

DYNAMICS OF FREQUENCY AND PECULIARITIES OF THE STRUCTURE OF CONGENITAL MALFORMATIONS IN SOUTH UKRAINE (MONITORING STUDY)

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Background. In Ukraine, the unfavorable demographic situation makes monitoring of the birth rate of children with congenital malformations urgent issue to identify regional features of epidemiology and develop methods for prenatal diagnosis and prognosis.

Objective. Objective of this study is to characterize the frequency dynamics, to identify structural features of congenital malformations of newborns in Kherson region over a 20-year period (2000-2019) and to compare the prevalence of various nosological forms of malformations in the region, in Ukraine and in European countries.

Methods. Research methods: epidemiological, medical-statistical.

Results. In Kherson region, the average frequency of congenital malformations over the past 20 years is: for newborns – $31.57 \pm 1.25\%$; for live births – $31.38 \pm 1.11\%$; for stillborns – 197.7 ± 0.65 per 10,000. In the structure of defects, cardiovascular malformations are leading (31.77%), musculoskeletal malformations (25.14%), genital malformations (17.5%). Increased prevalence of developmental anomalies in the region is mainly associated with an increase in the frequency of model malformations recorded by EUROCAT ($r=0.69$, $p<0.05$). The increase in the total frequency of congenital malformations is caused by increased number of births of children with cardiovascular defects (by 4.67‰), genital defects (by 1.21‰), other congenital malformations (by 1.55‰), multiple malformations (by 0.37‰).

Conclusion. Monitoring results showed an increase in congenital malformations incidence in Kherson region over a 20-year period by 7.94‰ possibly caused by population decline due to negative natural and mechanical growth. The prevalence of hereditary defects is at the same level. The frequency of some nosological forms significantly exceeds in the region compare to that in Ukraine and Europe: cardiovascular defects – in 1.5 times, genital malformations – in nearly 3 times, musculoskeletal defects – almost twice.

KEYWORDS: congenital malformations; chromosomal pathology; population; newborns.

Introduction

An unfavorable demographic situation in Ukraine (decrease in birth rate, high mortality and disability, negative natural population growth) necessitates monitoring of the genetic load of human populations, which averages 50-70 per 1000 newborns (5-7%): congenital malformations account for 2-5%, hereditary diseases – 1.5% (chromosomal – 0.5%, genetic – 1%), diseases with a significant hereditary predisposition – 3-3.5% [1]. Monitoring the birth rate of children with congenital malformations is necessary for identifying the epidemiology of its various nosological forms and for development of methods for prenatal diagnosis and prognosis [2]. According to current concepts, congenital malformations are defects in morphogenesis in the early period of fetal life of genetic and/or epigenetic etiology [3].

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The spectrum of mutations in genes that control the form-developing processes in embryogenesis may be ethno specific. Therefore, during monitoring of the prevalence and structure of malformations, the influence of ethnic factors should be taken into account, as well as not only epidemiological, but also genetic and demographic aspects [4,5].

Thus, the aim of the study was to define the dynamics of frequency, to identify the structural features of congenital malformations of newborns in Kherson region over a 20-year period (2000-2019) and to compare the prevalence of various nosological forms of congenital malformations in the region, Ukraine and European countries.

Methods

The study was conducted in Kherson region, covering all 18 territorial-administrative regions. For the analysis, the 20-year observation period (2000-2019) was divided into five-year

periods (2000-2004, 2005-2009, 2010-2014, 2015-2019).

The objects of the study were newborns (live and stillborn) with isolated and multiple congenital malformations, which were born to residents of Kherson region during the study period. The obtained material was analyzed using the registration of all forms of malformations included in the list of ICD-10 of section Q in order to assess their frequency and structure.

