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Research article

THE RISK OF INFANT MORTALITY AMONG THE OFFSPRING OF THE WORKERS OF RADIATION HAZARDOUS PRODUCTION

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Infant mortality is an indicator of healthcare quality and social well-being in a society and could be used as an important parameter in assessing the effects produced by parental occupational exposures on the offspring health.

The objective of the study: to analyze the risk of infant mortality in the cohort of the 1st generation offspring of the workers of Mayak Production Association (PA), the first atomic production facility in Russia.

Infant mortality and its components were analyzed in a cohort of children (n = 24,780) born in 1949–1973; the main group comprised 14,435 offspring of Mayak PA workers; the comparison group contained 10,345 children of unexposed parents. Incidence and relative risk of early and late neonatal, postneonatal and infant mortality were assessed taking into account the offspring sex, calendar period of birth, nosologies, parental age, categories of accumulated doses of parental preconception occupational exposure. Relative risk was calculated with 95 % confidence interval.

A higher incidence of postneonatal and infant mortality as a whole was established among the offspring of unexposed parents. Infectious pathology as a cause of death was registered among the offspring of Mayak PA workers statistically significantly less often than in the comparison group. Infant mortality rate in the main group was lower in parental age categories of 21–25 and 31–35 years as well as among younger fathers. A higher rate of infant mortality in certain categories of accumulated doses of occupational preconception gamma-exposure was caused by the contribution of infectious nosologies. Infant mortality due to malignant neoplasms in the main group requires further epidemiological analysis.

A retrospective analysis demonstrated higher rates of infant mortality and of its components among the children of unexposed parents that could be possibly explained through the "healthy worker effect" and better social well-being of Mayak PA personnel.

Keywords: *infant mortality, early neonatal death, late neonatal death, postneonatal death, radiation-hazardous production, Mayak PA, offspring of exposed parents, preconception exposure, gamma-exposure, doses to the gonads.*

Medical and demographic rates of infant, children and maternal mortality are the indicators of population health and healthcare organization in the society [1, 2]. Infant mortality is considered as a barometer of social well-being and its rate is used to assess the quality of life of the population and the level of social and economic development of the society [3].

A variety of risk factors for the health of infants, in particular, medical and biological factors such as obstetric and extragenital pathologies of mothers, the course of pregnancy and childbirth [4], as well as factors characterizing social and economic conditions in the population [5, 6] is widely discussed in publications. Late effects of parental exposure to various anthropogenic factors including radiation and the related risk of mutagenic effects in germ cells have long been a trouble for scientific community [7, 8].

Radiation exposure as a factor that potentially causes predisposition to mortality at early age is under special attention. Thus, there is a certain concern regarding unfavorable outcomes of pregnancies and genetic diseases (transgenerational of hereditary effects) induced by the effects of radioactive fallouts to population [9]. In analyses of long-term trends

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of infant mortality rates in the USA and some European countries (France, UK, Spain, Germany and Italy), the authors assume that atmospheric nuclear weapons tests could be responsible for several millions infantile deaths in the Northern Hemisphere [10]. Other authors point at the increase of perinatal losses in prefectures contaminated due to the accident at Fukushima Daiichi NPP in Japan in 2011 [11]. Meanwhile, the issues of medical effects among the offspring due to occupational contact of their parents with ionizing radiation sources are still a matter of scientific discussion [12].

This research work describes a retrospective cohort study of mortality among children population of Ozyorsk, a Closed Administrative and Territorial Unit (CATU) located close to the first Russian atomic production facility Mayak Production Association (PA) that has been in operation since 1948.

The objective of the study: to analyze the risk of infant mortality and its components in the cohort of 1st generation offspring of Mayak PA workers.

Material and methods. The following databases of the laboratory of Radiation Epidemiology of SUBI were used as the sources of information for the study: Registry of Mayak PA personnel[1], Children Registry of Ozyorsk population[2], Cause of death Registry of Ozyorsk population [13], and Health Registry of Ozyorsk children population [14]. Information on preconception (prior to conception) occupational doses of external gamma-exposure to the gonads was obtained from the database "Mayak Workers Dosimetry System 2013" [15].

Groups of children for a retrospective study were composed as follows. The main group contained children of Mayak PA workers born in Ozyorsk in 1949–1973, 14,580 children (51.7 % or 7543 were boys, and 48.3 % or 7037 were girls); 14,435 of them were live-born (51.7 % (7457) were boys, and 48.3 % (6987) were girls).

Children Registry of Ozyorsk population comprises information on 43,680 children born in 1949–1973; 35,149 of them were born in the city. After including 14,580 offspring of Mayak PA workers into the main group, a thorough check was performed among the other 20,569 children searching for preconception exposure of their parents (occupational exposure prior to conception among construction workers, military personnel, liquidators of radiation accidents, migrants from the territories contaminated with radiation). Finally, the comparison group comprised 10,427 children of unexposed parents born in Ozyorsk in 1949–1973: 50.8 % or 5301 were boys, and 49.2 % or 5126 were girls; 10,345 of them were live-born (50.8 % (5026) were boys, and 49.2 % (5085) were girls).

Comparability of the groups was provided through the fact of birth within the city of Ozyorsk and the same follow up period that assumes the absence of climatic and geographic differences in living conditions and equal level of medical care for the population.

