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PREVALENCE AND STRUCTURE OF CONGENITAL MALFORMATIONS IN THE KHERSON REGION

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Abstract. The problem of differentiated prevalence of congenital malformations and reproductive losses in the Ukrainian populations becomes particularly relevant in the context of increasing the influence of adverse environmental, genetic and demographic factors that may affect their gene pool. The frequency and dynamics of congenital abnormalities is a reliable indicator of environmental quality. With the decline in the population of the Kherson region and the decline in the birth rate, the frequency of congenital malformations of newborns increased from 22.3 ± 5.4‰in 2000–2008 years to 40.1 ± 8.2‰in 2009–2017). The overall frequency of congenital malformations increased in almost all districts of the Kherson region (from 20.2 ± 1.4 to 27.6 ± 1.3 ‰), which is most noticeable in the regional center (from 23.1 ± 4.4 to 52, 5 ± 22.0 ‰) and on average 37.8 ± 11.3 ‰ Significant differences in this indicator were found between the rural populations of the region. The most common are circulatory system malformations (28.5‰), then - musculoskeletal system malformations (26.05‰), urinary system malformations (15.25‰), and maxillofacial defects (mainly cleft lip) (9.25‰,, chromosomal abnormalities (3.9‰), defects in the digestive system (3.75‰), defects in the nervous system (3.0‰) in the structure of congenital malformations among newborns. The proportion of multiple malformations in the overall structure of birth defects is 2.27% The study of the dynamics of the structure of congenital malformations showed a rapid and statistically significant increase in the prevalence of circulatory system malformations among newborns (from 23.7‰in the period 2000–2006 to 35.3‰in the period 2007–2015).A promising area of research is to study the causes of differences in the prevalence of congenital malformations among the urban and rural populations, as well as among the rural populations of different regions of the same region.

Key words: population, congenital malformations, medical and genetic monitoring.

Анотація. Проблема диференційної поширеності вроджених вад розвитку і репродуктивних втрат в українських популяціях стає особливо актуальною в контексті посилення впливу несприятливих екологічних, генетичних і демографічних чинників, які можуть впливати на їх генофонд. Частота і динаміка вродженої патології є надійним показником якості навколишнього середовища. В умовах скорочення чисельності населення Херсонської області та зниження коефіцієнта народжуваності частота вроджених вад розвитку новонароджених збільшилася (з 22,3 ± 5,4 ‰ в 2000-2008 роках до 40,1 ± 8,2 ‰ в 2009-2017 роках). Загальна частота вроджених вад розвитку зросла майже в усіх районах Херсонської області (від 20,2 ± 1,4 до 27, 6± 1,3 ‰), що найбільш помітно в регіональному центрі (з 23,1 ± 4,4 до 52, 5 ± 22,0 ‰) та в середньому 37,8 ± 11,3 ‰ Значні відмінності цього показника виявлені між районними популяціями регіону. У структурі вроджених вад розвитку провідне місце займають вади системи кровообігу (28,5‰), далі - вади скелетно-м'язової системи (26,05‰), вади сечової системи (15,25‰), щелепно-лицьові дефекти (в основному ущелина губи) (9,25‰), хромосомні дефекти (3,35‰), дефекти органів травлення (3,75‰), дефекти нервової системи (3,0‰). Частка множинних вад розвитку в загальній структурі вроджених дефектів становить 2,27% Вивчення динаміки структури вроджених вад виявило на швидке та статистично значуще зростання поширеності вад системи кровообігу серед новонароджених (з 23,7‰ в період 2000-2006 рр. до 35,3‰ в період 2007-2015 рр.). Перспективною областю досліджень є вивчення причин відмінностей у поширеності вроджених вад розвитку серед міського і сільського населення, а також серед сільського населення різних районів одного регіону.