When conducting a comparative analysis of the incidence of malformations in populations, it is necessary to take into account standard markers – those forms of them that are often encountered and are unambiguously diagnosed by doctors of all specialties in one age cohort. Such forms have a well-defined phenotype and are well diagnosed at birth. These are: multiple congenital malformations and compulsory model defects (Q00-Q99). Long-term monitoring of populations for such markers makes it possible to assess the prevalence and dynamics of malformations and conduct their comparative analysis in populations, which is one of the tasks of the European international register EUROCAT (European surveillance of congenital anomalies).

Since the number of abortions is not large enough to have a significant impact on the prevalence of defects, calculations for this indicator were carried out in a cohort of newborn children. Most cases of malformations among all pregnancies occur in children born alive; therefore, it is the assessment of the dynamics of their prevalence in this cohort, and not all births, that is the most acceptable form of analysis of epidemiological data [6].

The prevalence of malformations was calculated as the ratio of the number of newborns with congenital malformations to the total number of newborns multiplied by 1000 (‰). Similar calculations were carried out in cohorts of live and stillborn children. The data for a comparative analysis of the frequencies of congenital malformations were taken from the open official website of the European register of the international organization EUROCAT [<http://www.eurocat-network.eu>].

The theoretical indicator of the number of hereditary congenital malformations was calculated as the sum of cases of chromosomal pathology of living children and half of the remaining part of congenital malformations (without chromosomal diseases), since it is established that about half of cases of congenital

malformations (regardless of clinical manifestation) are caused by genetic factors [7].

Statistical processing of the research results was carried out using MS Excel: determining of the average value, error of the average value, growth rate. Using the Statistica 6.0 software package, the statistical connection of features was determined by the Spearman rank correlation method.

Results

In total, in 2000-2019, 222,191 newborn babies were born in Kherson region; 220,067 of them were live-born and 2,124 still-born. Congenital malformations were found in 7015 newborns, including 6973 live births and 42 stillborns. The obtained data allowed estimating the population frequency of congenital malformations in children of Kherson region, which is: for newborns – $31.57 \pm 1.25\%$; for live births – $31.38 \pm 1.11\%$; for stillbirths – 197.7 ± 0.65 per 10,000. Based on the data of the Regional Department of Statistics in Kherson region, the average annual number of live births in the region for the last 20 years has been calculated, which is 11,003 children (with an average statistical deviation of up to 5%).

Theoretical calculations of the prevalence of congenital malformations in the region show that approximately 556 newborns (5%) may be born with signs of congenital pathology. Since the contribution of the genetic component to the structure of malformations is on average about 50% (the other half is a consequence of teratogenesis) [8], thus for Kherson region the hereditary component of malformations is expected at the level of 278 people per year (2.5% of the number of newborns). Actual calculations of the prevalence of congenital malformations are presented in Table 1.

According to Table 1, with the decrease in the birth rate in the region, the prevalence of congenital malformations is rising (from 20.6‰ in 2004 to 37.6‰ in 2017) and on average over a 20-year period was 31.4‰. Among all congenital malformations, the actual number of cases of hereditary forms (181 people per year) turned out to be lower than the theoretically calculated indicator (278 people per year); it did not undergo significant changes in recent years and averaged within 52% of all anomalies; this testifies the stable level of mutation process in the region. But in a long-time tendency, the share of hereditary forms is gradually increasing: in 2000 it was 1.29%, in 2019 it was 1.62%. There is a gradual increase in the

frequency of multiple malformations: from 0.29 to 0.66‰.

Since the incidence of neonatal malformations and spontaneous miscarriages correlates with their prevalence among live births, we analyzed the dynamics of nosological forms of congenital anomalies in the last cohort (Table 2).

According to Table 2 in the structure of congenital malformations malformations of the cardiovascular system are leading (31.77% of all cases, an average annual increase of 9.1%), the frequency of which is constantly increasing from 5.1 to 9.93‰ on average over the past 20 years. Congenital malformations of the musculoskeletal system (25.14% of all cases, the prevalence slightly decreases from 7.93 to 6.13 and averages 7.35) are the second. Stably high frequency of malformations of the genital organs (on average 5.23‰; in the structure – 17.5% of the total number of cases).

