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НОВЫЙ ДЕНЬ В МЕДИЦИНЕ
NEW DAY IN MEDICINE**

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MODERN VIEW OF THE RISK OF DEVELOPMENT OF INTRAUTERIN ANOMALIES OF DEVELOPMENT

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✓ Resume

We have studied the assessment of the significance of various risk factors for the birth of a child with congenital developmental anomalies in the Bukhara region. A method for the rational formation of risk groups among pregnant women is proposed, which will increase the level of timely diagnosis of congenital malformations and reduce perinatal and infant mortality in the Bukhara region. The risk factors were folate deficiency (24.9%), vitamin D deficiency (9.8%), zinc deficiency (12.9%) and chronic iodine deficiency (7.5%). In the course of the analysis, congenital malformations of the nervous system were revealed (34.03%), the second place was taken by multiple congenital malformations - (19.9%), the third - congenital malformations of the circulatory system (2.27%). To study the frequency and structure of CM and fetal chromosomal abnormalities detected using prenatal technologies, the study group (n=80) was formed by random sampling ("every third") of all cases of examination of pregnant women using prenatal diagnostic methods. . In the course of the study, a predominance in the main group of women aged 20-24 years (50.8%) was established. The proportion of women of young and young age (18-24 years) was 2 times higher than in the comparison group (48.6% versus 24.7%, $p<0.01$), while the proportion of women aged 35 years and older - 4 times lower (7.9% versus 32.5%, $p<0.01$). Summing up the results of our study, we can conclude that the structure of CM detected perinatally is dominated by CM of the nervous system (34.4%), multiple malformations (19.9%), and congenital malformations of the circulatory system (2.27%). In CM of the nervous system, the highest sensitivity and specificity is the increase in AFP, as well as ultrasound markers detected in the 1st trimester; with multiple CM - a decrease in PAPP and ultrasound markers in the 2nd trimester, with CM of the circulatory system - ultrasound markers detected in the 2nd-3rd trimesters, with chromosomal abnormalities - a change in the level of hCG and ultrasound markers in the 2nd-3rd m trimesters.

Key words: congenital malformations, chromosomal abnormalities, prenatal diagnosis.

СОВРЕМЕННЫЙ ВЗГЛЯД РИСКА РАЗВИТИЯ ВНУТРИУТРОБНЫХ АНОМАЛИЙ РАЗВИТИЯ

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✓ Резюме

Изучена оценка значимости различных факторов риска рождения ребенка с врожденными пороками развития в Бухарской области. Предложен метод рационального формирования групп риска среди беременных, что позволит повысить уровень своевременной диагностики врожденных пороков развития и снизить перинатальную и младенческую смертность в Бухарской области. Факторами риска были дефицит фолиевой кислоты (24,9%), дефицит витамина D (9,8%), дефицит цинка (12,9%) и хронический дефицит йода (7,5%). В ходе анализа были выявлены врожденные пороки развития нервной системы (34,03%), второе место заняли множественные врожденные пороки развития - (19,9%), третье - врожденные пороки развития системы кровообращения (2,27%).

Ключевые слова: врожденные пороки развития, хромосомные аномалии, пренатальная диагностика

ТУГМА НУҚСОНЛАР РИВОЖЛАНИШ ХАВФ ОМИЛЛАРИ ЗАМОНАВИЙ ЁНДАШУВ

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✓ Резюме

Бухоро вилоятида тугма нуқсонлари бўлган ҳомила тузилишида турли хил хавф омилларининг аҳамиятини баҳолашни ўргандик. Ҳомиладор аёллар ўртасида хавф гуруҳларини оқилона ривожлантириш усуллари таклиф этилмоқда, бу эса Бухоро вилоятида тугма нуқсонларни ўз вақтида таъхислаш даражасини ошириш, перинатал ва чақалоқлар ўлими камайтиришни имконини беради. Хавф омиллари фолат танқислиги (24,9%), D витамини танқислиги (9,8%), рух танқислиги (12,9%) ва сурункали йод танқислиги (7,5%) эканлиги аниқққланди. Таҳлиллар давомида асаб тизимининг нуқсонлари аниқланган (34,03%), иккинчи ўринда кўп тугма нуқсонлар (19,9%), учинчи ўринда қон айланиш тизимининг тугма нуқсонлари (2,27%) жой олган