Ключові слова: популяція, вроджені вади розвитку, медико-генетичний моніторинг

Анотація. Проблема диференційованої розповсюдженості вроджених вад розвитку і репродуктивних втрат в українських популяціях стає особливо актуальною в контексті посилення впливу несприятливих екологічних, генетичних і демографічних факторів, які можуть впливати на їх генофонд. Частота і динаміка вродженої патології є надійним показником якості середовища. В умовах скорочення чисельності населення Херсонської області і зниження коефіцієнта народжуваності частота вроджених вад розвитку новонароджених збільшилась (з 22,3 ± 5,4 ‰ в 2000-2008 роках до 40,1 ± 8,2 ‰ в 2009-2017 роках). Загальна частота вроджених вад розвитку зросла майже по всіх районах Херсонської області (від 20,2 ± 1,4 до 27,6 ± 1,3 ‰), що найбільше помітно в регіональному центрі (з 23,1 ± 4,4 до 52,5 ± 22,0 ‰) і в середньому 37,8 ± 11,3 ‰. Значні відмінності цього показника виявлені між районами популяції регіону. В структурі вроджених вад розвитку провідне місце займають вади системи кровообігу (28,5%), далі – вади скелетно-м'язової системи (26,0%), вади сечової системи (15,2%), щелепно-лицеві дефекти (в основному розщелина губи) (9,2%), хромосомні дефекти (3,3%), дефекти органів травлення (3,7%), дефекти нервової системи (3,0%). Доля множинних вад розвитку в загальній структурі вроджених дефектів складає 2,27%. Вивчення динаміки структури вроджених вад показало швидке і статистично значиме зростання частоти вад системи кровообігу серед новонароджених (з 23,7% в період 2000-2006 рр. до 35,3 % в період 2007-2015 рр.). Перспективною областю досліджень є вивчення причин відмінностей в розповсюдженості вроджених вад розвитку серед міського і сільського населення, а також серед сільського населення різних районів одного регіону.

Ключевые слова: популяция, врожденные пороки развития, медико-генетический мониторинг.

Introduction. Over the past decades, the increasing technogenic and anthropogenic impact on the biosphere dramatically worsens the ecological situation and environmental pollution products are included in the trophic chain "soil-water-plants-man", increasing the incidence and mortality of the vulnerable part of humanity-children [1].

There is an increase in the number of diseases recognized by the World Health Organization as indicator diseases that characterize the ecological state of the territories. These are congenital malformations, neoplasms, diseases of the endocrine system. In almost all countries of the former USSR, an increase in the frequency of developmental defects has been noted. The study of the genetic foundations of the origin and distribution in the population of the congenital and hereditary pathology, primarily birth defects, chromosomal and widespread gene diseases, continues to be relevant issues. The basis for medical genetic preventive measures aimed at reducing the burden of congenital malformations, chromosomal and genetic diseases is the precise knowledge of their prevalence in the region, taking into account the population-genetic structure of the population, the geographical, ecological and hygienic features of the territory, and the quality of medical care to the population [3, 4]. Frequency and dynamics of congenital pathology is a reliable indicator of the quality of the environment [5].

Monitoring congenital malformations (the system for determining and monitoring prevalence in a population) is the only effective instrument for controlling the level of birth defects and is used to study their etiology [7]. An ideal monitoring system would be the detection of newly occurring mutations in the sex and somatic cells [2]. Practically the ones that are well manifested are systems for monitoring congenital malformations, including "model forms" that are clearly and uniquely diagnosed. His birth of such individuals is essential for the monitoring of mutations in the germ cells, since the appearance of a baby with these abnormalities in clinically healthy parents will mean a mutation that originated de novo [6].

The problem of the differential prevalence of congenital malformations and reproductive losses in Ukrainian populations becomes particularly relevant in the context of increasing the environmental and genetic and demographic factors that can influence their gene pool. The incidence of congenital malformations can be used as an indicator of external mutagenic and teratogenic effects. Among the perspective directions of modern studies of mutational load in human populations, genetic experts consider the exact determination of the frequency of congenital pathology, in particular, "model" developmental defects, spontaneous abortions and stillbirths, as the first priority [4].