There is a gradual increase in the frequency of multiple malformations – from 0.29 to 0.66‰, and a slight increase in their share in the overall structure of anomalies (by 0.8%). The prevalence of chromosomal abnormalities (1.0-1.17‰) is characterized by relative stability, which confirms the previous assumption about the constancy of the level of the mutation process in the region.

The greatest lethality is caused by defects of the central nervous system (Q00-Q07), in particular anencephaly, multiple congenital malformations (Q89.7) and chromosomal abnormalities (Q90-Q99).

Then a comparative analysis of the prevalence of congenital malformations in Kherson region was carried out regarding Ukraine and European countries (according to the international register EUROCAT) (Table 3). It has been noted that there is a significant increase in the frequency of malformations of the car-

Table 1. Dynamics of congenital malformations prevalence (Kherson region, 2000-2019)

Years	Number of live births	Congenital malformations											
		Total	Frequency, ‰	Genetically determined congenital malformations:							total genetically determined	part, %	
				Q90-Q99	cases of chromosomal pathology				from congenital malformations	from live births			
					Ds	Ps	Es	Ts					
2000	10 184	255	25.0	8	8	-	-	-	131.5	51.6	1.29		
2001	9 757	243	24.9	9	9	-	-	-	126.0	51.9	1.29		
2002	9 972	280	28.1	11	8	-	1	-	145.5	52.0	1.46		
2003	10 502	216	20.9	15	14	-	-	-	115.5	53.5	1.10		
2004	10 363	201	20.6	8	5	-	-	-	104.5	52.0	1.00		
2005	10 150	307	30.2	11	7	1	-	1	159.0	51.8	1.57		
2006	11 475	397	34.6	13	13	-	-	-	205.0	51.6	1.83		
2007	11 570	444	38.4	21	18	3	-	-	232.5	52.4	1.79		
2008	12 473	556	44.6	18	16	1	-	1	287.0	51.6	2.30		
2009	12 323	384	31.2	21	18	1	1	-	202.5	52.7	1.64		
2010	12 388	391	31.6	18	13	-	1	-	204.5	52.3	1.65		
2011	12 085	418	34.6	15	9	1	-	-	216.5	51.8	1.79		
2012	12 643	428	33.8	16	14	-	-	-	222.0	51.9	1.76		
2013	12 300	388	31.5	15	15	-	-	-	201.5	51.9	1.64		
2014	12 308	433	35.2	11	10	-	-	-	222.0	51.3	1.80		
2015	11 372	352	31.0	17	13	-	2	-	184.5	52.4	1.62		
2016	10 769	350	32.5	11	9	-	2	-	180.5	51.6	1.68		
2017	9 964	375	37.6	4	3	-	-	-	189.5	50.5	1.90		
2018	9 095	293	32.2	13	12	-	1	-	153.0	52.2	1.68		
2019	8 374	262	31.3	9	9	-	-	-	135.5	51.7	1.62		
M	11003.4	348.65	31.4	13.2	11.2	0.4	0.4	0.1	180.9	51.9	1.62		
m	281.48	20.15	1.28	1.02	0.9	-	-	-	10.36	0.13	0.065		

Note: Ds – Down syndrome; Ps – Patau syndrome; Es – Edwards syndrome; Ts – Turner syndrome.

Table 2. Dynamics of the frequency and structure of congenital malformations of compulsory registration (Q00-Q99) among live births in Kherson region