Пренатал технологиялардан фойдаланган ҳолда аниқланган ҳомила хромосома аномалияларининг частотаси ва тузилишини ўрганиш учун тадқиқот гуруҳи (n=80) ҳомиладор аёлларни пренатал диагностика усулларида фойдаланган ҳолда текширишнинг барча ҳолатларидан тасодифий танлаб олиш (ҳар учдан бир) йўли билан тузилган. Тадқиқот давомида 20-24 ёшли аёлларнинг асосий гуруҳида (50,8%) устунлик аниқланди. Ёш (18-24 ёш) аёллар улуши солиштирма гуруҳдагига нисбатан 2 баравар юқори (48,6% га нисбатан 24,7%, $p<0,01$), 35 ва ундан катта ёшдаги аёллар улуши эса 4 баравар кам (32,5% га нисбатан 7,9%, $p<0,01$). Тадқиқотимиз натижаларини сарҳисоб қилсак, перинатал тарзда аниқланган нуқсонлар тузилишида асаб тизимининг нуқсонлари (34,4%), кўп нуқсонлар (19,9%) ва қон айланиш тизимининг тугма нуқсонлари (2,27%) устунлик қилади деган хулосага келишимиз мумкин. Асаб тизимининг энг юқори сезувчанлик ва ўзига хослик АФП нинг ортиши, шунингдек, 1 триместрда аниқланган ултратовуш белгиларидир; бир нечта нуқсонлар билан - 2 триместрда ПАПП ва ултратовуш белгиларининг пасайиши, қон айланиш тизимининг ўзгаришлари - 2-3 триместрда ултратовуш белгилари, хромосома аномалиялари билан - ХГЧ даражасининг ўзгариши ва 2-чида ултратовуш маркерлари туради.

Калит сўзлар: тугма нуқсонлар, хромосома аномалиялари, пренатал таъхис.

Relevance

Today, congenital malformations (CM), which rank second in the structure of perinatal mortality, remain an urgent problem in modern perinatology [1, 2]. Prenatal diagnosis of developmental anomalies, which makes a significant contribution to infant and child mortality, disability and morbidity, is an important task of modern healthcare. According to EUROCAT, every year in the world, 1 out of 33 newborns has a congenital malformation (CMD), almost 300 thousand children with defects die in the first 4 weeks of life, approximately 3.2 million children have disabilities of varying severity due to this pathology. In Uzbekistan in recent years a significant decrease in perinatal mortality our indicators are still significantly higher than in Europe [9-11]. In the Bukhara region he showed that on average it ranges from 6.8% to 8.7% of congenital malformations. Improvement of methods of antenatal diagnostics, screening of pregnant women for the presence of congenital fetal pathology, the introduction of modern perinatal technologies are recognized as one of the main tasks of reducing perinatal mortality in Uzbekistan [1, 4-6].

From a medical point of view, in the complex of methods for the prevention and prevention of hereditary and congenital pathology belongs prenatal diagnostics, which helps to prevent the birth of children with severe fetal malformations incompatible with life, with socially significant and fatal chromosomal diseases [1, 10]. Many authors believe that one of the most rational and promising directions that help reduce the likelihood of developing a disease is its prediction, which allows you to

determine the most rational tactics for managing a patient, take into account and use all possible preventive and therapeutic measures.

Materials and methods. To study the frequency and structure of congenital malformations and fetal chromosomal abnormalities, detected using prenatal technologies like ultrasound biochemical testing of blood the study group ($n = 80$) was formed by random sampling ("every third") from all cases of examination of pregnant women using prenatal diagnostic methods. The age of women ranged from 19 to 40 years. In order to identify risk factors (predictors) for the most common congenital malformations and chromosomal abnormalities in the fetus and determine the possibility of their mathematical prediction, the study group was subdivided into the main group and the comparison group. The main group consisted of pregnant women with congenital malformations diagnosed in the fetus during pregnancy or after childbirth ($n = 45$). The comparison group consisted of patients who, according to generally accepted criteria (ultrasound, biochemical test to estriol, HCG, AFP) had a risk of having a child with congenital malformation during pregnancy. The control group was formed from women who applied to the screening center of Bukhara region who did not have the risk of having a child with congenital anomalies, examined at their own request and subsequently gave birth to healthy children ($n = 35$). The significance of differences was assessed using Student's and Fisher's tests. The difference between the compared values was recognized as significant at $p < 0.05$. To determine the diagnostic significance of the indicators, the method of G.P. Kotelnikov and A.S. Spiegel, who made it possible to determine the sensitivity, specificity, predictive value of a positive result, and the predictive value of a negative result. The odds ratio was used as a criterion for determining whether the trait under study is a risk factor for the disease.