Causes of death were considered according to "International Statistical Classification of Diseases and Related Health Problems" (ICD) of the 9th and 10th revision. Mortality rates were calculated for 1000 children: early neonatal mortality as a ratio of the number of children who died during the first 7 days to the number of children born alive; late neonatal mortality as a ratio of the number of children who died in the period from 8 to 28 days to all the live-born children excluding those who died in the first week of their life; postneonatal mortality as a ratio of the number of children who died at the age from 29 days to one year to all the live-born children excluding those who died during the first 28 days of their life; infant mortality a ratio of the num-

[1] Koshurnikova N.A., Shilnikova N.S., Okatenko P.V., Kreslov V.V., Bolotnikova M.G., Sokolnikov M.E., Khokhriakov V.F., Suslova K.G. [et al.]. Characteristics of the cohort of workers at the Mayak nuclear complex. *Radiat. Res.*, 1999, vol. 152, no. 4, pp. 352–363.

[2] Petrushkina N.P., Koshurnikova N.A., Kabirova N.R., Okatenko P.V., Khokhryakov V.V. Radiation risk assessment for communities living near the atomic plants. Report 1. Procedures of radiation risk assessments. Child's Register. *Voprosy radiatsionnoi bezopasnosti*, 1996, no. 2, pp. 46–50 (in Russian).

ber of children who died within the period from the date of birth to 12 months to all the live-born children.

STATISTICA Version 10 software (StatSoft, USA) was used for our comparative analysis: incidences were compared using a Pearson's chi-squared test and two-tailed Fisher's exact test[3]. The differences were considered statistically significant at $p < 0.05$. Calculation of the relative risk (RR) was performed with 95 % confidence interval (CI) using the following formula:

$$RR = (a / (a + b)) / (c / (c + d)),$$

where a is a number of deaths among the offspring of the main group; b is alive offspring of the main group; c is deaths in the comparison group; d is alive offspring of the comparison group; with 95 % confidence interval:

$$95\ \%\ \mathrm{CI} = \exp\left(\ln(\mathrm{RR}) - 1.96 \cdot \mathrm{SE}\{\ln(\mathrm{RR})\}\right)$$
$$\text{to}\ \ \exp\left(\ln(\mathrm{RR}) + 1.96 \cdot \mathrm{SE}\{\ln(\mathrm{RR})\}\right)$$

and mean square error of the logarithmic RR:

$$\mathrm{SE}\{\ln(\mathrm{RR})\} = \sqrt{\frac{1}{a} + \frac{1}{c} - \frac{1}{a+b} - \frac{1}{c+b}}.$$

Incidence and RR of death at age under one year was analyzed taking into account the offspring sex, periods of birth, parental age at the date of childbirth. The following 5-year periods were considered: 1949–1953, 1954–1958, 1959–1963, 1964–1968, and 1969–1973. Analysis of parental age was performed based on the following intervals: 20 years and younger, 21–25 years, 26–30 years, 31–35 years, 36 and older.

RR of death of the offspring regarding preconception exposure of the parents at Mayak PA was calculated in each of the following dose categories of external gamma-exposure of the gonads: zero dose (no doses registered for the worker in the studied period); 0.1–20, 20.1–50, 50.1–100, 100.1–500, 500.1–1000, 1000.1 and more mGy.

Results and discussion. A comparative analysis of infant mortality and its components in the groups is presented in Table 1. Three hundred and seventy-two cases of infant deaths were registered in the main group of offspring during the whole follow up period (57.5 % were boys, 42.5 % were girls). Among the offspring of unexposed parents, the number of children who had died under the age of one year made 322 (56.8 % were boys, 43.2 % were girls) that statistically significantly exceeds the rate in the main group: $\chi^2 = 6.35$, $p = 0.012$.

Early neonatal mortality made 39.3 % (146/372) of all the cases of death at age under one year in the main group and 32.6 % (105/322) in the comparison group, and didn’t differ between the groups. Late neonatal mortality took 5.9 % (22/372) in the mortality structure of the main group and 6.8 % (22/322) in the comparison group. There were no statistically significant differences in the rates of late neonatal mortality between the groups both as a whole and taking into account the offspring sex.

The contribution of postneonatal mortality within the groups was large, 54.8 % (204/372) in the main group and 60.6 % (195/322) in the comparison group. The rate of postneonatal death was statistically significantly higher in the comparison group regarding the total observation ($\chi^2 = 8.47$, $p = 0.004$), as well as in the comparative analysis by sex ($\chi^2 = 4.54$, $p = 0.033$ among boys; $\chi^2 = 4.06$, $p = 0.044$ among girls).

Calculation of the relative risk demonstrated similar results: the rates of postneonatal mortality among boys, girls and both sexes as well as infant mortality as a whole were higher among the offspring of unexposed parents.

Dynamics of infant mortality and of its components regarding 5-year periods of birth is presented at Figure 1. Temporal trends of early neonatal mortality were proportional in

[3] Glantz S.A. Primer of biostatistics. Fourth Edition. New York, McGraw-Hill, Health Professions Division, 1997, 473 p.