Form CM (patient's medical record-10)	Units	Monitoring periods (years)				On average over 20 years	Rank	Average increase rate, %
		2000-2004	2005-2009	2010-2014	2015-2019			
Congenital malformations:								
Nervous system (Q00-Q07)	abs.	7.8	10,6	7,8	7.2	8.35	8	+0.55
	‰	0.77	0,93	0,64	0.73	0.76		+ 0.05
	%	3.40	2,62	2.01	2.34	2.59		- 0.81
Ear, face and neck (Q10-Q18)	abs.	1.8	5.0	5.6	4.4	4.2	11	+ 2.4
	‰	0.18	0.44	0.46	0.44	0.38		+ 0.2
	%	0.78	1.24	1.44	1.43	1.22		+ 0.44
Congenital heart defects (Q20-Q28)	abs.	52.0	130.0	150.6	102.8	108.9	1	+ 56.9
	‰	5.10	11.35	12.27	10.37	9.93		+ 4.67
	%	22.67	32.13	38.83	33.46	31.77		+ 9.1
Respiratory (Q30-Q34)	abs.	4.0	5.2	5.4	3.0	4.4	10	+ 0.4
	‰	0.39	0.45	0.44	0.30	0.40		+ 0.01
	%	1.74	1.29	1.39	0.98	1.35		- 0.39
Cleft lip with or without palate (Q35-Q37)	abs.	10.0	11.8	10.2	9.2	10.3	7	+ 0.3
	‰	0.98	1.03	0.83	0.93	0.94		- 0.04
	%	4.36	2.92	2.63	3.0	3.23		- 1.13
Other congenital malformations of the digestive system (Q38-Q45)	abs.	10.0	19.0	12.4	10.0	12.85	6	+ 2.85
	‰	0.98	1.66	1.01	1.0	1.17		+ 0.18
	%	4.36	4.70	3.20	3.26	3.88		- 0.48
Genital (Q50-Q56)	abs.	41.0	61.4	64.6	62.2	57.3	3	+ 16.3
	‰	4.02	5.36	5.26	6.27	5.23		+ 1.21
	%	17.87	15.18	16.66	20.25	17.50		- 0.37
Limb (Q65-Q79)	abs.	80.8	99.6	81.2	60.8	80.6	2	- 0.2
	‰	7.93	8.70	6.62	6.13	7.35		- 0.58
	%	35.22	24.62	20.94	19.79	25.14		- 10.08
Other congenital malformations (Q80-Q89)	abs.	8.8	34.8	33.8	29.4	26.7	4	+ 17.9
	‰	0.86	3.04	2.75	2.97	2.41		+ 1.55
	%	3.84	8.60	8.72	9.57	7.68		+ 3.84
Multiple malformations (Q89.7)	abs.	3.0	10.6	8.2	7.4	7.3	9	+ 4.3
	‰	0.29	0.93	0.67	0.75	0.66		+ 0.37
	%	1.31	2.62	2.11	2.41	2.11		+ 0.80
Chromosomal abnormalities (Q90-Q99)	abs.	10.2	16.6	14.0	10.8	12.9	5	+ 2.7
	‰	1.0	1.43	1.18	1.08	1.17		+ 0.17
	%	4.45	4.10	3.61	3.52	3.92		- 0.53
of which Down syndrome (Q90)	abs.	8.8	14.4	12.2	9.2	11.15	-	+ 2.35
	‰	0.90	1.26	0.99	0.93	1.02		+ 0.12
	%	90.2	86.7	72.7	85.2	83.7		- 6.5
on average per year (Q00-Q99)	abs.	229.4	404.6	393.8	307.2	333.8	-	+ 104.4
	‰	22.51	35.33	31.60	31.0	30.11		+ 7.6
	%	100.0	100.0	100.0	100.0	100.0		
Other congenital malformations	abs.	9.0	17.2	25.8	23.6	18.9	4	+ 9.9
	‰	0.88	1.50	2.10	2.38	1.72		+ 0.84
	%	3.67	4.08	6.24	7.13	5.28		+ 1.61
In total all congenital malformations	abs.	238.4	421.8	419.6	330.8	352.7	-	+ 114.3
	‰	24.06	36.83	33.70	33.36	32.0		+ 7.94

Note: abs. – the number of cases of birth of a child with congenital malformation of this nosology over 5 years (monitoring period) on average

Table 3. Dynamics of the frequency of various nosological forms of congenital malformations among live births [https://eu-rd-platform.jrc.ec.europa.eu/eurocat/eurocat-data/prevalence_en]

