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EARLY MARKERS FOR THE DIAGNOSIS OF INTRAUTERINE FETAL ANOMALIES

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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%).

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

РАННИЕ МАРКЕРЫ ДИАГНОСТИКИ ВНУТРИУТРОБНЫХ АНОМАЛИЙ РАЗВИТИЯ ПЛОДА

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✓ ***Резюме***

Нами было изучено оценка значимости различных факторов риска рождения ребенка с врожденными аномалиями развития на территории Бухарской области. Предложено методика рационального формирования групп риска среди беременных, что позволит повысить уровень своевременной диагностики врожденных аномалий развития и снизить перинатальную и младенческую смертность в Бухарском регионе. Факторами риска оказались фолиеводефицитное состоянии (24,9%), дефицит витамина Д (9,8%), дефицит цинка (12,9%) и хронические йод дефицитное состоянии (7,5%). По ходу анализа выявлено ВУАП нервной системы (34,03%), второе место заняли множественные врожденные пороки развития – (19,9%), третье – ВУАП системы кровообращения (2,27%).

Ключевые слова: врожденные пороки развития, хромосомные аномалии, перинатальная диагностика.

TUG'MA NUQSONLARNI RIVOJLANISHINING XAVF OMILLARINI ERTA TAHLIL QILISH

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Biz Buxoro viloyatida tug'ma rivojlanish anomaliyasi bo'lgan bola tug'ilishi uchun turli xil xavf omillarining ahamiyatini baholashni o'rganib chiqdik. Buxoro viloyatida tug'ma nuqsonlarni o'z vaqtida tashxislash darajasini oshirish va perinatal va bolalar o'limini kamaytirishga imkon beradigan homilador ayollar o'rtasida xavf guruhlarini oqilona shakllantirish usuli taklif etilmoqda. Xavf omillari folat etishmovchiligi (24,9%), D vitamini etishmovchiligi (9,8%), rux etishmovchiligi (12,9%) va yodning surunkali etishmasligi (7,5%) edi. Tahlil jarayonida asab tizimining tug'ma nuqsonlari aniqlandi

(34,03%), ikkinchi o'rinni ko'plab tug'ma nuqsonlar egalladi - (19,9%), uchinchi qon aylanish tizimining tug'ma nuqsonlari (2,27%).

Kalit so'zlar: tug'ma nuqsonlar, xromosoma anomaliyalari, prenatal tashxis.

Relevance

Today, intrauterine fetal abnormalities (VUA) remainan urgent problem in modern perinatology, which occupy the second place in the structure of perinatal mortality [1, 2.25]. Perinatal diagnosis of developmental abnormalities, which makes a significant contribution to infant and child mortality, disability and morbidity, is an important task of modern healthcare. According to EUROCAT data, 1 out of 33 newborns in the world annually have a congenital malformation (CRD), 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. Despite a significant decrease in perinatal mortality in Uzbekistan in recent years, our indicators are still significantly higher than in Europe [9,11,24]. In the Bukhara region, it was shown that on average it accounts for 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,

introduction of modern perinatal technologies are recognized as one of the main tasks of reducing perinatal mortality in Uzbekistan [1, 4,6,10,11,25].

Various pathogenic factors have an unequal damaging effect on the fetus and the entire fetoplacental system. In this regard, it is quite difficult to separate the degree of influence of one factor from another, to assess whether they act independently of each other or in combination [1, 15, 18, 20].

Specific preventive measures to prevent the development of most fetal birth defects do not exist, since they are mainly sporadic [10, 12, 16, 20]. Therefore, at present, prenatal diagnosis of intrauterine fetal abnormalities is the most effective measure to prevent the birth of children with congenital anomalies [10, 21, 24]. Despite the introduction of modern technologies of prenatal diagnostics in Uzbekistan (ultrasound screening, biochemical examinations for markers of fetal malformations, invasive methods of examination), the frequency of congenital pathology does not decrease, which leads to the search for new approaches to the prevention and identification of risk factors for congenital malformations of the fetus [20,24]. There is a need to form groups with different degrees of risk for the development of intrauterine fetal abnormalities, taking into account the specifics of the impact of antenatal damaging factors and optimizing prenatal diagnostics, and therefore the purpose and objectives of the study were determined [24,26].

The purpose of the study: To develop significant risk factors for the formation of VUA and markers of the development of VPD

Materials and methods

To study the frequency and structure of intrauterine fetal malformations (VUA) 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. The women ranged in age from 19 to 40. In order to identify risk factors (predictors) of the presence of the most common VOAP and chromosomal abnormalities in the fetus, the study group was divided into the main group and the comparison group. The main group consisted of pregnant women with VUA diagnosed in the fetus during pregnancy or after the birth of the child (n=45). The comparison group consisted of patients who, according to generally accepted criteria, had a risk of having a child with VUAP during pregnancy. The control group was formed from women who applied to the screening center of the Bukhara region, who did not have a risk of having a child with intrauterine abnormalities , who were examined on their own and subsequently gave birth to healthy children (n=35). To determine the diagnostic significance of the indicators, the sensitivity, specificity, and prognostic value of the negative result were determined by the method of early diagnosis of ultrasound and biochemical markers in the screening center. The odds ratio was used as a criterion for determining whether the trait

Result and discussion

In the course of the study, the prevalence of women aged 20-24 years in the main group was established (50.8%). The proportion of women younger and younger age (18-24 years) was 2 times (48,6% vs 24.7 per cent, $p<0.01$), while the proportion of women aged 35 years and older is 4 times lower (7,9% against 32.5%, $p<0.01$).