Table 1

Infant mortality and its components in the groups

Main group			Comparison group			Relative risk [95% CI]					
Boys (n = 7457)	Girls (n = 6978)	Total (n = 14,435)	Boys (n = 5260)	Girls (n = 5085)	Total (n = 10,345)	Boys		Girls		Total	
abs. (for 10^3)	abs. (for 10^3)	abs. (for 10^3)	abs. (for 10^3)	abs. (for 10^3)	abs. (for 10^3)	RR	CI	RR	CI	RR	CI
Early neonatal mortality											
83 (11.1)	63 (9.0)	146 (10.1)	64 (12.2)	41 (8.1)	105 (10,2)	0.92	0.7–1.3	1.12	0.8–1.7	0.99	0.8–1.3
Late neonatal mortality [1]											
13 (1.8)	9 (1.3)	22 (1.5)	9 (1.7)	13 (2.6)	22 (2.1)	1.02	0.4–2.4	0.51	0.2–1.2	0.72	0.4–1.3
Postneonatal mortality [2]											
118* (16.0)	86* (12.5)	204* (14.3)	110 (21.2)	85 (16.9)	195 (19.1)	0.76*	0.6–0.98	0.74*	0.5–0.99	0.75*	0.6–0.9
Infant mortality											
214 (28.7)	158 (22.6)	372* (25.8)	183 (34.8)	139 (27.3)	322 (31.1)	0.83	0.7–1.01	0.83	0.7–1.04	0.83*	0.7–0.96

Note: [1] – excluding children who died during the first 7 days of life, [2] – excluding children who died during the first 28 days of life, * – statistically significant differences.

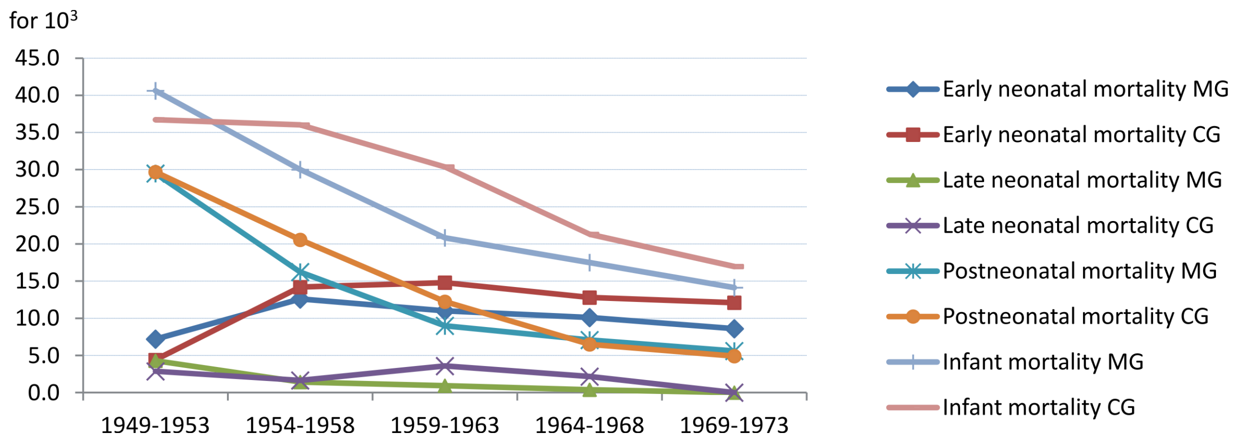

Figure 1. Dynamics of infant mortality and its components for 1949–1973: MG – main group, CG – comparison group

both groups: minimum values in the period 1949–1953, stable rates in 1954–1963 and gradual decrease by 1969–1973. A comparative analysis of early neonatal mortality in each calendar period demonstrated no differences between the groups.

The rates of late neonatal, postneonatal and infant mortality in the groups were rather comparable: the highest rates were registered in 1949–1953 that steadily decreased by the end of the followed period. Statistically significant differences were established only among children born in 1959–1961 when the rate of infant mortality in the comparison group was higher than in the main group (χ^2 = 3.88, p = 0.049).

Assessment of the relative risk in relation to the period of birth of the offspring (Table 2) demonstrated the same trends: infant mortality was statistically significantly higher among children born in 1959–1963 in the comparison group than in the main group, RR = 0.67 (0.5–0.99). A comparative analysis of early and late neonatal mortality taking into account 5-year periods of birth demonstrated no significant differences.

Table 2

Relative risk of death at age under one year by calendar periods of childbirth

Periods	Mortality types	Main group, n = 14,435			Comparison group, n = 10,345			*RR* [95% CI]
		abs.	Number of children in the group[3]	for 10^3	abs.	Number of children in the group[3]	for 10^3	
1949–1953	Early neonatal	22	3053	7.2	17	3869	4.4	1.64 [0.9–3.1]
	Late neonatal[1]	13	3031	4.3	11	3852	2.9	1.5 [0.7–3.3]
	Postneonatal[2]	89	3018	29.5	114	3841	29.7	0.99 [0.8–1.3]
	Infant	124	3053	40.6	142	3869	36.7	1.11 [0.9–1.4]
1954–1958	Early neonatal	45	3565	12.6	35	2471	14.2	0.89 [0.6–1.4]
	Late neonatal	5	3520	1.4	4	2436	1.6	0.86 [0.2–3.2]
	Postneonatal	57	3515	16.2	50	2432	20.6	0.79 [0.5–1.2]
	Infant	107	3565	30.0	89	2471	36.0	0.83 [0.6–1.1]
1959–1963	Early neonatal	36	3264	11.0	21	1416	14.8	0.74 [0.4–1.3]
	Late neonatal	3	3228	0.9	5	1395	3.6	0.26 [0.1–1.1]
	Postneonatal	29	3225	9.0	17	1390	12.2	0.74 [0.4–1.3]
	Infant	68	3264	20.8	43	1416	30.4	0.67* [0.5–0.99]
1964–1968	Early neonatal	26	2571	10.1	12	939	12.8	0.79 [0.4–1.6]
	Late neonatal	1	2545	0.4	2	927	2.2	0.18 [0.02–2.0]
	Postneonatal	18	2544	7.1	6	925	6.5	1.09 [0.4–2.7]
	Infant	45	2571	17.5	20	939	21.3	0.82 [0.5–1.4]
1969–1973	Early neonatal	17	1982	8.6	20	1650	12.1	0.71 [0.4–1.4]
	Late neonatal	–	1965	–	–	1630	–	–
	Postneonatal	11	1965	5.6	8	1630	4.9	1.14 [0.5–2.8]
	Infant	28	1982	14.1	28	1650	17.0	0.83 [0.5–1.4]

Note: [1] – excluding children who had died during the first 7 days of life; [2] – excluding children who had died during the first 28 days of life, [3] – number of children in the group born in this period, * – statistically significant differences.

