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MULTIPLE CONGENITAL ANOMALIES: EPIDEMIOLOGY AND A CLINICAL ANALYSIS

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МНОЖИННІ УРОДЖЕНІ АНОМАЛІЇ: ЕПІДЕМІОЛОГІЯ ТА КЛІНІЧНИЙ АНАЛІЗ

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РЕЗЮМЕ

Метою роботи було вивчення епідеміологічних показників множинних аномалій в новонароджених та плодів Чернівецької області. Матеріалом для даного дослідження слугували новонароджені та плоди із множинними вадами, матері яких постійно проживають у Чернівецькій області. Дослідження частоти МУВР проводилося на базі медико-генетичного центру Чернівецького обласного діагностичного центру. Моніторингом охоплено 51129 новонароджених, у 134 (7,54%) випадках виявлено множинні аномалії. Пренатальним ультразвуковим скринінгом виявлено 54 плоди із множинними вадами розвитку (МУВР). Вивчено частоту та динаміку частоти множинних уроджених вад у Чернівецькій області за період 2004–2008 рр. У новонароджених множинні уроджені вади займають четверте місце за поширеністю (2,6‰). При пренатальній діагностиці переважали плоди із МУВР траплялися у жінок, які проживають у передгірських районах — 28,0% випадків, та у плодів чоловічої статі (64,8%). Виявлено здебільшого поєднання вад кістково-м'язової системи із вадами нервової системи. Вади нервової системи у складі множинних вад траплялися у 81,5%, що може слугувати підставою для вдосконалення системи первинної профілактики множинних аномалій.

МНОЖЕСТВЕННЫЕ ВРОЖДЕННЫЕ АНОМАЛИИ: ЭПИДЕМИОЛОГИЯ И КЛИНИЧЕСКИЙ АНАЛИЗ

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РЕЗЮМЕ

Целью работы было изучение эпидемиологических показателей множественных аномалий у новорожденных и плодов Черновицкой области. Материалом исследования были новорожденные и плоды с множественными пороками, матери которых постоянно проживают в Черновицкой области. Исследования частоты множественных пороков развития (МВПР) проводились на базе медико-генетического центра Черновицкого областного диагностического центра. Мониторингом охвачено 51129 новорожденных, у 134 (7,54%) случаях виявлены множественные аномалии. Пренатальным ультразвуковым скринингом выявлено 54 плода с МВПР. Изучена частота и динамика частоты множественных врожденных пороков в Черновицкой области за период 2004–2008 гг. У новорожденных множественные врожденные пороки занимают четвертое место по распространенности (2,6‰). При пренатальной диагностике чаще плоды с МВПР диагностировались у женщин, проживающих в предгорных районах — 28,0% случаев, и у плодов мужского пола (64,8%). Выявлено частое сочетание пороков костно-мышечной системы с пороками нервной системы в составе множественных пороков (81,5% случав), что может служить отправной точкой для совершенствования системы первичной профилактики множественных аномалий.

Key words: multiple congenital defects, newborns, fetuses.

One of the most important trends of modern prenatal medicine is early diagnostics of pathology of the embryo and fetus to avoid giving birth to a child with congenital (hereditary and acquired) diseases [5].

Congenital developmental defects are a heterogenous group of pathological states that includes isolated, systemic and multiple anomalies of the organs and systems of various ethiology: genetic, environmental and multifactorial. An evaluation of the rate of giving birth to children with congenital defects is one of the adequate means up controlling hereditary variability [4].

Among the causes of children's invalidism congenital developmental defects (CDDs) in children rank first and second — in the pattern of children's mortality of the infants of the first year of life [1]. In recent years the development of embryology, comparative anatomy, medical genetics, perinatology, pediatrics and teratology have made it possible not only to describe defects morphologically, but to detect the causes of their development [2]. And this, in its turn, is their primary prophylaxis. As is generally known congenital malformations, namely, multiple anomalies have a multifactorial nature of the development in 80–90% of the cases. The results of experimental studies and clinical observations have demonstrated that the majority of developmental defects is a consequence of embryopathies, when a lesion occurs, starting from the 16th day after fertilization up to the end of the 8th week of the intrauterine life. During this period the influence of teratogens is maximal and may bring about gene mutations, chromosomal aberrations, enzymatic disorders etc. [3].

The purpose of the research. To study the epidemiologic indicators of multiple developmental defects in newborns and fetuses of the Chernivtsi region.

MATERIALS AND METHODS

Newborns and fetuses with multiple congenital developmental defects (MCDDs) served as the material for this particular research, their mothers had been permanently living in the Chernivtsi region. The research of the prevalence, of MCDDs was carried out on the base of the Medicogenetical Centre (MGC) of the Chernivtsi Regional Diagnostic Centre (CRDC). A retrospective method of research was used covering the period, ranging from 2004 to 2008 by means of studying registration genetic maps (from N149/y) and accounts of the CRDS, of Ukraine's MHP — born N49-healthy «A report on rendering medicogenetic aid». The findings of an ultrasound examination of gravidas, taking medical advice at the Diagnostic Centre and the results of their analyses were also used. An ultrasound investigation of women was carried out during the terms of 11–16 and 16–28 weeks of pregnancy in accordance with the program of mass screening for the purpose of detecting developmental defects in a fetus.