Nosological form of congenital malformations	Kherson region. ‰		Ukraine. ‰		EUROCAT. ‰	
	Years:					
	2001-2005	2013-2017	2001-2005	2013-2017	2001-2005	2013-2017
nervous system	0.87	0.93	1.006 (0.657-1.475)	1.85 (1.615-2.111)	1.274 (1.232-1.317)	1.162 (1.126-1.199)
ear, face and neck	0.24	0.41	1.277 (0.879-1.794)	0.126 (0.07-0.207)	0.458 (0.433-0.484)	0.157 (0.144-0.171)
congenital heart defects	5.86	10.48	7.20 (6.203-8.311)	7.878 (7.383-8.398)	7.473 (7.371-7.576)	6.96 (6.872-7.050)
respiratory	0.38	0.35	0.039 (0.00-0.219)	0.117 (0.064-0.197)	0.261 (0.243-0.281)	0.334 (0.315-0.354)
cleft lip with or without palate	1.00	0.97	1.161 (0.783-1.658)	0.804 (0.651-0.981)	0.854 (0.820-0.889)	0.726 (0.697-0.755)
digestive system	1.00	0.85	1.084 (0.720-1.566)	1.348 (1.148-1.573)	1.627 (1.579-1.675)	1.558 (1.516-1.601)
genital	3.81	6.12	0.735 (0.443-1.149)	2.369 (2.102-2.662)	2.090 (2.036-2.145)	2.108 (2.059-2.157)
limb	7.74	6.51	4.103 (3.360-4.962)	4.638 (4.260-5.041)	4.781 (4.699-4.863)	3.691 (3.627-3.757)
including poly-dactyly	1.09	1.15	1.123 (0.752-1.612)	1.407 (1.202-1.636)	0.859 (0.825-0.894)	0.915 (0.883-0.948)
chromosomal abnormalities	1.05	0.97	1.123 (0.752-1.612)	1.591 (1.373-1.834)	1.767 (1.717-1.817)	1.689 (1.646-1.733)
teratogenic syndromes with malformations	0.50	0.85	0.426 (0.212-0.762)	0.553 (0.427-0.703)	0.105 (0.093-0.118)	0.109 (0.098-0.12)
Total	24.75	31.4	17.109 (15.55-18.27)	22.061 (21.227-22.920)	22.740 (22.562-22.920)	20.520 (20.368-20.674)

diovascular system of children born alive (from 5.86‰ in 2001-2005 to 10.48‰ in 2013-2017) among the populations of Kherson region. Moreover, these indicators are significantly higher than the prevalence of this nosological form in Ukraine (7.2 and 7.88 respectively) and in European countries (7.47 and 6.96‰ respectively). A similar trend is observed in the dynamics of the frequency of congenital malformations of the genital organs: an increase in the average annual indicator in Kherson region from 3.81 to 6.12‰ (in Ukraine – from 0.74 to 2.37‰), although in European countries this indicator has stabilized at the level of 2.09-2.11‰.

Discussion

Among all developmental anomalies the frequency of model forms and multiple defects is a sign that largely reflects the intensity of the mutation process in populations. Genetic factors and the mutational component (of at least 40%) largely contributes to the etiology of multiple congenital malformations [9].

The prevalence of malformations in the populations of Kherson region is inversely correlated with the prevalence of spontaneous abortions ($r = -0.52 \pm 0.12$; $tr = 2.4 > t_{05} = 2.12$), which indicates the “sifting” effect of natural selection that eliminates nonviable genotypes in the embryonic period of ontogenesis [10].

The increase in the prevalence of developmental anomalies in the region is mainly due to the increase in the frequency of model malformations recorded by the EUROCAT ($r=0.69$, $p<0.05$). Fetal malformations that can affect the development of intrauterine and infant mortality and lead to human disability are called model congenital malformations or strict accounting malformations. They are highlighted by the EUROCAT for greater objectivity of research.