Just a few publications refer to the issues of infant mortality at early years of follow up indicating that it was a difficult period of overcoming demographic consequences of the war under severe lack of resources [16]. According to the national statistics, data infant mortality in 1947–1964 decreased from 130 to 25 for 1000 births; infant mortality rate in the 70-ies and 80-ies varied from 23.6 to 22.1 for 10^3 and depended a lot on regional specific conditions[4]. A.A. Baranov in his analysis of 30-year trends in USSR infant mortality indicates that "season variations with peak rates in July and September were one of the characteristic features" [17].

Analysis of mortality structure in the groups (Fig. 2) demonstrated that among the offspring of exposed parents "Other disorders originating in the perinatal period" (ICD-10 codes: P00–P96) took the leading place in the infant mortality structure: 132 cases (35.5 % of all the outcomes); this subclass took the second place in the comparison group with 97 cases (30.1 %), $\chi^2 = 0.035$, $p > 0.05$.

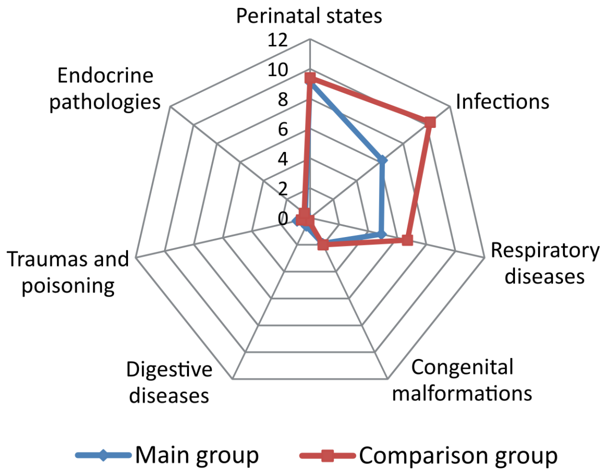

Figure 2. Rates of certain subclasses of infant mortality (for 10^3).

Infectious diseases as a cause of death of children aged under one year took the second place among the offspring of exposed parents (23.9 % or 89 cases) and the leading place among the offspring of unexposed parents (32.9 % or 106 cases); this rate was statistically significantly higher in the comparison group: $\chi^2 = 12.86$, $p = 0.00034$. Respiratory diseases took the third place in both groups: 71 cases (19.1 %) in the main group and 69 cases (21.4 %) in the comparison group; $\chi^2 = 0.035$, $p > 0.05$. No statistically significant differences were found comparing other subclasses (endocrine pathologies, congenital malformations, neural and digestive diseases).

Early neonatal mortality due to prematurity was statistically significantly more often observed in the comparison group, 2.2 against 1.2 for 10^3 in the main group ($\chi^2 = 4.1$, $p = 0.04$). Pneumonia with unspecified germ, congenital abnormalities of the heart and great vessels and perinatal period states mostly presented by extreme immaturity, the consequences of birth injuries and respiratory distress syndrome were the most often causes of death in the late neonatal period in both groups. No statistically significant differences were established between the groups in the late neonatal period.

Infections prevailed in the structure of postneonatal mortality: respiratory diseases, particularly, bronchopneumonia with unspecified germ, and intestinal infections among which deaths from shigellosis were registered especially often. It should be noted that in the period 1950–1956 an extremely unfavorable epidemiological situation regarding dysentery with severe infectious forms and high mortality rate was registered in Ozyorsk. Thus, 77 lethal outcomes from intestinal infections (5.4 for 10^3) were registered in the postneonatal period in the main group, and 47 of them were due to shigellosis (3.3 for 10^3); 85.1 % of these were in 1950–1956. Mortality rate due to intestinal infections in the comparison group was statistically significantly higher: 79 cases or 7.7 for 10^3 ($\chi^2 = 5.13$, $p = 0.024$); of them were 49 cases of shigellosis or 4.8 for 10^3 ($\chi^2 = 3.44$, $p > 0.05$), and 79.6 % of these cases were in the period 1950–1956.

In addition to intestine damages, infectious pathology in the postneonatal period was presented by childhood quarantine infections, viral hepatitis and tuberculosis. It was noted that tuberculosis was statistically significantly more often registered as a cause of death in the comparison group than in the main group: 1.27 against 0.2 for 10^3 (*F*-test = 0.0017). Single cases of miliary tuberculosis and extrapulmonary forms of tuberculosis – meningeal and bone tissue tuberculosis –

[4] Anderson B.A., Silver B.D. Trends in mortality of the Soviet population. *Sov. Econ.*, 1990, vol. 6, no. 3, pp. 191–251; Millle F., Shkolnikov V.M., Hertrich V., Vallin J. Sovremennye tendentsii smertnosti po prichinam smerti v Rossii: 1965–1994 [Current trends in mortality by cause of death in Russia: 1965–1994]. Paris, INED; Moscow, Center for Demography and Human Ecology, 1996, 140 p. (in Russian).

were diagnosed in the offspring of unexposed parents. Postneonatal pneumonia cases were registered as causes of death in the postneonatal period significantly more often among the children of unexposed parents: 5.28 against 3.5 per 10^3 in the main group, $\chi^2 = 4.46$, $p = 0.035$. Eventually, after summing up all observations, infections turned out to be the registered cause of death in the postneonatal period much more often in the offspring of unexposed parents: 104 cases or 10.2 for 10^3 against 88 cases or 6.17 for 10^3 in the main group, $\chi^2 = 12.3$, $p = 0.0005$.