In the analysis of socio-geographical conditions of stay established that the vast majority of pregnant women lived on the territory with a modified (9.8 per cent) and heavily modified (86,3%) the type of living conditions ($p<0.01$), but significant differences between the main group and the comparison group in terms of the type of

conditions of accommodation were not identified. Women of the main group and the comparison group were mainly residents of cities (83%), including in 49% –the city of Bukhara, respectively, rural women made up only 17% ($p<0.01$). It should be noted that in the main group of residents of cities in the region were larger than in the comparison group (39,8% vs 28.3%, and $p<0.05$), whereas in the comparison group was dominated by women from Bukhara (55,4% and 39.1%, $p<0.01$).

In the study of occupation pregnant women of the main group and the comparison group found that prevailed employees (39.7%) and the unemployed (30,4%). In the group of patients with VAAP in the fetus (the main group), non-working women were significantly more common 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 professional exposure to risk factors. The structure of occupational hazards was dominated by electromagnetic radiation (50.5%), contact with biomaterial (13.3%) and chemicals (12.4%). In the main group, increased professional speech load was more often observed (18.4% and 5.4%, respectively, $p<0.01$).

One of the most significant factors determining the risk of VUA is diseases with a hereditary history. The analysis showed that the greatest share was occupied by VUA in the family history, which in the main group was 92.8% ($p<0.001$). Among the VUA in the anamnesis, the most common malformations were observed, their number was predominant in the main group (87.6%, $p1-2<0.001$), the number of CA (Down's disease) in the anamnesis, on the contrary, was greater in the comparison group (16.4%, $p1-2<0.001$). When analyzing the prevalence of chronic extragenital pathologies in pregnant women, their high frequency was found in the main group and the comparison group – 88.6%. Diseases of the respiratory system (24.0%), digestive system (26.8%), and urinary system (17.0%) predominated in the structure of chronic extragenital pathologies of pregnant women. In the main group revealed the predominance in the prevalence of allergic diseases compared with controls (18.5% and 1.9%, respectively, $p<0.01$), including drug Allergy (8,9%, $p<0.005$) and polyvalent Allergy (4,3%, $p<0.05$).

Reproductive history is burdened with a high frequency was observed among women of the main group and the comparison group (the artificial termination of pregnancy is 67.2%, spontaneous abortions, and 12.8% of cases). In these groups, preterm birth was observed more often than in the control group (6.7%, 14.5% and 1.2%, respectively, $p1-3<0.05$, $p2-3<0.05$). The analysis of the study of pregnancy parity in women of the compared groups showed that the main group was dominated by primiparous women (66.3%), mainly primiparous women (42.4%), while in the comparison group – repeat births (56.7%) and repeat pregnancies (71.9%), ($p1-2<0.01$, $p1-3<0.05$). In the main group, first-time pregnant women were 1.5 times more common than in the comparison group (42.4% and 28.1%, $p<0.005$), and second-time first-time pregnant women were 1.6 times more common (23.9% vs. 15.2%, $p<0.05$). At the same time, the control group was also dominated by first-time mothers (77.3%) and re-pregnant women (63.9%), which reflects the peculiarities 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 a threatening early self-abortion (28.8%), ARVI during pregnancy was observed in 21.6% of cases, vomiting of pregnant women – in 13.4%. However, in the main group of these complications were found significantly less frequently than in the comparison group and in the control group ($P1-2<0,05$, $P13<0,05$).

In the study of pregnancy outcomes in the main group of women were naturally dominated by termination of pregnancy for medical reasons in 1-m (9.2 percent) and 2-3-m (61.9%) of the trimester of pregnancy that was determined by the necessity of elimination of the affected non-viable fetuses, delivery in time was observed in 17.7% of women ($P1-2<0.01$), and 2.4% were observed spontaneous abortion and antenatal fetal death. Naturally, in the comparison group, preterm birth was 3.7 times less frequent than in the main group (8.8%, $p<0.01$). The structure of chronic micronutrient deficiencies among pregnant women is dominated by folic acid deficiency (24.9%), vitamin D deficiency (9.8%), zinc deficiency (12.9%) and chronic iodine deficiency (7.5%).