The prevalence of chromosomal abnormalities (1.0-1.17‰) is characterized by relative stability, which confirms the previously stated assumption about the constancy of the level of the mutation process in the region. Among the nosological forms of chromosomal defects the

largest specific weight is of Down syndrome (83.7%) and a frequency of 0.9-1.02‰.

The frequency of malformations of the musculoskeletal system in Kherson region is 6.51-7.74‰ (in Ukraine and Europe 4.1-4.64‰ and 4.1-3.37‰, respectively). In addition, an alarming trend was revealed of increased prevalence of multiple congenital malformations (from 0.5‰ to 0.85‰); their frequency significantly exceeds these indicators not only in Ukraine (0.43-0.55 ‰) but also in European countries (0.069-0.109 ‰).

The cluster of nosological forms of defects with a stable prevalence in Kherson region, which does not exceed the corresponding figure in Ukraine and European countries, should include malformations of the nervous system, congenital malformations of the face, neck, ears, cleft, lip and palate, other malformations of the digestive system, polydactyly (1.09‰ in 2001-2005 and 1.15‰ in 2013-2017; in Ukraine – 1.12 and 1.41‰; in European countries – 0.86 and 0.92‰, respectively), chromosomal abnormalities (in Kherson region – 1.05‰ and 0.97‰; in Ukraine – 1.12 and 1.59‰; in European countries – 1.77 and 1.69‰ respectively).

The prevalence of malformations of the respiratory system in Kherson region (0.38‰ in 2001-2005 and 0.35 ‰ in 2013-2017, respectively) significantly exceeds this level in Ukraine for the same period (0.04‰ and 0.12‰, respectively) and is at the level of prevalence in European countries (0.26‰ and 0.33‰, respectively).

Conclusion

The frequency of congenital malformations in Kherson region over the past 20 years is: for

newborns – 31.57 ± 1.25 ‰; for live births – 31.38 ± 1.11 ‰; for stillbirths – 197.7 ± 0.65 per 10.000. The increase in the prevalence of congenital malformations in the region is mainly due to an increase in the frequency of model malformations which are subject to mandatory registration by the EUROCAT system ($r=0.69$, $p<0.05$). In the structure of congenital malformations defects of the cardiovascular system (31.77%), of the musculoskeletal system (25.14%) and of genital organs (17.5%) are leading. The frequency of malformations of the cardiovascular system, genitals and musculoskeletal system, multiple congenital malformations in Kherson region significantly exceeds the prevalence of these nosological forms in Ukraine and European countries. Among hereditarily determined forms the frequency of chromosomal abnormalities (1.0-1.17‰) is characterized by relative stability, which confirms our hypothesis about the constancy of the level of mutation process in the region. Among the nosological forms of chromosomal defects the largest share is for Down syndrome (83.7%) with a frequency of 0.9-1.02. Reducing the burden of congenital anomalies in the population is possible through integration of research in epidemiology, genetic demography and epigenetics.

Conflict of Interests

Author declares no conflict of interest regarding this study.

Acknowledgments

The author expresses sincere gratitude to Svetlana Yevhenievna Onishchenko, a geneticist at Kherson Children's Clinical Hospital, for assistance in collecting primary medical and statistical material.

ДИНАМІКА ЧАСТОТИ ТА ОСОБЛИВОСТІ СТРУКТУРИ ВРОДЖЕНИХ ВАД РОЗВИТКУ НА ПІВДНІ УКРАЇНИ (МОНІТОРИНГОВЕ ДОСЛІДЖЕННЯ)

О. Лановенко

ХЕРСОНСЬКИЙ ДЕРЖАВНИЙ УНІВЕРСИТЕТ. ХЕРСОН. УКРАЇНА

Вступ. В Україні в умовах несприятливої демографічної ситуації актуальним є моніторинг народжуваності дітей з вродженими вадами розвитку для виявлення регіональних особливостей епідеміології та розробки методів пренатальної діагностики та прогнозування.