It is worth mentioning that among the children of exposed parents two cases of death due to malignant neoplasms (MN) were registered in the postneonatal period. Leukemia of unspecified cell type was diagnosed in 1954 in a boy aged 3 months born to the workers of the radiochemical plant exposed to preconception gamma-radiation; the doses made 5.1 mGy to the ovaries and 385.8 to the testicles, in utero gamma-exposure dose made 8.78 mGy. Brain MN was diagnosed in 1968 in a girl aged 5 months whose father was a reactor plant worker, dose of preconception occupational external gamma-exposure to the testicles made 2.33 mGy. No lethal outcomes due to MN at age under one year were observed among the offspring of unexposed parents.

It should be noted that the compared groups contained only children born and residing in Ozyorsk. From the moment of launching the main production facility "medical care for Ozyorsk population along with the workers of the city-forming facility was provided by the FMBA of Russia in a form of medical and sanitary units and clinical hospitals" [18] that assumes the same standards of healthcare and medical equipment.

Table 3 demonstrates distribution of the offspring deceased at age under one year by parental age at childbirth and the relative risk of death in various categories of maternal and paternal age.

Average maternal age at childbirth in the main group was 26 years (range from 15 to 46 years); average paternal age, 27.5 years (range 17–54 years). In the comparison group, average maternal age was the same at 26 years (range 15–49 years) while average paternal age was somewhat higher at 28.3 years (15–56). Characteristics of parental age among death cases did not differ a lot from the whole–cohort data: average maternal age in the main group was 26 years (17–43), average paternal age was 27.3 years (19–50); in the comparison group, 26 years (16–45) and 28 years (19–47) respectively.

In both groups, most often children were born to mothers aged 21–25 and fathers aged 26–30. Infant mortality cases in the groups were more often registered among boys born to young mothers (40.0 for 10^3 in the main group and 43.0 for 10^3 in the comparison group, $p > 0.05$) and mothers aged 36 and older (37.8 and 48.2 for 10^3 respectively, $p > 0.05$), and among the offspring of young fathers (34.3 for 10^3 among the boys of main group, $p > 0.05$; and 53.4 for 10^3 among the girls of main group, F-test = 0.031).

Statistically significant estimates of the relative risk were obtained for maternal age category of 21–25 years in which infant mortality in the comparison group was higher for girls, 0.68 (0.5–0.96), and for both sexes, 0.75 (0.6–0.95), and for maternal age category of 31–35 for girls, 0.5 (0.3–0.97). Infant mortality was statistically significantly lower among the offspring of Mayak PA workers in the following paternal age categories: 20 years and younger, 21–25 years and 31–35 years.

Research of the differences in infant mortality rates in different subgroups of mothers aged under 20 in USA demonstrated that children born to younger mothers had an increased risk of death [19]. A relation between elderly age of fathers and unfavorable outcomes for both a mother and a child was described by Y.S. Khandwala et al. [20]. Meanwhile, according to the data from the Sweden Registry for mortality research, a higher survivability was established in the offspring of elderly parents [21]. The authors emphasize the importance of the trend of giving birth to "later children in wealthier and healthier" environment. Alongside, M. Balaj et al. [22] mention the value of parents' education level pointing out the fact that a lower education level of mothers and fathers are risk factors of children mortality even taking into account other markers of social and economic status of the family. Research of the interrelation between the parental level of education and infant mortality based on statistical data of natural migration of the population in Japan demonstrated that a lower level of maternal education was in fact related to children mortality [23].

