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RISK OF DEVELOPING CONGENITAL MALFORMATIONS IN INFANTS WHOSE MOTHERS LIVE UNDER UNFAVOURABLE GEOCHEMICAL CONDITIONS

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Abstract. The objective of the paper was to determine the risk of congenital malformations in children whose mothers lived in areas with different geochemical characteristics.

Material and methods. We have analysed 492 protocols of autopsy on newborn infants and fetuses, which died in the uterus or after birth during 2004-2014 in Chernivtsi due to the geochemical disadvantages of the places where the pregnant women lived.

Results. When pregnant women live in the areas with a chronic exposition to heavy metals the risk of the fetal death and that of newborn infants increases by 6,1 times compared to conditionally clean areas. It has been established that in the structure of birth defects in deceased children, whose mothers lived in places of geochemical disadvantage, there was a reliable risk of congenital heart disease and of multiple congenital malformations.

Conclusions. The peculiarities of the distribution of incidence of congenital malformations in ecologically unfavorable areas are: the prevalence of congenital heart disease (OR = 2.13 (95DI 1.05-4.31), multiple congenital heart diseases OR = 1.8 (95CI 1.1- 2.8), especially in the male population (OR = 2.7 (95CI 1.04-7.4).

Key words: congenital malformations, newborn infants, heavy metals, soil pollution.

According to WHO, 4-6% of children with congenital malformations (CMF) are born annually in the world, and about 30% of all perinatal losses are due to congenital malformations that are incompatible with life. CMF may be caused by various environmental factors, therefore, their incidence in the population may be regarded as an indicator of environmental disadvantage [4,5,6].

At the same time, it should be noted that the pathogenic influence of geochemical factors on the development of CMF has not been sufficiently studied. This is partly due to the fact that pathogenic soil stimuli such as heavy metals and radionuclides are considered to be inert enough to enter the body of a pregnant woman and, subsequently, transplacentally to the fetus and cause structural, metabolic or epigenetic changes [1,2]. But given that these pathogenic factors can enter the body through food chains, groundwater and inhalation while the upper layer of soil is weathering, then this point of view seems insufficiently substantiated [3]. Proceeding from this, the idea of the risk of congenital malformations depending on the geochemical characteristics of the parents' residence is justified.

Objective is to determine the risk of congenital malformations in children whose mothers lived in areas with different geochemical characteristics.

Material and methods.

We have analysed 492 protocols of autopcies on newborn infants and fetuses, who died in the uterus or after birth during 2004-2014 in Chernivtsi. The dissections were carried out at the Department of Morbid Anatomy (acting head Hrechko D.I.) in Chernivtsi. The analysis included cases of perinatal, neonatal and infantile losses with congenital malformations ages under 1 year.

The geochemical characterization of the places where the mothers, whose children died, lived, was determined by the results of the study performed by the geological association "Pivnichukrgeology" (1993) and byYu. Fedkovych Chernivtsi National University 1992). The content of heavy metals in the soil was estimated by the integral coefficient of pollution, which was calculated as the sum of the ratio of the content of individual heavy metals to the maximum permissible concentration. Depending on the results from the places, where the mothers, whose children had died, lived, they were referred to as "contaminated with heavy metals" (CHM), or as conditionally "clean" (CFM). The division point was considered to be the values, which went beyond the limits $+2\ \sigma$ from the mean.

Depending on the geochemical characteristics of the places, where the mothers, whose children had died, lived, two groups of observation were formed. The first one (I) included 354 fatal cases, which had happened in the places belonging to the CHM. And the second one (II) -133 cases of death of fetuses and newborns in the families, which lived in the places attributed to the CFM.

The obtained data were analyzed by means of the methods of biostatistics using the principles of clinical epidemiology, the computer packages STATISTICA StatSoft Inc. and Excel XP for Windows on a personal computer using parametric and nonparametric computation methods [8]. The risk of congenital malformations in deceased children was estimated by the odds ratio (OR) and the relative risk (RR) with a 95% confidence interval (95% CI), as well as by the value of the attribute risk (AR) [7].

Results.

