chernobyl NPP. The same conclusion can be drawn in respect of findings [4-5,9].

It is known that the rejection of link between radiation and an increase in the leukemia by infants [4-5,6] and children [9] observed after the Chernobyl accident is mostly based on results of analysis of the leukemia in infants and children of Belarus [7,10-12]. No statistical significance of the increase in leukemia incidence as well as no correlation between the incidence and correlation between contamination level was established in the reports [7,10-12]. However the reports [7,10-12] had significant methodical shortages. In case of reports [10,11] incidences in leukemia registered before the accident at the Chernobyl NPP were compared with data established in 1986-1992. The authors [10,12] could not find the statistical significance in the increase in leukemia in 1986-1992. However, data registered in Belarus after the period 1986-1992 demonstrate a decreasing trend of spontaneous childhood leukemia to the incidence before the Chernobyl accident.

An inappropriate method of analysis was used also in the report [12]. In this case the childhood leukemia in children of Belarus was analyzed by comparing annual incidences. Moreover boys and girls were analyzed separately. Such analysis was performed separately for different regions of Belarus. As a result, the children's population of Belarus was divided in the big number of subgroups. This splitting excluded any possibility to find the increase in the childhood leukemia in Belarus.

The indicated shortages and the influence of demographic factors are reasons for decreasing findings made in reports [7,10-12]. However, specialists in radiation protection concluded on the basis of these findings that there was no increase in infants and childhood leukemia in Belarus after the Chernobyl accident at whole [13,14]. As a result, they concluded the increase in infants and children leukemia observed in reports [4-6,9] had no any link to radiation.

Data established in the present report demonstrate that all these conclusions made in reports [13,14] are incorrect. The statistical significant short-time increase in the leukemia incidence occurred after the

Chernobyl accident in Belarus. The most probable reason of this increase is irradiation of Belarus as a result of the Chernobyl accident. The same conclusion can be made in respect of the increase in the leukemia incidence observed in some countries of Europe [4-6,9].

It is to notice here that ecological method was used in the present report as well as in reports [4-10-12,15-17] for analysis of the incidence in infants and children's leukemia. This method has significant limitations in interpreting of established results because both exposure and outcome are determined at the level group level. Therefore, ecological studies do not allow an assurance that the individuals who are exposed are actually those who develop the disease [35]. As a result of these limitations, ecological studies have significant problems by answering a very important question about possible threshold in inducing of the disease. For example, according to the assessment carried out in the report [36] doses of the whole body irradiation of the Belarusian population caused by the Chernobyl accident are in the range from some fractions of millisievert up to some hundreds of millisievert. It is impossible to determine on the basis of data estimated for the Belarusian children in the presented report if there is a threshold in case of the childhood leukemia.

Qualitative answer on the last question can give in case of the childhood leukemia ecological studies carried out in range of lower doses.

The highest dose of the whole body irradiation accumulated by of Finland in the first 2 years after the Chernobyl accident was 0.97 mSv [8]. It is known that irradiation dose of some small number of persons (critical group) in any irradiated group is by 3-5 times higher than the arithmetic mean dose. Assumption that radiation-induced leukemia in case of children of Finland developed in the critical group indicates, that ionizing radiation can induce radiation-induced leukemia at least at doses of the whole body irradiation in the range 3-5 mSv. This means that if the threshold exists in reality it can not be higher than 3-5 mSv in case of the childhood leukemia.

It was demonstrated in the previous section that radiation risk of the childhood leukemia in Belarus agrees very well with radiation risk established for children of Finland [8]. It is also quite close to radiation risk found for inhabitants of Hiroshima and Nagasaki irradiated at the age 0-9 years [37]. According the authors [37] excessive relative risk of leukemia incidence in persons irradiated at the age 0-9 years and followed up to the age 20 years is 44/Sv. This corresponds to a relative risk of 4.4% per mSv. This is a fully unexpected result. According the paradigm of radiation protection [38] radiation risk depends on doses and dose rates of irradiation. It is well known that doses and doses rates of the Belarusian population differ very significantly from doses and dose rates of survived inhabitants of Hiroshima and Nagasaki. The main contribution to the whole body doses of the Belarusian population, as can be seen from Table 1, gave irradiation in 1986-1989. In case of atomic bomb survivors the main fraction of dose was delivered within 1 minute [39]. Individual dose of the whole body irradiation of the Belarusian children was by 2 orders in magnitude lower than population dose of the atomic bomb survivors. The higher radiation risk of the incidence in leukemia in children of Belarus than in atomic bomb survivors despite of such immense difference in irradiation doses gives the clear evidence that using of the DRREF factor in case of chronic or protracted irradiation is not relevant at least in case of the childhood leukemia.

Conclusions

The analysis of the childhood leukemia in Belarus carried out for the period 1980-2004 indicates that the accident at the Chernobyl NPP caused manifestation of additional leikemias in the Belarusian children. Their number is about 83 cases in the period 1986-1992. The excessive relative risk of leukemia assessed for this period is 7,8% per 1 mSv. This value agrees very well with radiation risk found after the Chernobyl accident in Finland. Quite good agreement exists also of radiation risks estimated in this report with radiation risks established for atomic bomb survivors irradiated at the age 0-19 years. This is an unexpected result because of very significant difference in temporal patterns of irradiation of the Belarusian children and atomic bomb survivors. The dose rates of irradiation of the whole body in case of children of Belarus were approximately 10^{14} times lower than dose rates of atomic bomb survivors irradiation. The population doses of the whole body irradiation of the Belarusian children were lower by two orders in magnitude lower than in case of atomic bomb survivors. Despite these differences in doses and dose rates radiation risks of the leukemia incidence in children of Belarus are by some factors higher than in atomic bomb survivors. This indicates that the hypothesis about decrease of radiation risk with decrease of doses and dose rates is not relevant at least in case of the childhood leukemia.

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