Table 3

Relative risk of death at age under one year by parental age at childbirth

Parental age	Sex	Main group, *n* = 14,435			Comparison group, *n* = 10,345			*RR* [95 % CI]
		abs.	Number of children in the group[1]	for 10^3	abs.	Number of children in the group[1]	for 10^3	
The group as a whole	Boys	214	7457	28.7	183	5260	34.8	0.82 [0.7–1.002]
	Girls	158	6978	22.6	139	5085	27.3	0.83 [0.7–1.04]
	Total	372	14435	25.8	322	10345	31.1	0.83* [0.7–0.96]
Maternal age								
20 years and younger	Boys	33	825	40.0	32	744	43.0	0.93 [0.6–1.5]
	Girls	20	757	26.4	14	652	21.5	1.23 [0.6–2.4]
	Total	53	1582	33.5	46	1396	33.0	1.02 [0.7–1.5]
21–25 years	Boys	84	2938	28.6	73	2080	35.1	0.82 [0.6–1.1]
	Girls	61	2796	21.8	66	2063	32.0	0.68* [0.5–0.96]
	Total	145	5734	25.3	139	4143	33.6	0.75* [0.6–0.95]
26–30 years	Boys	55	2420	22.7	42	1482	28.3	0.8 [0.5–1.2]
	Girls	52	2255	23.1	33	1496	22.1	1.05 [0.7–1.6]
	Total	107	4675	22.9	75	2978	25.2	0.91 [0.7–1.2]
31–35 years	Boys	31	983	31.5	21	643	32.7	0.97 [0.6–1.7]
	Girls	15	892	16.8	20	594	33.7	0.5* [0.3–0.97]
	Total	46	1875	24.5	41	1237	33.1	0.74 [0.5–1.1]
36 years and older	Boys	11	291	37.8	15	311	48.2	0.78 [0.4–1.7]
	Girls	10	278	36.0	6	280	21.4	1.68 [0.6–4.6]
	Total	21	569	36.9	21	591	35.5	1.04 [0.6–1.9]
Paternal age[2]								
20 years and younger	Boys	8	233	34.3	2	141	14.2	2.42 [0.5–11.2]
	Girls	2	204	9.8	7	131	53.4	0.18* [0.04–0.9]
	Total	10	437	22.9	9	272	33.1	0.69 [0.3–1.7]
21–25 years	Boys	72	2508	28.7	65	1761	36.9	0.78 [0.6–1.1]
	Girls	53	2391	22.2	49	1675	29.3	0.76 [0.5–1.1]
	Total	125	4899	25.5	114	3436	33.2	0.77* [0.6–0.99]
26–30 years	Boys	66	2855	23.1	55	1789	30.7	0.75 [0.5–1.1]
	Girls	56	2662	21.0	43	1854	23.2	0.91 [0.6–1.3]
	Total	122	5517	22.1	98	3643	26.9	0.82 [0.6–1.1]
31–35 years	Boys	28	1224	22.9	38	934	40.7	0.56* [0.4–0.9]
	Girls	19	1145	16.6	30	859	34.9	0.47* [0.3–0.8]
	Total	47	2369	19.8	68	1793	37.9	0.52* [0.4–0.8]
36 years and older	Boys	14	477	29.4	23	633	36.3	0.81 [0.4–1.6]
	Girls	9	452	19.9	10	553	18.1	1.1 [0.5–2.7]
	Total	23	929	24.8	33	1186	27.8	0.89 [0.5–1.5]

Note: [1] – number of children in a group born to parents of this age; [2] – paternal age is unknown for 284 children of the main group and 15 children of the comparison group; * – statistically significant differences.

Table 4

Characteristics of preconception external gamma-exposure of the parents, mGy

	Number of offspring	Dose range	Average value ± mean square deviation	Median [interquartile range Q25; Q75]
Preconception exposure of the ovaries				
The whole group	4821	0–4075.6	286.8 ± 470.9	74.4 [0.4; 367.4]
Deaths at age under one year	158	0–1930.4	276.2 ± 474.1	55.3 [0; 303.8]
Preconception exposure of the testicles				
The whole group	12356	0–5653.1	382.2 ± 614.8	126.9 [16.1; 461.8]
Deaths at age under one year	273	0–3987.5	349.9 ± 605.2	110.6 [0; 461.4]

Table 4 demonstrates dose estimates of preconception external gamma-exposure of the parents in the main group at Mayak PA. Parameters of accumulated doses of external gamma-exposure are presented for the whole group and for children who died at age under one year.

Maximum doses of occupational exposure of mothers in the whole main group reached 4075.6 mGy; 1930.4 mGy among the mothers whose children died aged under one year. Similar trends were noted when analyzing preconception exposure of the testicles: maximum dose in the whole cohort 5653.1 mGy; for infant mortality cases, 3987.5 mGy. The values of average characteristics of the doses of preconception exposure of ovaries and testicles were lower in the subgroup of infant mortality compared to the whole group.

Distribution of the children in the main group by dose categories of parental occupational exposure demonstrated that maximum number of the offspring were registered in the preconception dose ranges of 100.1–500 mGy (26 % of the children of mothers working at Mayak PA and 30.3 % of the children of fathers working at the facility) and in zero dose category (24.5 % and 15.8 % respectively). Analysis of infant mortality demonstrated that maximum number of death cases at age under one year was registered in these categories 24.1 % in the dose category of 100.1–500 mGy and 27.2 % in "zero dose" : in case of preconception exposure of the ovaries; 28.2 % and 26 % respectively in case of preconception exposure of the testicles.

Assessment of infant mortality taking into account dose ranges of external gamma-exposure in comparison to the offspring of unexposed parents of corresponding sex is presented in Table 5.

Table 5

Relative risk of death at age under one year by dose ranges of preconception exposure of the parents (comparing to the same-sex children of unexposed parents)

Dose ranges, mGy	Sex	Main group			Comparison group			*RR* [95 % CI]
		abs.	Number of children in the group[1]	for 10^3	abs.	Number of children in the group	for 10^3	
1	2	3	4	5	6	7	8	9
Preconception exposure of the ovaries								
Zero dose	Boys	21	590	35.6	183	5260	34.8	1.02 [0.66–1.6]
	Girls	22	592	37.2	139	5085	27.3	1.36 [0.87–2.1]
	Total	43	1182	36.4	322	10345	31.1	1.17 [0.85–1.6]
from 0.1 to 20.0	Boys	9	302	29.8	183	5260	34.8	0.86 [0.44–1.66]
	Girls	8	281	28.5	139	5085	27.3	1.04 [0.52–2.1]
	Total	17	583	29.2	322	10345	31.1	0.94 [0.58–1.51]