The **purpose of this study** was to analyze the prevalence of congenital malformations of hereditary etiology among newborns based on monitoring studies of their dynamics in the Kherson region over an 18-year period (2000-2017) and to determine the general structure of congenital malformations in the region.

Data for study and methods. The study was conducted in accordance with the main criteria of the EUROCAT European Register: 1) conducting research in limited populations (accounting for newborns with developmental abnormalities whose parents live in a given locality); 2) accounting for 19 nosological forms.

When calculating the population frequency of malformations for the city or region of the Kherson region, materials from the regional medical and statistical register were used on the total number of newborns born alive and stillborn children, as well as on the number of cases of spontaneous miscarriages, births of children with developmental disabilities subject to strict registration (medical form 21, 13, 49). The obtained data were processed using standard statistical methods: the calculation of the standard deviation of the error of the mean, the error of the arithmetic average of the characteristic. Statistical calculation of the obtained results (calculation of confidence intervals and the reliability of differences) was carried out using the programs STATISTICA and Microsoft Excel 9-2000.

Results and their interpretation. In the Kherson region, isolated single congenital malformations (97.7%) have the largest share and only 2.3% are multiple, including chromosomal abnormalities. In the conditions of reduction of the population of Kherson oblast and reduction of fertility rate, the frequency of congenital developmental defects among newborns has increased (from 22.3± 5,4 ‰ in 2000-2008 to 40,1 ± 8,2‰ in 2009-2017 (Table 1).

Table 1.

The frequency of congenital malformations among newborns in the Kherson region (2000-2017)

District	Years		
	2000-2008	2009-2017	2000-2017
Belozersky	18,9 ± 4,2	53,3 ± 6,3*	36,3 ± 5,3*
Berislavsky	52,5 ± 12,8*	38,4 ± 6,9	45,2 ± 7,0*
V.Aleksandrovsky	27,1 ± 7,4	23,2 ± 6,0	25,2 ± 4,6
V.Lepetichsky	7,3 ± 1,6	21,5 ± 5,2	14,4 ± 3,0
V.Rogachiksky	13,9 ± 5,3	12,6 ± 3,9	13,3 ± 3,1
Vysokopolsky	22,0 ± 5,6	36,6 ± 5,7	29,2 ± 4,4*
Genichesky	24,0 ± 3,5	11,6 ± 3,3	17,8 ± 2,9
Golopristansky	14,1 ± 3,1	45,6 ± 10,0	29,7 ± 6,9*
Gornostaevsky	10,8 ± 3,6	16,1 ± 5,2	13,4 ± 3,0
Ivanovsky	12,2 ± 4,1	29,5 ± 7,3	20,8 ± 4,3
Kalanchaksky	20,0 ± 5,3	22,3 ± 4,3	21,0 ± 3,4
Kakhovsky	23,0 ± 2,8	28,4 ± 2,3	25,7 ± 1,8
N. Serogosy	8,8 ± 1,3	15,2 ± 5,3	12,0 ± 2,9
Novovorontsovsky	10,7 ± 2,0	15,4 ± 2,2	13,0 ± 1,6
Novotroitsky	18,2 ± 4,2	22,6 ± 4,1	20,4 ± 2,9
Skadovsky	33,2 ± 5,2*	32,3 ± 6,7	32,8 ± 4,7*
Tsyurupinsky	30,6 ± 3,3*	32,6 ± 2,7	31,2 ± 2,1*
Chaplynsky	17,0 ± 2,2	40,0 ± 27,5	28,6 ± 5,9*
Total in the district	**20,2 ± 1,4**	**27,6 ± 1,3**	**23,8 ± 1,4**
City of Kherson	23,1 ± 4,4	52,5 ± 22,0*	37,8 ± 11,3
Total in the region	**22,3 ± 5,4**	**40,1 ± 8,2**	**30,2 ± 6,4**

* The differences are statistically significant at $p < 0.05$

The incidence of congenital malformations in cities is significantly higher ($\chi^1 = 4.02$), and in rural areas of the region - significantly lower ($\chi^1 = 22.5$) compared with the general regional indicator.