During the period under study the monitoring involved 51129 newborns, multiple anomalies having been diagnosed in 134 (7,54%) cases. Prenatal ultrasound screening has revealed MCDDs in 54 fetuses. The dynamics of the frequency MCDDs over the years has been analyzed and compared with the findings of the International Register EUROCAT [8].

The population rate of MCDDs was calculated as a ratio of the number of live born and stillborn infants with multiple anomalies of live- and stillborns. The calculation was performed per 1000 births.

The EUROCAT formula was used:

$$\text{Total Prevalence Rate} = \frac{\text{№ Cases } (LB + FD + IA)}{\text{№ Births } (LB + FD)} \bullet 1000$$

where: LB — live births, FD — Fetal Deaths/Still Births from 20 week gestation, IA — induced abortion following prenatal diagnosis.

RESULTS AND THEIR DISCUSSION

51129 infants in all were born over the period from 2004 to 2008 1777 congenital developmental defects being registered among them making up 34,61±3,31‰. While analyzing the prevalence of CDDs in newborns, multiple congenital defects rank fourth (2,6‰). The first place is occupied by CDDs and deformities of the musculoskeletal system (17,2‰); the second place — CDDs of the blood circulation system (4,6‰); the third place — CDDs of the genital organs (3,8‰) [6,7]. The dynamics of the incidence of MCDDs over the period under study is presented in Table 1.

Over the period from 2004 to 2006 the incidence of MCDDs significantly increased 1,85 times, in 2007 its essential abatement was noted to 1,78‰ whereas in 2008 it increased to the maximal level over the period of case monitoring — 3,6‰.

By comparing the incidence of MCDDs in the Chernivtsi region with the finding of EUROCAT and Ukraine an identity of the indices with the data in Ukraine, Malta and Portugal is marked (table 2).

This may point to imperfect primary prophylaxis of these particular anomalies, namely, a neglect of the intake of folic acid before planned pregnancy and errors, when performing prenatal diagnostics. The intake of folic acid should start 2–3 months prior to planned pregnancy (the diurnal dose is 400–800 mg per diem) and must be prolonged, at the minimum, up to the 3^{d} month of pregnancy. However, the majority of women do not plan their pregnancy and learn about its onset only after 2–3 weeks. In this case, the intake of folates may be not efficient, since such disturbances of the development as anomalies of the heart and vessels arise during the first three weeks and the closure of the neural tube occurs in the 4th week [6].

Table 1

Dynamics of the prevalence of multiple congenital developmental defects in newborns of the Chernivtsi region (‰)

Nosology	Years					
	2004	2005	2006	2007	2008	Total
Multiple congenital developmental depects	1,74	2,62	3,23	1,78	3,60	2,59
Total number up defects	30,02	33,20	34,34	35,29	40,19	34,61

Table 2

A comparative disease incidence of MCDDs in newborns according to the findings of the registers of the Chernivtsi region and EUROCAT (‰)

Nosology	Regions					
	1	2	3	4	5	6
Multiple congenital developmental defects	2,59	2,10	0,90	1,60	2,40	2,10
Total	34,61	23,32	33,17	14,26	28,15	11,12

Note: 1 — the Chernivtsi region; 2 — Ukraine; 3 — Austria; 4 — Ireland; 5 — Malta; 6 — Portugal [5].

While performing prenatal ultrasound screening 54 MCDDs were detected, making up 13,4% of the total number of defects. The greatest number of MCDDs was diagnosed during the period of 16–28 weeks of pregnancy — 36 cases (66,7%). In the fetuses of women, living in the rural area MCDDs occurred in 39 (72%) cases, whereas in city dwellers — in 15 (28%) cases. The incidence of MCDDs among the districts of the region is represented in Fig. 1.

The analysis shows that MCDDs prevailed in gravidas of the foothill districts of the region (28,0%) and in fetuses of the male gender (64,8%) (Fig. 1).