It has been established that the largest proportion of children who died during 2004-2014 were born to the families living in places of contamination with heavy metals (CHM). For instance, $86 \pm 1.83\%$ of the fatalities occurred in families living in places where the soil was contamined with heavy metals and only in $14 \pm 3.0\%$ ($P < 0.05$) cases the pregnant women lived in the areas with relatively favourable geochemical situation. The odds ratio of loss of children, whose mothers lived in places of geochemical disadvantage, was 6.1 (95CI 3.7 - 10.04) with a relative risk of this event 37 (95CI 16.9 -83.8) and the attribute risk – 0.61(95CI 3.7 – 10.04) 0.72. For instance there were 25 $\pm$ 2.28% such cases in group I and $20.2 \pm 3.48\%$ in group II ($P>0.05$). Almost half of the deceased children whose mothers lived in contaminated areas were abortive fetuses or those prematurely born. At the same time, the incidence of congenital malformations in these groups of comparison did not coincide in a number of systems (Table 1).

Table 1. Incidence of congenital malformations in children whose mothers lived in the areas with different geochemical conditions

Comparison groups	Number	Incidence of congenital malformations (%)				
		Central nervous system	Gastrointestinal tract	Cardiovascular system	Multiple congenital malformations	Musculoskeletal system
Group I (CHM) *	359	6.1±1.26	2.0±0.74	6.7±1.31	5.6±1.21	3.1±0.91
Group II (CFM) **	133	6.7±2.17	3.7±1.63	3.0±1.47	3.7±1.63	3.0±1.47
P		>0.05	>0.05	<0.05	<0.05	>0.05

* CHM – contamination with heavy metals

** CFM – the soil which is relatively clean from heavy metals

The findings allowed us to believe that the infants from the first group, who died, had more congenital heart defects and multiple congenital malformations than those from the first group, whose mothers lived in conditionally favourable areas. In addition, there were malformations in the development of the respiratory (1.1 ± 0.55%) and urinary (0.6 ± 0.41%) systems in group I, while there were no cases of these CMF in the comparison group. It should be noted though that the odds ratio in the development of congenital heart disease in group I relative to the comparison group was OR = 2.2 (95CI 1.4 - 3.5), and of multiple malformations OR = 1.51 (95CI 0.88-2.6).

It should be noted that congenital heart defects were more common in male ftuses and newborns of group I and the risk of developing such congenital malformations in relation to the second group was 26 (95CI 8.8-76.1) OR = 2.7 (95CI 1.04-7.4).

Table 2 presents the structure of congenital malformations, which led to the loss of children, whose mothers lived in places with different geochemical characteristics.

Table 2. Distribution of the incidence of congenital malformations in different organ systems due to the geochemical characteristics of the habitat

Incidence of congenital malformations in the structure											
Geochemical characteristic of the habitat	Number of children with CMF	Central nervous system		Gastrointestinal tract		Cardiovascular system		Multiple congenital malformations		Musculoskeletal system	
		Abs.	%	Abs.	%	Abs.	%	Abs.	%	Abs.	%
CHM	90	22	24.4	7	7.8	24	27	20	22.2	2	3.5
CFM	27	9	33.3	5	18.5	4	14.8	5	18.5	4	14.8
Pφ		> 0.05		> 0.05		< 0.01		< 0.01		> 0.05	

The structure of congenital malformations in the children whose mothers lived in the areas with different geochemical characteristics coincided with the trends identified in the analysis of the incidence of this pathology in the comparison groups. For instance, the odds ratio of developing congenital heart defects in relation to other malformations in group I was OR = 2.13 (95CI 1.05-4.31), the attribute risk was 0.12, and the risk of multiple congenital malformations in these children in relation to the comparison group reached OR = 1.8 (95CI 1.1-2.8) and the attribute risk 0.14.

Thus, a ten-year analysis of autopsy showed that women with perinatal, neonatal and infant losses, in most cases, lived in places of soil pollution with heavy metals. In this case, the deceased infants had a significant risk of developing heart defects, which was significantly higher in boys. In the structure of the congenital malformations , among the causes of lethality in places of geochemical disadvantage, there was a reliable risk of developing congenital heart defects and multiple congenital malformations.

Conclusions.

1. When pregnant women live in the areas with a chronic exposition to heavy metals the risk of the fetal death and that of newborn infants increases by 6,1 times compared to conditionally clean areas.
2. When mothers live in ecologically unfavourable areas of the city, their children have an increased chance to develop congenital heart defects (OR=2.2(95CI 1.4 – 3.5) and multiple congenital malformations 1.51(95CI 0.88 – 2.6)
3. The peculiarities of the distribution of the incidence of congenital malformations in ecologically unfavorable habitats are: the prevalence of congenital heart defects (OR = 2.13 (95CI 1.05-4.31), multiple congenital heart defects, OR = 1.8 (95CI 1.1-2.8), especially in males (OR = 2.7 (95CI 1.04-7.4).

Prospects of research: to study the influence of soil and air contamination on the onset, development and prognostication of various pathologies in infants.

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