End of the Table 5

1	2	3	4	5	6	7	8	9
from 20.1 to 50.0	Boys	12	233	51.5	183	5260	34.8	1.48 [0.84–2.6]
	Girls	4	183	21.9	139	5085	27.3	0.8 [0.3–2.1]
	Total	16	416	38.5	322	10345	31.1	1.24 [0.75–2.02]
from 50.1 to 100.0	Boys	13	254	51.2	183	5260	34.8	1.47 [0.85–2.55]
	Girls	3	196	15.3	139	5085	27.3	0.56 [0.18–1.74]
	Total	16	450	35.6	322	10345	31.1	1.14 [0.7–1.87]
from 100.1 to 500.0	Boys	23	652	35.3	183	5260	34.8	1.01 [0.66–1.55]
	Girls	15	602	24.9	139	5085	27.3	0.91 [0.54–1.54]
	Total	38	1254	30.3	322	10345	31.1	0.97 [0.7–1.36]
from 500.1 to 1000.0	Boys	5	263	19.0	183	5260	34.8	0.55 [0.23–1.32]
	Girls	7	262	26.7	139	5085	27.3	0.98 [0.46–2.1]
	Total	12	525	22.9	322	10345	31.1	0.73 [0.42–1.3]
from 1000.1 and more	Boys	12	221	54.3	183	5260	34.8	1.56 [0.88–2.75]
	Girls	4	190	21.1	139	5085	27.3	0.77 [0.29–2.06]
	Total	16	411	38.9	322	10345	31.1	1.25 [0.76–2.1]
Total	Boys	95	2515	37.8	183	5260	34.8	1.09 [0.85–1.38]
	Girls	63	2306	27.3	139	5085	27.3	0.99 [0.75–1.34]
	Total	158	4821	32.8	322	10345	31.1	1.05 [0.87–1.27]
Preconception exposure of the testicles								
Zero dose	Boys	32	1010	31.7	183	5260	34.8	0.91 [0.63–1.32]
	Girls	39	946	41.2	139	5085	27.3	1.51* [1.06–2.14]
	Total	71	1956	36.3	322	10345	31.1	1.17 [0.91–1.5]
from 0.1 to 20.0	Boys	15	642	23.4	183	5260	34.8	0.67 [0.4–1.13]
	Girls	6	657	9.1	139	5085	27.3	0.33* [0.15–0.75]
	Total	21	1299	16.2	322	10345	31.1	0.52* [0.33–0.81]
from 20.1 to 50.0	Boys	11	591	18.6	183	5260	34.8	0.54* [0.3–0.98]
	Girls	7	560	12.5	139	5085	27.3	0.46* [0.22–0.97]
	Total	18	1151	15.6	322	10345	31.1	0.5* [0.31–0.81]
from 50.1 to 100.0	Boys	14	651	21.5	183	5260	34.8	0.62 [0.36–1.1]
	Girls	10	638	15.7	139	5085	27.3	0.57 [0.3–1.08]
	Total	24	1289	18.6	322	10345	31.1	0.59* [0.39–0.9]
from 100.1 to 500.0	Boys	50	1935	25.8	183	5260	34.8	0.74 [0.55–1.01]
	Girls	27	1806	15.0	139	5085	27.3	0.55* [0.36–0.82]
	Total	77	3741	20.6	322	10345	31.1	0.66* [0.52–0.85]
from 500.1 to 1000.0	Boys	20	748	26.7	183	5260	34.8	0.77 [0.49–1.2]
	Girls	13	682	19.1	139	5085	27.3	0.69 [0.39–1.22]
	Total	33	1430	23.1	322	10345	31.1	0.74 [0.52–1.06]
from 1000.1 and more	Boys	17	771	22.0	183	5260	34.8	0.63 [0.39–1.04]
	Girls	12	719	16.7	139	5085	27.3	0.61 [0.34–1.09]
	Total	29	1490	19.5	322	10345	31.1	0.62* [0.43–0.91]
Total	Boys	159	6348	25.0	183	5260	34.8	0.72* [0.58–0.89]
	Girls	114	6008	19.0	139	5085	27.3	0.69* [0.54–0.89]
	Total	273	12356	22.1	322	10345	31.1	0.71* [0.61–0.83]

Note: [1] – number of children in the group in the given dose interval of parental exposure; * – statistically significant differences.

The number of children whose mothers were exposed to occupational contact with ionizing radiation prior to conception made 4821; 158 of them died at age under one year (60.1 % were boys, 39.9 % were girls). No actual pattern was found by analyzing the categories of maternal preconception exposure and incidence of infant mortality among the offspring: average infant mortality in the main group corresponded to the values in the comparison group. Maximum infant mortality in the main group was registered among male offspring in dose ranges of 20.1–50 mGy (51.5 for 10^3), 50.1–100 mGy (51.2 for 10^3) and over 1 Gy (54.3 for 10^3). However, a comparative analysis revealed no statistically significant differences in *RR* in any of the dose categories of preconception exposure of the ovaries.

The number of main group offspring whose fathers were exposed to occupational contact with ionizing radiation prior to conception made 12,356; 273 cases of infant mortality were registered among them (58.2 % boys, 41.8 % girls). The highest infant mortality rate (41.2 for 10^3) was observed among girls with fathers in the “zero dose” category of occupational exposure. RR assessment in this category demonstrated that infant mortality among the girls of exposed fathers was statistically significantly higher than among the girls of the comparison group, 1.51 (1.06–2.14). A detailed analysis of mortality structure in this dose category demonstrated a statistically significant increase of intestinal infections among the daughters of exposed fathers (13.7 for 10^3) compared to the girls of unexposed parents (7.1 for 10^3), $\chi^2 = 4.39$, $p = 0.036$.