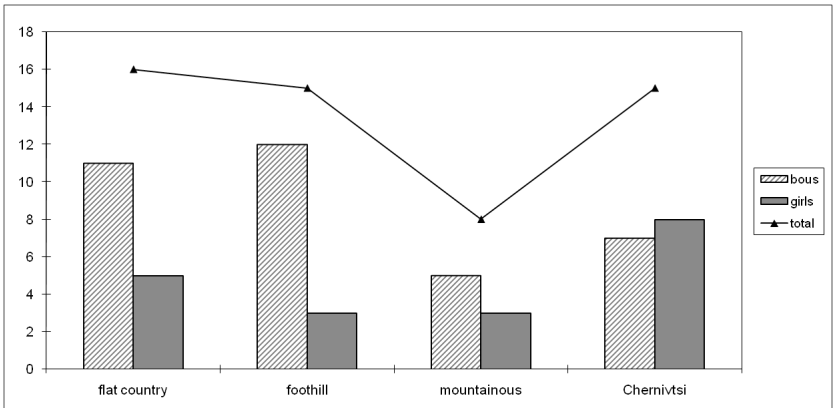

Fig. 1. The incidence of multiple anomalies detected by means of prenatal screening, depending on the mother's place of residence (abs. figures)

Fetuses with MCDDs most often occurred in women aged 34 years (74,1%), during the first pregnancy (70,1%), accompanied with hydramnion (18,5%), fetoplacental insufficiency (42,6%) and threatened abortion (42,6%). Pregnancies with MCDDs terminated in 53,7% of the cases with a justifiable abortion, in 46,3% with delivery.

When studying the pattern of multiple anomalies, we analyzed the frequency of their combination (Table 3).

We have revealed (Table 3) the most frequent combination of the defects of the musculoskeletal system with the defects of the nervous system, and the defects of the cardiovascular system with the defects of the nervous system. Apart from this, there occurred defects of the central nervous system (81,5%) in the pattern of multiple defects.

CONCLUSIONS

1. Multiple anomalies rank fourth in newborns as far as prevalence is concerned (2,6‰).

Table 3

Frequency of combinations of anomalies in the composition the multiple defects

	Nonimmune edema of the fetus	Defects of the gastrointestinal tract	Defects of the cardiovascular system	Defects of the maxillofacial region	Defects of the musculoskeletal system	Renal defects	Defects of the genital system	Defects of the lungs	Other
Defects of the central nervous system	5	5	10	5	14	3	-	-	2
Defects of the gastrointestinal tract	1	-	2	1	-	3	-	1	2
Defects of the cardiovascular system	1	-	-	2	4	2	-	-	-
Defects of the musculoskeletal system	1	-	-	1	-	5	-	1	-
Renal defects	-	-	-	1	-	-	1	1	1

2. In case of prenatal diagnosis fetuses with MCDDs occurred in women who live in the rural area — 72% of the cases, namely, in the foothill districts (28,0%) and fetuses of the male gender (64,8%).

3. MCDDs are largely registered in women aged under 34 years (74,1%), in case of the Ist pregnancy (70,1%) that is accompanied with hydramnion (18,5%), fetoplacental insufficiency (42,6%) and threatened abortion (42,6%).

4. A combination of the defects of the musculoskeletal system with the defects of the nervous system (81,5%) has been detected in the pattern of multiple defects in the majority of cases.

OUTLOOKS OF FURTHER STUDIES

A high incidence of congenital developmental defects in infants requires measures as to bringing up-to-date their primary prophylaxis and early prenatal diagnostics.

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REFERENCES

1. Антонова И. В. Роль экзогенных факторов в формировании врожденных пороков развития (обзор) / И. В. Антонова, Е. В. Богачева, Ю. Ю. Китаева //Экология человека.— 2010.— № 6.— С. 30–35.

2. Барашнев Ю. И. Диагностика и лечение врожденных заболеваний у детей (путеводитель по клинической генетике) / Ю. И. Барашнев, В. А. Бахарев, П. В. Новиков.— М.: Триада-Х, 2004.— С. 6–13.

3. Метаболизм фолатов и врожденные аномалии развития /А.С. Вайнер, Д. А. Жечев, А. А. Кечин [и др.] // Мать и дитя в Кузбассе.— 2011.— Т. 45, № 2.— С. 3–10. 6

4. Панкова Е. Е., Мониторинг врожденных пороков развития в Краснодарском крае / Е. Е. Панкова, С. А. Матулевич, В. И. Голубцов // Кубанский научный медицинский вестник.—2009.— Т. 106, № 1.— С. 79–82.

5. Пренатальная диагностика у беременных юного возраста в Приморском крае / А. Ю. Смирнова, Ф. Ф. Антоненко, М. Б. Хамошина, О. А. Дударь // Бюллетень СНЦ СО РАМН.— 2006.— Т. 47, № 1.— С. 94–96.

6. Ризничук М. О. Поширеність уроджених вад розвитку в дітей Чернівецької області / М. О. Ризничук, В. П. Пішак // Клінічна та експериментальна патологія.— 2011.— Т. 10, № 1 (35).— С. 140–143.

7. Ризничук М. О. Частота і структура уроджених вад розвитку в дітей Чернівецької області та чинники ризику їх формування: автореф. дис. канд. мед. наук / М. О. Ризничук.— Чернівці, 2012.— 24 с.

8. EUROCAT. Instructions for the Registration and Surveillance of Congenital Anomalies. 2005. WEB: http: // www.eurocat.ulster.ac.uk / pubdata.