Research results and discussion. In the course of the study, the predominance in the main group of women aged 20-24 (50.8%) was established. The proportion of young and young women (18-24 years old) was 2 times higher than in the comparison group (48.6% versus 24.7%, $p < 0.01$), while the proportion of women aged 35 and older - 4 times lower (7.9% versus 32.5%, $p < 0.01$).

When analyzing socio-geographical living conditions (city or village), it was found that the overwhelming majority of pregnant women lived in an area with a changed (9.8%) and

strongly changed (86.3%) type of living conditions ($p < 0.01$), but there were significant differences between the main group and the comparison group for the factor of the type of living conditions was not identified. Women in the main group and in the comparison group were mainly residents of cities (83%), including 49% in the city of Bukhara, respectively, rural women accounted for only 17% ($p < 0.01$). It should be noted that in the main group, women from the cities of the region were more than in the comparison group (39.8% versus 28.3%, $p < 0.05$), while in the comparison group, women from Bukhara predominated (55.4 % and 39.1%, $p < 0.01$).

When studying the type of occupation of pregnant women in the main group and the comparison group, it was found that office workers (39.7%) and non-working people (30.4%) prevailed among them. In the group of patients with congenital malformations in the fetus (main), there were non-working women significantly more often than in the comparison group (33.3% and 20.2%, respectively, $p < 0.05$). 18.1% of pregnant women in the main group and the comparison group had occupational exposure to risk factors. The structure of occupational hazards was dominated by electromagnetic radiation (50.5%), contact with biomaterial (13.3%) and chemical substances (12.4%). In the main group, an increased professional speech load was more often observed (18.4% and 5.4%, respectively, $p < 0.01$).

One of the most significant factors that determine the risk of congenital malformations are diseases in a hereditary history. The analysis showed that the greatest specific weight was occupied by congenital malformations in the family history, which in the main group was 92.8% ($p < 0.001$). Among congenital malformations in the history, malformations were most often noted, their number prevailed in the main group (87.6%, $p_{1-2} < 0.001$), the number of CA (Down's disease) in the history, on the contrary, was higher in the comparison group (16.4%, $p_{1-2} < 0.001$).

When analyzing the prevalence of chronic extragenital pathologies of pregnant women, their high frequency was found in the main group and the comparison group - 88.6%. In the structure of chronic extragenital pathologies of pregnant women, diseases of the respiratory system (24.0%), digestion (26.8%) and urinary system (17.0%) prevailed. In the main group, the prevalence of the prevalence of allergic diseases was revealed in comparison with the control (18.5% and 1.9%, respectively, $p < 0.01$), including drug allergy (8.9%, $p < 0.005$) and polyvalent allergy (4.3%, $p < 0.05$).

A burdened reproductive history with a high frequency was noted among women in the main group and in the comparison group (artificial termination of pregnancy - 67.2%, spontaneous abortion - 12.8% of cases). In these groups, preterm labor was observed more often than in the control group (6.7%, 14.5% and 1.2%, respectively, $p_{1-3} < 0.05$, $p_{2-3} < 0.05$).

Analysis of the study of the parity of pregnancy in women of the compared groups showed that primiparous women prevailed in the main group (66.3%), mainly primiparous (42.4%), while in the comparison group, multiparous (56.7%) and re-pregnant women prevailed. (71.9%), ($p_{1-2} < 0.01$, $p_{1-3} < 0.05$). In the main group, primiparous women met 1.5 times more often than in the comparison group (42.4% and 28.1%, $p < 0.005$), and re-pregnant primiparas - 1.6 times more often (23.9% versus 15.2%, $p < 0.05$). At the same time, primiparous (77.3%) and re-pregnant women (63.9%) also dominated in the control group, which reflects the characteristics of the reproductive behavior of women in the region.

When analyzing the course of this pregnancy, it was found that the most frequent complication was threatening early self-abortion (28.8%), acute respiratory viral infections during pregnancy were noted in 21.6% of cases, vomiting of pregnant women - in 13.4%. However, in the main group, these complications were significantly less frequent than in the comparison group and in the control group ($P_{1-2} < 0.05$, $P_{13} < 0.05$).

