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Comparative Analysis of the Prevalence of Congenital Heart Defects in the East Kazakhstan Region

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At present, the frequency and forms of congenital anomalies including malformations of the heart and blood vessels are poorly understood. More than 400 nuclear explosion tests were conducted at the Semipalatinsk Nuclear Test Site, and significant amounts of radioactive substances were released. In the present study, we researched inborn abnormalities in general and cardiovascular abnormalities in the Republic of Kazakhstan and administrative regions of the East Kazakhstan region among children using the official statistics data. Five years of data from the official statistics on the incidence of congenital abnormalities in the various regions of Kazakhstan were examined. We used indicators of congenital malformations (birth defects), deformations and chromosomal abnormalities, and congenital defects of the heart and circulatory system in children aged 0 to 14 years. These anomalies are classified in International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) as the Q00-99, Q20-28. The average incidence, level of significance (p), and 95% confidence interval were calculated for each area of the Republic of Kazakhstan and 19 settlements in the East Kazakhstan region. The results show a relatively high prevalence of congenital anomalies in the whole country and in the East Kazakhstan region.

Key words: semipalatinsk nuclear test site, East Kazakhstan region, congenital malformations, congenital heart defects

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INTRODUCTION

In most countries, congenital anomalies remain a relevant public health problem, but they are also an important risk factor for child mortality and disability. Studies in Europe and North America have shown that up to a third of all perinatal losses may be due to anatomical defects. In stillborn infants, congenital anomalies are detected in 15-20% of cases. According to the National Center on Birth Defects in the United States each year 10 to 20 million children are born throughout the world with congenital anomalies [1]. Congenital heart defects (CHD) are one of the leading causes of death in infants, so the timely detection of them is important, and hemodynamic instability can determine the quality of children's lives beginning in the neonatal period. CHD is present from birth in definition. The most practical measurement of CHD occurrence is birth prevalence per 1,000 live births [2]. According to the literature [3], the frequency of CHD in infants is an average of 2 to 5 per 1,000. The estimate of 8 per 1,000 live births is accepted as the best approximation generally [4].

The lack of a clear trend towards reducing the number of children born with various malformations, including CHD, highlights the significance of ongoing research on the subject. In the Republic of Kazakhstan, official statistics on infant mortality show that congenital anomalies were present in up to 22.8% of cases, ranking second among all causes [5]. According to the report, the incidence of congenital diseases in Kazakhstan was 4%-6%, including congenital abnormalities at 2.5% [5].

Every year, according to the National Register of Genetics of the Republic of Kazakhstan, from 2,500 to 3,500 children are born in Kazakhstan with congenital and hereditary diseases, constituting a rate ranging from 20.0 to 24.3 per 1,000 live births, and the proportion of congenital malformations among cases of perinatal mortality in a number of ecologically unfavorable regions is highest among conditions associated with perinatal mortality [6]. In 9% of cases of CHD was due to a variety of factors including radiation, viral infections, diseases of the mother during pregnancy, drugs and chemicals, and heavy metals, while only 10% of cases of CHD were caused by chromosomal abnormalities or single gene mutations [3, 7, 8].

It is known, that 468 nuclear tests were performed at the Semipalatinsk Nuclear Test Sites (SNTS) before 1990 caused irreparable damage to human health and the environment and caused an increase in overall morbidity and mortality [9, 10]. About 54% of the area occupied by the nuclear test sites was in East Kazakhstan. The zones of maximum and high radiation risk are recognized to be in the cities Semey, Ust-Kamenogorsk, Kurchatov, Ridder, and in the regions of East Kazakhstan: Borodulichinsky, Zharminsky, Ayagozky, Glubokovsky, Shemonaikhinsky, and Ulansky areas [11], but no analysis of the incidence of congenital anomalies, depending on the degree of remoteness from the test site has been recently published. At the same time the highest levels of disease were recorded in the Akmola region at 783.6 cases per 100,000 populations, the South Kazakhstan region - at 967.4, the Zhambyl region - at 707.0, and in Almaty city - at 788.1. Until now, the frequency of congenital abnormalities have not been fully studied, including malformations of the heart and blood vessels, and their prevalence among the causes of infant mortality in Semey and East Kazakhstan has not been established. Also, the impact of various exogenous and endogenous circumstances, the long term consequences of the activites at the SNTS twenty five years after the test site was closed, the risk of having a baby with a congenital anomaly have been important today.

The aim of this study was to determine the incidence of congenital malformations and CHD in Kazakhstan and in the East Kazakhstan region among children aged 0 to 14 years.