In the course of the study, the structure of VUA identified in the main group was dominated by: VUA of the nervous system (34.03%), the second place was taken by multiple congenital malformations – (19.9%), the third – VUA of the circulatory system (2.27%). In the main group, in the 1st trimester of pregnancy, VOAP and ultrasound markers of chromosomal abnormalities were detected in 16.3% of cases. 83.2% of patients were diagnosed with isolated VUAP or UZD of chromosomal abnormalities, and 16.7% had combined changes. The most frequently detected VUA were those of the nervous system (22-36. 7%), VUA of the digestive system (10-31.3%), and VUA of the genitourinary system (5-9. 4%). The effectiveness of the echography method in the study conducted in the 1st trimester of pregnancy

in relation to chromosomal diseases was noted in 16.7% of cases. One of the significant risk factors for the formation of VOAP in the fetus is specific deviations from the norm of serum pregnancy markers (SMB). In the conducted study, 16-71% of patients with various types of VUA had these deviations. As a result of the analysis, it was found that in congenital pathologies they have a relatively low sensitivity and high specificity. The greatest sensitivity was a decrease in RARR (0.38), and the lowest-a decrease in AFP (0.07). The specificity ranged from 0.44 to 0.91, the highest was found for an increase in AFP (0.91), as well as for a decrease in hCG and AFP (0.88 and 0.81, respectively), the lowest – for an increase in hCG (0.44). PCO is defined as a relatively stable value for almost all SMBs (from 0.5 to 0.59), the highest – for a decrease in RARP and the lowest – for an increase and decrease in AFP. When analyzing data on individual types of congenital anomalies, it was found that in the case of VUA of the nervous system, the greatest sensitivity is an increase in AFP (0.83), in the case of multiple VUA – a decrease in RARP (0.75), in the case of CRV of the musculoskeletal system – a decrease in RARP (0.67), in the case of chromosomal abnormalities – a decrease and an increase in hCG (0.67). During the analysis of changes, their high specificity was established for almost all types of VUA (from 0.53 for reducing RARP in most VUA to 0.95 for increasing hCG in VUA of the digestive system), the highest value was noted for increasing AFP in VUA 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 in the combination of several ultrasounds compared to isolated ultrasounds (1.9 times more often-13.3% vs. 9.4%). The greatest sensitivity to CA belongs to congenital heart defects (VUA): 57.1% in isolated VUA and 20.7% in combination with other ultrasound examinations. Markers such as vascular plexus cysts, diaphragmatic hernia, polyhydramnios, hypoplasia of the nasal bone were isolated in isolated cases, but their sensitivity to chromosomal abnormalities was 100%. High sensitivity to chromosomal abnormalities (50%) was noted for atresia of the duodenum 12, intestinal obstruction, cystic-adenomatous lung VOAP, as well as for fetal development delay (66.7%) and cystic neck hygroma (37%) in combination with other ultrasounds.

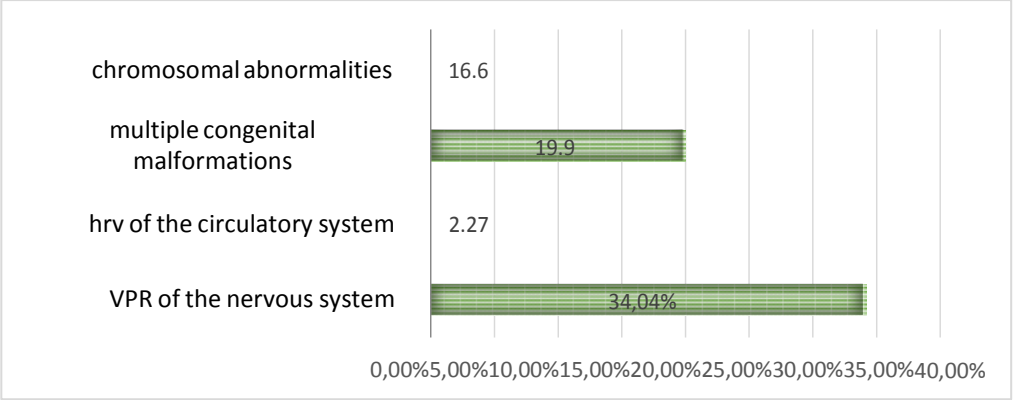

Figure-1.Results of screening tests of the occurrence of VUAP

Conclusion

Summing up our study, we can conclude that the structure of VUA detected perinatally is dominated by VUA of the nervous system (34.4%), multiple malformations (19.9%) and CPR of the circulatory system (2.27%). In VUA of the nervous system, the greatest sensitivity and specificity is an increase in AFP, as well as ultrasound markers detected in the 1st trimester; in multiple VUA-a decrease in RARR and ultrasound markers in the 2nd trimester, in VUA of the circulatory system – ultrasound markers detected in the 2nd-3rd trimesters, in chromosomal abnormalities-a change in the level of hCG and ultrasound markers in the 2nd-3rd trimesters.

Predictors of the presence of the fetus in a pregnant woman with VUA are a history of VPR, deviations according to ultrasound data in the 1st and 2nd trimester, changes in RARP-A, and the age of women 16-24 years.

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