The frequency of genetically determined congenital malformations was significantly higher (1.33 ± 0.018‰) than the average in Ukraine (0.99 ± 0.014‰) in the Kherson region for the period 2002-2013 years.

Down syndrome (population frequency 1.08 ± 0.095 ‰) occupies a leading place in their structure, Patau syndrome (0.057 ± 0.018 ‰) comes second, followed by Edwards syndromes (0.028 ± 0.01‰) and Turner (0.020 ± 0.01‰). In the Kherson region, there is a gradual increase in the frequency of genetically

determined malformations of the newborn (χ^2 = 30.1). Such an increase in prevalence in the hereditary birth defects population was due to an increase in the frequency of Down syndrome (from 0.83 to 1.04 ‰) with a maximum also in 2006-2009 (1,375 ‰) and Patau syndrome (from 0.025 ‰ to 0,04 ‰) with the maximum indicator in 2006-2009 - 0,105 ‰.

The overall population prevalence of genetically determined anomalies in newborns was higher in the regional center (3.7 ‰) than in areas of the region (2.34‰). But on average in recent years there has been a statistically significant increase in the frequency of the hereditary pathology of newborns in rural populations of the region (from 1.09 to 1.95), while in the regional center we observed the opposite trend - its gradual decrease (from 3.89‰ to 3,06 ‰).

The overall frequency of congenital malformations increases in almost all areas of the Kherson region (from 20.2 ± 1.4‰ to 27.6 ± 1.3‰), most significantly in the regional center (from 23.1 ± 4.4 to 52,5 ± 22.0‰) and averaged 37.8 ± 11.3‰. Significant differences in this indicator were found between some populations of the region: the overall incidence of congenital malformations is significantly higher in Belozersky (36.3 ± 5.3 ‰), Berislavsky (45.2 ± 7.0), Vysokopolsky (29.2 ± 4.4 ‰), Golopristansky (29.7 ± 6.9 ‰), Skadovsky (32.8 ± 4.7 ‰), Tsyurupinsky (31.2 ± 2.1 ‰), Chaplynsky (28.6 ± 5.9‰) districts. On the contrary, the incidence of congenital malformations among newborns is significantly lower in the Velikolektiichsky, V.Rogachiksky, Genichesky, Gornostaevsky, N. Serogosy, Novovorontsovsky districts (12.0-17.8‰). We have identified areas of the region in which the prevalence of chromosomal pathology is statistically significantly higher than the regional average level over the past five years: Berislav district (4.05 per 1000 newborns), Skadovsky (3.1‰), Genichesky (2.64‰).

The most common are circulatory system malformations (28.5%), then - musculoskeletal system malformations (26.05%), urinary system malformations (15.25%), and maxillofacial defects (mainly cleft lip) (4.25%)„ chromosomal abnormalities (3.35%), defects in the digestive system (3.75%), defects in the nervous system (3.0%) in the structure of congenital malformations among newborns (Fig.1).

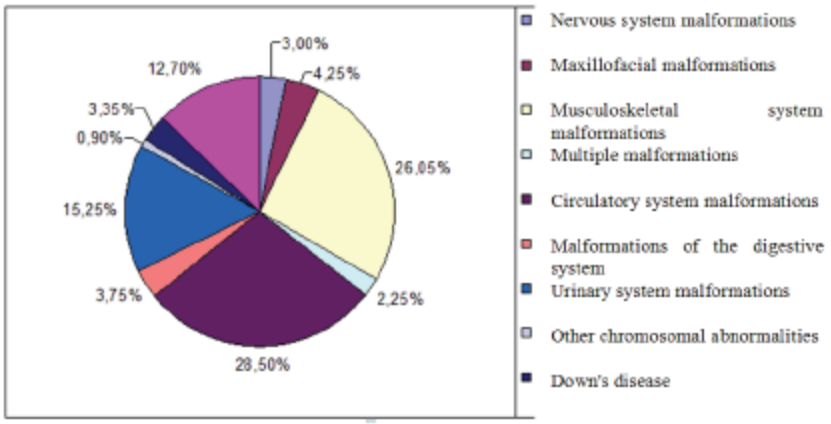

Fig.1. Structure of congenital malformations of strict accounting (model forms) in the Kherson region (2000-2015).