Infant mortality in many of dose categories of preconception exposure of the testicles turned out to be statistically significantly lower than in control. A final risk assessment for all the children whose fathers were exposed to long-term occupational exposure also demonstrated a lower rate of infant mortality than in the comparison group: 0.72 (0.58–0.89) for male offspring, 0.69 (0.54–0.89) for female offspring, 0.71 (0.61–0.83) for both sexes.

In the research of children cancer survivors by L.B. Signorello et al. [24], it was reported that radiation exposure of the ovaries and uterus significantly increased a risk of stillbirth and neonatal death of the offspring in accumulated doses over 10 Gy. D.M. Green et al. [25] observed reproductive outcomes following radiation cancer therapy and noted that newborns of women with exposure doses to the uterus over 5 Gy were more likely to be small for their gestation age, though there were no differences related to the proportion of congenital malformations, cytogenetic syndromes or monogenic defects between the offspring. Meanwhile, analysis of the relation between radiation exposure and risk of congenital abnormalities and death in the perinatal period among the offspring of Japan population exposed to atomic bombing demonstrated a relation between the studied effects and parental exposure though direct effect of radiation was not proved [26]. According to earlier research work in the cohort of children population of Ozyorsk comparing the rate and structure of mortality at age under one year among the children born in 1974–1988 no statistically significant differences were found between the offspring of Mayak PA workers and children of unexposed parents[5].

Thus, the summary assessment of infant mortality and its components demonstrated higher rates of postneonatal and infant mortality and infectious pathology among the offspring of unexposed parents. It could be possibly explained through the “healthy worker effect” [27] among the parents who were Mayak PA workers due to a thorough medical investigation prior to employment to the production facility with harmful working conditions and selection of individuals with no obvious chronic pathologies. One could not deny that the parents of the main group of children could be initially different in health characteristics from the parents in the comparison group [28].

[5] Petrushkina N.P., Koshurnikova N.A., Kabirova N.R., Okatenko P.V. Radiation risk assessment for population from the areas close to the atomic industry enterprises. Information 3. Infant mortality among the newborns of 1974–1988. *Voprosy radiatsionnoi bezopasnosti*, 1996, no. 4, pp. 15–22 (in Russian).

From the other point of view, it is important to note the specific social and economic conditions in the CATU [29, 30]. The families of Mayak PA workers used to have better financial and living conditions compared to the families of those working in city organizations. Analysis of infant mortality in relation to social groups of parents demonstrated that 61.3 % (228/372) of the mothers in the main group belonged to the category of "labor workers", 21.2 % (79/372) were "civil servants", and 10.5 % (39/372) of mothers were students. In the comparison group, 53.7 % (173/322) mothers of the children who died at age under one year were "labor workers", 15.5 % (50/322) were "civil servants", and 19.9 % (64/322) were students. Analysis of paternal occupation demonstrated that in the main group 68 % (253/372) of the fathers belonged to the group of "labor workers", 16.9 % (63/372) were "civil servants"; in the comparison group, 59.6 % (192/322) and 20.2 % (65/322), respectively, and 0.3 % (1/322) was registered as a college student.

Statistically significant differences were obtained for a social group of "labor workers" that comprised a larger number of parents in the main group than in the comparison one ($\chi^2 = 4.05$, $p = 0.044$, among mothers, $\chi^2 = 5.3$, $p = 0.022$, among fathers), and $\chi^2 = 12.1$, $p < 0.001$ for the category "students" that was mostly presented by mothers of the comparison group.

Research works of the social aspects of infant mortality are numerous. Thus, assessment of the effect of medical organization factors and social reasons to mortality in late neonatal period in the Ural Federal District indicated that "social reasons prevail" and reach 60 % [31]. Researchers of children and perinatal mortality in Russia point out social factors as the basis of deaths due to external causes [32]. When developing measures in order to decrease infant and maternal mortality in the country, three groups of factors are usually stressed that define different living conditions: financial well-being, medical care quality, and social environment [5]. Taking into account the fact that the observed children were all born and lived in the CATU and, correspondingly, had the same quality of medical care, the issues of social well-being and initial health status of the parents turn out to be the priority.

Further planned research of this topic includes analysis of perinatal and infant mortality taking into account such non-radiation factors as gestation age, delivery parity and other obstetric and gynecologic risk factors related to unfavorable outcomes during the first year of life [33, 34]. MN cases as causes of death at age under one year in the main group requires further follow up in older age groups of the offspring.

Conclusions. The retrospective epidemiological study of infant mortality and its structural components was carried out in the cohort of children born in CATU Ozyorsk in 1949–1973 (n = 24,780); 14,435 of them were from the families of workers of the radiation-hazardous enterprise.

The comparative analysis of mortality at age under one year demonstrated that postneonatal and infant mortality was in whole statistically significantly higher among the offspring of unexposed parents in comparison to the main group. Our study established a significant effect of infectious pathology on the frequency of outcomes and–clear predominance of postneonatal mortality cases due to infectious diseases in the comparison group.

An assessment of infant mortality taking into account accumulated doses of production preconceptional exposure to external gamma-radiation found some dose intervals where the risk in the main group was higher, that was due to infectious pathology.

The analysis of non-radiation factors, in particular, the parental age and occupation, revealed higher rates of infant mortality among the offspring of unexposed parents in some age categories and significant differences in the groups by type of parental employment.

Taking into account the variety of non-radiation factors resulting in infant mortality, a detailed factor analysis is required in the future in the cohort of the CATU children population.

At this stage of the work, the noted features of mortality among the offspring of exposed parents are probably due to the "healthy worker effect" in the cohort of Mayak PA workers and to more favorable living conditions for their families which could have an important effect on the infant morbidity and mortality.

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