Мета. Мета дослідження – охарактеризувати динаміку частоти і виявити особливості структури вроджених вад розвитку новонароджених дітей у Херсонській області за 20-річний період (2000-2019 рр.), порівняти поширеність різних нозологічних форм вад розвитку в регіоні, в Україні і в країнах Європи.

Методи. Методи дослідження: епідеміологічний, медико-статистичний.

Отримані результати. У Херсонській області середня популяційна частота вроджених вад розвитку за останні 20 років становить: для новонароджених – $31,57 \pm 1,25\%$; для народжених живими – $31,38 \pm 1,11\%$; для мертвонароджених – $197,7 \pm 0,65$ на 10 000. У структурі провідне місце займають вади розвитку серцево-судинної системи (31,77%), опорно-рухового апарату (25,14%), статевих органів (17,5%). Збільшення поширеності вроджених вад розвитку в регіоні в основному пов'язано зі збільшенням частоти модельних вад, що реєструються EUROCAT ($r=0.69$, $p<0.05$). Підвищення загальної частоти вроджених вад відбувається за рахунок збільшення кількості народжених дітей з вадами серцево-судинної системи (на 4,67%), статевих органів (на 1,21%), інших вад розвитку (на 1,55%), множинних вад (на 0,37%).

Висновки. Результати моніторингу свідчать про зростання поширеності вроджених вад розвитку в Херсонській області за 20-річний період на 7,94%. Причиною такого явища може бути скорочення чисельності населення через негативний природний і механічний приріст. Поширеність спадково обумовлених вад залишається на постійному рівні. У регіоні частота деяких нозологічних форм вад значно перевищує цей показник в Україні і країнах Європи: вад серцево-судинної системи – в 1,5 рази, статевих органів – майже в 3 рази, опорно-рухового апарату – майже в 2 рази.

КЛЮЧОВІ СЛОВА: вроджені вади розвитку; хромосомна патологія; популяція; новонароджені діти.

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References

1. Bochkov NP. Clinical Genetics. 2th ed. Moskva: Geotar-Med; 2001. 448 p. [In Russian].
2. Zhuchenko LA, Letunovskaya AB, Demikova NS. The frequency and dynamics of congenital malformations in children in the Moscow region, according to the register of congenital malformations for the period 2000-2005. Rossiyskiy Vestnik Perinatologii i Pediatrii. 2008;53(2):30-8 [In Russian].
3. Hobbs CA, Chowdhury S, Cleves MA. Genetic epidemiology and nonsyndromic structural birth defects from candidate genes to epigenetic. JAMA Pediatrics. 2014; 168(4):371-77.
DOI: 10.1001/jamapediatrics.2013.4858
4. Lanovenko OG. Dynamics of Congenital Development Disorders Prevalence in Ukrainian Regions and their Structure in Kherson Region. 2018; 12(2):45-2. [In Ukrainian].
DOI: 10.30970/sbi.1202.561
5. Egbe A, Uppu S, Lee S, Stroustrup A, Ho D, Srivastava S. Congenital malformations in the newborn population: a population study and analysis of the effect of sex and prematurity. Pediatrics&Neonatology.2015; 56(1):25-30.
6. Mikitenko DA. Ukraine: regional aspects of the genetic load of congenital and hereditary pathology. Sibirskiy Meditsinskiy Zhurnal. 2013; (3):18-3. [In Russian].
7. Community genetic services in Europe. Report on a survey: WHO. Copenhagen: European Services;1991. No 38. 147 p.
8. Minkov IP. Monitoring of congenital malformations: their prenatal diagnosis, role in pathology in children and ways of prevention. Perinatology and Pediatrics. 2000; (1): 8-3. [In Russian].
9. Lanovenko OG. Differentiation of local and rural populations of the Kherson region for the frequency of growth and development of reproductive costs. Visnyk Vinnyts'koho Natsional'noho Medychnoho Universytetu. 2018; 22(1):10-3. [In Ukrainian].

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