When studying the outcomes of pregnancy in the main group of women, abortion for medical reasons naturally prevailed in the 1st (9.2%) and 2-3rd (61.9%) trimesters of pregnancy, which was determined by the need to eliminate the affected nonviable fetuses, childbirth in term was noted in 17.7% of women ($p_{1-2} < 0.01$), in 2.4% spontaneous abortion and antenatal fetal death were noted. It is natural that in the comparison group, preterm birth was noted 3.7 times less often than in the main group (8.8%, $p < 0.01$).

In the structure of chronic micronutrient deficiencies among pregnant women, folate deficiency (24.9%), vitamin D deficiency (9.8%), zinc deficiency (12.9%) and chronic iodine deficiency (7.5%) prevail.

In the course of the study, in the structure of congenital malformations identified in the main group prevailed: congenital malformations of the nervous system (34.03%), the second place was taken by multiple congenital malformations - (19.9%), the third - congenital malformations of the circulatory system (2.27%). In the main group in the 1st trimester of pregnancy, congenital malformations and ultrasound markers of chromosomal abnormalities were detected in 16.3% of cases. In 83.2% of patients, isolated congenital malformations or ultrasound imaging of chromosomal abnormalities were diagnosed in 16.7% - the changes were combined. The most frequently detected congenital malformations of the nervous system (22–36.7%), congenital malformations of the digestive system (10–31.3%), and congenital malformations of the genitourinary system (5–9.4%). The effectiveness of the echographic method in the study in the 1st trimester of pregnancy in relation to chromosomal diseases was noted in 16.7% of cases. In this case, the most sensitive ultrasonography was such as cystic hygroma of the neck and hydrocephalus (75%).

One of the significant risk factors for the formation of VA in the fetus is specific deviations from the norm of serum pregnancy markers (SMB). In this study, 16-71% of patients had these abnormalities for various types of congenital malformations. As a result of the analysis, it was found that in congenital pathologies they have a relatively low sensitivity and high specificity. The decrease in PAPP (0.38) had the highest sensitivity, and the decrease in AFP (0.07) was the least sensitive. Specificity ranged from 0.44 to 0.91, the highest was found to increase AFP (0.91), as well as to decrease hCG and AFP (0.88 and 0.81, respectively), the lowest - to increase hCG (0.44) ... CVR is defined as a relatively stable value for almost all SMBs (from 0.5 to 0.59), the highest - to reduce the PAPP and the lowest - to increase and decrease AFP.

When analyzing the data on certain types of congenital anomalies, it was found that with congenital malformations of the nervous system, an increase in AFP (0.83) has the greatest sensitivity, with multiple congenital malformations - a decrease in PAPP (0.75), with congenital malformations of the musculoskeletal system - a decrease in PAPP (0.67), with chromosomal abnormalities - a decrease and increase in hCG (0.67). During the analysis of the changes, their high specificity was established for almost all types of VA (from 0.53 to reduce PAPP in most VA to 0.95 - to increase hCG in CMR of the digestive system), the greatest result was noted for an increase in AFP in CMR of the nervous system (0.55).

In the 2nd and 3rd trimesters of pregnancy, ultrasound was performed in the main group in 77.9%. According to our data, the greatest sensitivity was observed with a combination of several USMs

compared with isolated USMs (1.9 times more often - 13.3% versus 9.4%). The greatest sensitivity in relation to CA belongs to congenital heart defects (CHD): 57, 1% with isolated CHD and 20.7% when combined with other USM. Markers such as vascular plexus cysts, diaphragmatic hernia, polyhydramnios, nasal bone hypoplasia were isolated in isolated cases, but their sensitivity for chromosomal abnormalities was 100%. High sensitivity to chromosomal abnormalities (50%) was noted for duodenal atresia, intestinal obstruction, cystic-adenomatous congenital malformations of the lungs, as well as with delayed fetal development (66.7%) and cystic hygroma of the neck (37,%) in combination with other.