MATERIALS AND METHODS

The prevalence rates of congenital anomalies and of CHD were studied in the Republic of Kazakhstan (16 regions) and all the cities and regions of the East Kazakhstan region. The standard WHO definition was used (2015): "Congenital anomaly - a persistent morphological changes in the body of the organ or a large part of the body, appearing most often in utero, is outside the normal variations of the structure and violates its function" [12]. The study is based on official statistical data reported on patient’s chart number 12 of the Ministry of Health of the Republic of Kazakhstan on the prevalence of congenital anomalies and congenital anomalies of the circulatory system in children over a 6-year period (2007-2012) [13]. Also, data from the statistical compilation titled "Health of the Republic of Kazakhstan and activities of the healthcare organizations" for the period 2007-2012 were used [5]. The study included congenital malformations, deformations and chromosomal abnormalities in children aged 0-14 years, which are classified according to ICD-10 as - Q00-Q99, as well as congenital heart disease and diseases of circulatory system in children aged 0 to 14 years, classified in accordance with the ICD-10 as - Q20-Q28.

Statistical analysis of the material was carried out using the software package SPSS, version 17.0. (SPSS Inc., Chicago, IL, USA). The average annual incidence for the period was used to rank the regions and administrative units of the East Kazakhstan region from the minimum to maximum incidence. Regression analysis was used to determine the upward (positive) or descending (reverse) trend, i.e. the increase or decrease of the incidence over the study period. Results were presented as arithmetic means of the average levels of morbidity (non-standard coefficients (B) with 95% confidence intervals (CI). Also, the value of the level of importance of each factor was given. Given that the same administrative unit did not participate in the comparison more than once, the Bonferroni correction for multiple comparisons was not performed.

These studies were approved by the Ethics Committee of the Semey State Medical University (No. 2. 11.13.2013).

RESULTS

The highest incidences of congenital anomalies over the study period were observed in the Zhambyl, South Kazakhstan, North Kazakhstan, Akmola and Mangistau regions. The East Kazakhstan region, where most of the SNTS was located, had a long-term average incidence almost three times lower than the national average and six times lower than the Zhambyl region, where the incidence rate in this period was the highest in Kazakhstan (Table 1).

Moreover, the incidence of congenital anomalies in the East Kazakhstan region had a tendency to decrease, although this tendency did not reach statistical significance. It is interesting to note that none of the administrative units of the republic showed statistically significant trends in reducing the incidence of congenital anomalies. In addition, the South Kazakhstan, Pavlodar, Kostanay and Karaganda regions showed statistically significant increases in incidence over the study period, which resulted in an increase in incidence at the national level by an average of 56.7 (95% CI: 34.4-79.0) cases per 100,000 populations. However, the significant increase in the reported incidence was probably due to the improved diagnosis of congenital anomalies, and was not the result of a true increase in incidence. The differences between the incidence of the region ranked first and that ranked last was eigt-fold, which is an unlikely result.

In the territory of East Kazakhstan, the highest incidence rates of congenital abnormalities have been reported in the cities of Ridder, Kurchatov, and Ust-Kamenogorsk, and in the Glubokoe and Zharma areas. All of these areas have an average annual incidence above average for the area, which suggests the negative impact of the landfill. At the same time, in some rural areas assigned to the zone of maximum and increased risk, the incidence was significantly lower, which, however, may be due in part to the lower diagnostic capabilities in these areas (Table 2).

Marked and statistically significant reductions in incidence have been reported in the cities of Ridder and Kurchatov. At the same time, the Zharma region showed an increase in incidence. Considering that opposing trends recorded in ecologically unfavorable surrounding areas, we believe that the identified trends can be regarded as the result of random variation or regression to the mean.

The highest incidences of congenital anomalies of the circulatory system over the study period were observed in the Akmola, Almaty, South Kazakhstan, Pavlodar and Mangistau regions. The East Kazakhstan region, where SNTS is located, had a long-term average incidence almost 2 times lower than the national average and 3.5 times lower than the Akmola region, where the incidence rate in this period was the highest in Kazakhstan (Table 3).