The proportion of multiple malformations in the overall structure of congenital malformations is 2.27%. In the group of defects with multiple lesions of systems and organs, the proportion of cases with chromosomal pathology and syndromes of other etiology is almost the same - 8.0% and 9.1%.

In recent years, we have established a rapid and statistically significant increase in the incidence of congenital malformations of the circulatory system among all other nosological groups (from 23.7 % for the period 2000-2006 to 35.3% for the period 2007-2015). We noted a slight decrease in the frequency of gastrointestinal malformations (from 3.75% to 3.6 %), defects of the nervous system (from 3.0 ‰ to 2.4 ‰). The frequency of malformations in the development of the urinary organs has remained at the same level (15.5-15.0 %). A particular concern is the increase in prevalence in populations of congenital malformations caused

by chromosomal aberrations (from 4.2 to 5.3 ‰) and multiple developmental malformations (from 2.1 to 3.4 ‰) with a significant hereditary component.

Conclusions and future perspectives. Frequency and dynamics of congenital pathology is a reliable indicator of the quality of the environment. In the conditions of reduction of the population of Kherson oblast and reduction of fertility rate, the frequency of congenital developmental defects among newborns has increased (from 22.3± 5,4 ‰ in 2000-2008 to 40,1 ± 8,2‰ in 2009-2017. The incidence of congenital malformations in cities is significantly higher ($\chi^2 = 4.02$), and in rural areas of the region - significantly lower ($\chi^2 = 22.5$) compared with the general regional indicator.

The overall population prevalence of genetically determined anomalies in newborns was higher in the regional center (3.7 ‰) than in areas of the region (2.34‰). But on average in recent years there has been a statistically significant increase in the frequency of the hereditary pathology of newborns in rural populations of the region (from 1.09 to 1.95), while in the regional center we observed the opposite trend - its gradual decrease (from 3.89‰ to 3.06 ‰).

The overall frequency of congenital malformations increases in almost all areas of the Kherson region (from 20.2 ± 1.4‰ to 27.6 ± 1.3‰), most significantly in the regional center (from 23.1 ± 4.4 to 52,5 ± 22.0‰) and averaged 37.8 ± 11.3‰. Significant differences in this indicator were found between some populations of the region. Indicators of the frequency of congenital malformations can be used to assess the possible genetic consequences of their prevalence for the population.

The most common are circulatory system malformations (28.5%), then - musculoskeletal system malformations (26.05%), urinary system malformations (15.25%), and maxillofacial defects (mainly cleft lip) (4.25%)„ chromosomal abnormalities (3.35%), defects in the digestive system (3.75%), defects in the nervous system (3.0%) in the structure of congenital malformations among newborns. The proportion of multiple malformations in the overall structure of congenital malformations is 2.27%. In the structure of "model" malformations, the most common is hypospadias (frequency 1.9 ‰), polydactyly (1.3‰), Down's disease (1.1‰). There is a very low prevalence in the populations of the Kherson region of anencephaly (0.03‰) and malformations of the central nervous system.

A particular concern is the increase in prevalence in populations of congenital malformations caused by chromosomal aberrations (from 4.2 to 5.3 ‰) and multiple developmental malformations (from 2.1 to 3.4 ‰) with a significant hereditary component. The study of the dynamics of the structure of congenital malformations showed a rapid and statistically significant increase in the prevalence of circulatory system malformations among newborns (from 23.7% in the period 2000–2006 to 35.3% in the period 2007–2015).

A promising area of research is to study the causes of differences in the prevalence of congenital malformations among the urban and rural populations, as well as among the rural populations of different regions of the same region.

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