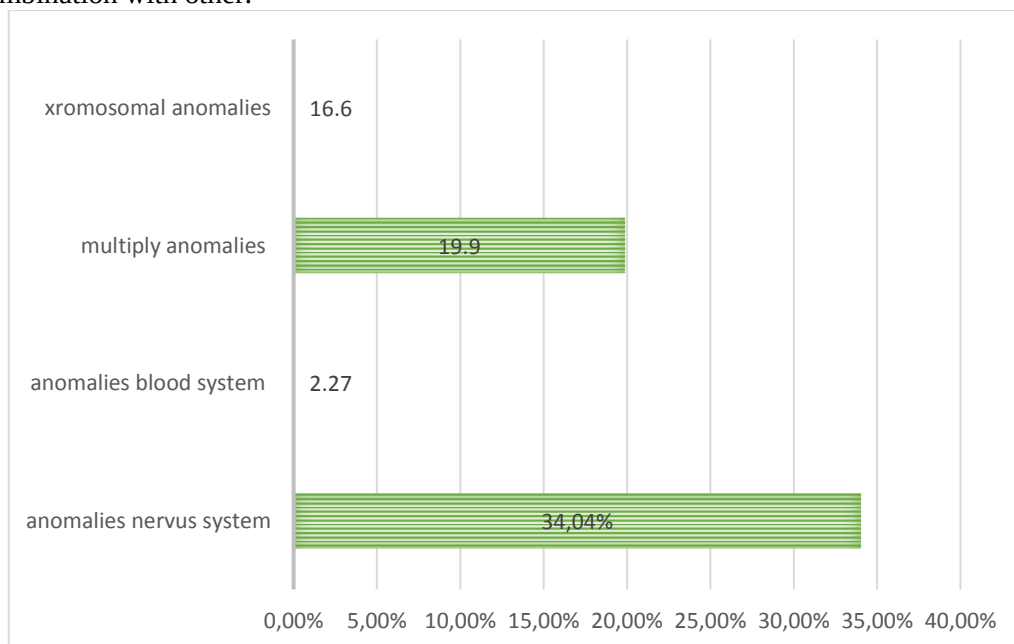
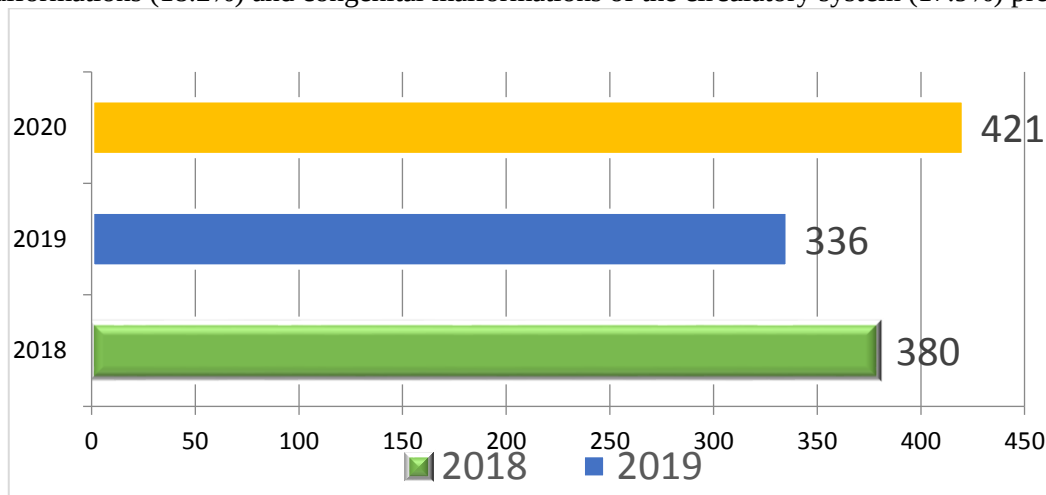


Figure 1 - Results of screening analyzes of the occurrence of CM

Summing up the results of our study, we can conclude that in the structure of congenital malformations detected perinatally, congenital malformations of the nervous system (20.3%), multiple malformations (18.2%) and congenital malformations of the circulatory system (17.9%) prevail.



2 Figure. In Bukhara in 2018-2020, the incidence of intrauterine defects in the fetus

In congenital malformations of the nervous system, an increase in AFP, as well as ultrasound markers identified in the 1st trimester, has the highest sensitivity and specificity; with multiple congenital malformations - a decrease in PAPP and ultrasound markers in the 2nd trimester, with congenital malformations of the circulatory system - ultrasound markers identified in the 2-3rd trimesters, with chromosomal abnormalities - a change in the level of hCG and ultrasound markers in 2-3- m trimesters.

Predictors of the presence of a fetal congenital malformation in a pregnant woman are a history of congenital malformations in a child, abnormalities according to ultrasound data in the 1st and 2nd trimester, changes in PAPP, the age of women 16-24 years.

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