Moreover, the incidence of congenital anomalies of the circulatory system in the East Kazakhstan region showed a statistically significant downward trend on average of 54.6 (95% CI: 21.5-87.7) per 100,000 populations. Statistically significant reductions in incidence were observed in the Atyrau, West Kazakhstan, Aktobe, Kyzylorda, Mangystau, South Kazakhstan, and Zhambyl regions, as well as

Table 1. The incidence of congenital anomalies in Kazakhstan by region. 2007 to 2012

Region. city	Long-term average annual value	Coefficient	95 % CI		p
Atyrau	309.7	20.0	-47.4	87.5	0.457
West Kazakhstan	364.6	162.0	-63.7	31.3	0.397
Karaganda	380.1	38.0	12.5	63.4	0.014
East Kazakhstan	394.9	-10.7	-33.8	12.3	0.266
Almaty	485.5	-44.9	-108.1	18.3	0.120
Aktobe	572.8	-10.6	-32.4	11.1	0.247
Kyzyl-Orda	628.9	23.3	-54.3	7.6	0.105
Astana	636.7	13.5	-64.7	91.8	0.656
Kostanai	734.8	167.5	104	231.1	0.002
The Republic of Kazakhstan	1040.8	56.7	34.4	79.0	0.002
Pavlodar	1081.9	169.2	95.2	243.3	0.003
Almaty	1163.7	116.5	-88.9	322.0	0.191
Mangistau	1352.3	237.1	-25.5	499.8	0.066
Akmola	1566.2	-41.3	-175.3	92.5	0.439
North Kazakhstan	1771.1	55.2	-347.8	458.2	0.723
South Kazakhstan	1855.0	101.0	22.1	179.9	0.024
Zhambyl	2403.4	69.0	-78.7	216.7	0.264

Table 2. The incidence of congenital anomalies in the East Kazakhstan by region. 2007 to 2012

District. city	Long-term average annual value	Coefficient	95% CI		p
Tarbagatai	152.6	16.8	-4.6	38.4	0.095
Kurchum	179.3	17.7	-40.8	76.2	0.449
Ayagoz	186.9	17.4	-20.0	54.9	0.265
Cato-Karagay	189.0	3.1	-47.1	53.3	0.872
Kokpekty	198.2	10.4	-44.7	65.6	0.627
Zaysan	206.9	10.3	-9.9	30.6	0.231
Urjar	237.5	46.0	-20.4	112.5	0.127
Ziryanovsk	240.7	20.2	-40.9	81.5	0.418
Ulan	241.7	27.1	-62.8	117.2	0.449
Boroschlihinsk	270.0	13.5	-20.8	47.9	0.336
Semey	296.3	-17.1	-63.2	28.8	0.359
Shemonaikha	308.0	-0.5	-11.7	10.6	0.901
Beskaragai	316.1	14.6	-37.1	66.3	0.477
May	320.6	16.8	-43.9	77.6	0.484
Zharma	337.2	70.1	23.7	116.4	0.014
Kurchatov	341.9	-128.6	-232.4	-24.9	0.026
Glubokovoe	352.6	61.5	-215.3	92.1	0.328
Ust- Kamenogorsk	493.7	25.4	-32.9	83.9	0.293
Ridder	968.9	-304.1	-469.0	-139.2	0.007

Table 3. The incidence of congenital anomalies of the circulatory system in Kazakhstan. 2007 to 2012

Region, city	Long-term average annual value	Coefficient	95% CI		p
Almaty	125.5	0.62	-26.6	27.9	0.064
Atyrau	129.4	-40.5	-80.0	-1.03	0.046
Karaganda	176.8	-47.6	-95.5	-0.32	0.051
East Kazakhstan	213.6	-54.6	-87.7	-21.5	0.010
West Kazakhstan	236.9	-52.0	836.0	-20.5	0.010
Aktobe	247.9	-61.7	-96.4	-27.0	0.008
Kyzylorda	277.2	-59.7	1 14.1	-5.25	0.038
North Kazakhstan	328.7	94.4	-295.2	106.2	0.261
Astana	330.4	-113.9	-178.1	-49.7	0.008
Mangistau	388.4	-123.6	-166.0	-81.3	0.001
The Republic of Kazakhstan	416.3	-71.9	-117.2	-26.6	0.012
Kostanay	431.8	82.5	29.7	135.2	0.012
Zhambyl	571.3	-205.7	-344.5	-67.0	0.015
South Kazakhstan	606.6	-76.6	-151.4	-1.97	0.046
Pavlodar	617.5	18.7	-13.1	50.6	0.078
Almaty	679.7	-139.7	-262.4	-17.1	0.034
Akmola	773.8	-48.4	-194.5	97.7	0.410

Table 4. The incidence of congenital anomalies of the circulatory system in the East Kazakhstan region. 2007 to 2012

District. city	Long-term average annual value	Coefficient	95 % CI		p
Caton-Karagay	44.0	-0.4	-8.9	7.5	0.879
Ayagoz	44.2	6.7	-4.0	17.5	0.159
Beskaragai	49.0	-4.8	-18.1	8.4	0.372
Shemonaikha	54.0	-5.2	-23.4	12.8	0.464
Kurchum	58.1	-3.9	-17.9	9.9	0.471
Ulan	68.8	20.3	-12.0	52.8	0.156
Kokpekty	73.4	6.0	-25.8	37.9	0.624
Urjar	75.0	20.0	-7.9	48.1	0.118
May	78.6	-8.1	-32.6	16.4	0.409
Tarbagatai	79.9	2.8	-5.9	11.7	0.400
Boroduliha	83.2	12.0	-15.4	39.5	0.291
Ziryanovsk	83.9	3.0	-25.1	31.1	0.782
Zaysan	87.1	3.3	-11.0	17.7	0.552
Semey	88.0	2.6	-7.0	12.3	0.493
Zharma	88.6	17.4	1.1	33.7	0.041
Glubokoe	89.4	2.4	-1.6	6.5	0.170
Ridder	90.7	-3.1	-19.1	12.8	0.614
Ust-Kamenogorsk	15.9	0.2	-22.8	23.2	0.982
Kurchatov	188.2	-71.7	-127.1	-16.3	0.023

in the cities of Astana and Almaty. The only region where an increase was recorded during the period was Kostanay. At the national level a downward trend in congenital anomalies and diseases of the circulatory system was also registered (Table 3).

The highest rates of incidence of anomalies of the circulatory system over the study period in the East Kazakhstan region were registered in the cities of Kurchatov, Ridder, Ust-Kamenogorsk, Semey and districts of Zharma, Glubokoe, i.e. in ecologically disadvantaged areas that are experiencing the most serious consequences of the SNTS activities. None of the administrative and territorial indicators of East Kazakhstan showed statistically significant changes in the dynamics of the incidence of abnormalities of the circulatory system (Table 4).

DISCUSSION

The results of our study show that the consequences of the activities of the Republic of Kazakhstan SNTS currently play a minor role. Regions with the maximum levels of morbidity due to congenital anomalies in general and to anomalies of the circulatory system are in opposite parts of the country, while the East Kazakhstan region has one of the lowest morbility rates in Kazakhstan. Moreover, this situation is unlikely to be related to the features and capabilities of diagnosis, as in East Kazakhstan, diagnostic medical staff has a pronounced wariness related to birth defects because of the ecological trouble the region.

At the same time at the regional level, the degree of influence of the impacts of the landfill is much more significant. The highest long-term incidence rates were recorded in urban and rural areas in this region and these areas also showed an increased maximum radiation risk. This variability in incidence can hardly be explained by varying diagnostic capabilities.

The results of the environmental study should be interpreted with caution, and the main features of the design of environmental studies should be taken into account. We used official statistics as our data, and thus the quality of our results depends on the quality of the reporting documentation. In addition, no information on the radiation levels in the study area was available, which made it impossible to analyze the link between radiation and congenital anomalies. On the other hand, this relationship is not in doubt, and the purpose of our study was to investigate the effects of the activity at the landfill on the incidence of congenital anomalies decades after the closure of the landfill. Another drawback of this study is our dependence on the reporting format adopted in the Republic of Kazakhstan; namely, the incidence was reported in children ranging in age from 0 to 14 years, which makes it impossible to compare the data with the results of most of the foreign and Russian studies [7, 14], which focused on the perinatal prevalence of congenital anomalies and twenty-eight percent of all major congenital anomalies consist of heart defects [15].

A report about prevalence rates of CHD in newborns varied widely and depends to some extent, lesion inclusion and exclusion criteria [16]. Different methods as certainment (e.g., physical examination, echocardiography, and registry data) yield varying prevalence rates of CHD in infancy [17]. However, we did not find studies about prevalence among the regions of one country.

Nevertheless, we did not set an aim to compare our results with those of other countries, and the different regions of Kazakhstan and East Kazakhstan shared the reporting format, which allowed; us to make comparisons within Kazakhstan, though these were not necessarily very informative.

CONCLUSION AND IMPLICATIONS

It should be noted that, despite the long-term activity at SNTS, three decades after it closed, the East Kazakhstan region recorded one of the lowest incidence of congenital anomalies. This suggests that the landfill activity played only a minor role in the relative risk of congenital anomalies in comparison with other risk factors all over Kazakhstan. At the same time, the data strongly suggest that within the East Kazakhstan region, even decades after the closure of the landfill, the highest incidence of morbilities is still observed in the territories of maximum radiation risk.

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