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Ecological Risk Factors for Intrauterine Anomalies of Fetal Development

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Abstract: To date, intrauterine anomalies of fetal development (IVAF), which occupy the second place in the structure of perinatal mortality, remain an urgent problem of modern perinatology. There is a need to form groups with varying degrees of risk for the development of UA, taking into account the specifics of the impact of antenatal damaging factors and optimizing prenatal diagnosis.

Keywords: congenital malformations, chromosomal abnormalities, prenatal diagnosis.

Introduction: To date, intrauterine anomalies of fetal development (IVAF), which occupy the second place in the structure of perinatal mortality, remain an urgent problem of modern perinatology [1, 2,

3]. Prenatal diagnosis of developmental anomalies, which make a significant contribution to infant and child mortality, disability and morbidity, is an important task of modern health care. According to EUROCAT, every year in the world 1 out of 33 newborns have a congenital malformation (CM), 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 rates are still significantly higher than in Europe [3-5]. In the Bukhara region, on average, congenital malformations are registered in 6.8-8.7% of newborns. Improving the methods of antenatal diagnosis, screening pregnant women for the presence of congenital fetal pathology, and the introduction of modern perinatal technologies are recognized as one of the main tasks in reducing perinatal mortality in Uzbekistan [1, 5–9].

Various pathogenic factors have an unequal damaging effect on the fetus and the entire fetoplacental system. In this regard, it is rather 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, 3, 10, 11].

There are no specific preventive measures to prevent the development of most fetal CMs, since they are mostly sporadic [3, 8, 12, 13]. Therefore, at present, prenatal diagnosis of intrauterine anomalies in the development of the fetus is the most effective measure to prevent the birth of children with congenital anomalies [8, 9]. Despite the introduction of modern prenatal diagnostic technologies in Uzbekistan (ultrasound screening, biochemical examinations for markers of fetal malformations, invasive examination methods), the frequency of congenital pathologies does not decrease, which leads to the search for new approaches to prevention and identification of risk factors for fetal CM [3]. There is a need to form groups with varying degrees of risk for the development of UA, taking into account the specifics of the impact of antenatal damaging factors and optimizing prenatal diagnosis, in connection with which the goal and objectives of the study were determined [3, 14].

The purpose of the study: To develop significant risk factors for the formation of UA and markers of the development of congenital malformations.

Materials and Methods: To study the frequency and structure of UAAP and fetal chromosomal abnormalities detected using prenatal technologies, a study group (n=80) was formed by random

sampling ("every third") of all examined 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 presence of the most common UA 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 a child (n=45). The comparison group consisted of patients who, according to generally accepted criteria, had a risk of giving birth to a child with VUA during pregnancy. The control group was formed from women who applied to the screening center of the Bukhara region, who did not have the risk of having a child with intrauterine anomalies, were examined at their own request and subsequently gave birth to healthy children (n=35). To determine the diagnostic significance of the indicators, the definition of sensitivity and specificity was used. The predictive value of a negative result was 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 studied trait is a risk factor for the disease.

Results and Discussion: The main group was dominated by women aged 20-24 years (50.8%). 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 was 4 times lower (7.9% versus 32.5%, $p<0.01$).

When analyzing the socio-geographical living conditions, it was found that the vast majority of pregnant women lived in a territory with a changed (9.8%) and greatly changed (86.3%) type of living conditions ($p<0.01$), but there were significant differences between the main group and the comparison group by the factor of the type of living conditions was not revealed. Women of the main group and the comparison group were predominantly residents of cities (83%), including 49% of the city of Bukhara; accordingly, rural women accounted for only 17% ($p<0.01$). It should be noted that in the main group there were more women from Bukhara region than in the comparison group (39.8% versus 28.3%, $p<0.05$), while in the comparison group women from Bukhara prevailed (55 4% and 39.1%, $p<0.01$).

When studying the occupation of pregnant women in the main group and the comparison group, it was found that employees (39.7%) and non-working persons (30.4%) prevailed among them. In the group of patients with VUA in the fetus (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 of 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 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 that determine the risk of AVAI is a family history of diseases. The analysis showed that the largest share was occupied by UARP in the family history, which in the main group was 92.8% ($p<0.001$). Among the UARP in history, malformations were most often noted, their number prevailed in the main group (87.6%, $p1\text{-}2<0.001$), the number of CA (Down's disease) in history, on the contrary, was higher in the comparison group (16.4%, $p1\text{-}2<0.001$). When analyzing the prevalence of chronic extragenital pathologies in pregnant women, their high frequency was established in the main group and the comparison group - 88.6%. In the structure of chronic extragenital pathologies of pregnant women, diseases of the respiratory organs (24.0%), digestion (26.8%) and urinary system (17.0%) prevailed. In the main group, a predominance of the prevalence of allergic diseases was revealed compared to 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 was noted with a high frequency among women of the main group and the comparison group (induced abortion - 67.2%, spontaneous abortions - 12.8% of cases). In these groups, more often than in the control group, preterm labor was observed (6.7%, 14.5% and 1.2%, respectively, $p1\text{-}3<0.05$, $p2\text{-}3<0.05$).

An analysis of the study of the parity of pregnancy in women of the compared groups showed that the main group was dominated by primiparous women (66.3%), predominantly primiparous (42.4%),

while in the comparison group - multiparous (56.7%) and multiparous (71.9%), (p1-2<0.01, p1-3<0.05). In the main group, primiparous women occurred 1.5 times more often than in the comparison group (42.4% and 28.1%, p<0.005), and multi-pregnant primiparas - 1.6 times more often (23.9% vs. 15 .2%, p<0.05). At the same time, primiparous (77.3%) and multi-pregnant women (63.9%) also dominated in the control group, 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 common complication was threatening early self-abortion (28.8%). SARS during pregnancy were observed in 21.6% of cases, vomiting of pregnant women - in 13.4%. However, at the same time, in the main group, the listed complications occurred significantly less frequently than in the comparison group and in the control group (P1-2<0.05, P13<0.05).

When studying the outcomes of pregnancy, in the main group of women, termination of pregnancy for medical reasons naturally prevailed in the 1st (9.2%) and 2nd-3rd (61.9%) trimesters of pregnancy, which was determined by the need to eliminate affected unviable fetuses. Delivery at term was noted in 17.7% of women (p1-2<0.01), in 2.4% spontaneous abortion and antenatal fetal death were noted. It is natural that in the comparison group, preterm births were 3.7 times less common than in the main group (8.8%, p<0.01).

In the structure of chronic microelement 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 UA, identified in the main group, UA of the nervous system prevailed (34.03%), the second place was occupied by multiple congenital malformations (19.9%), the third was UA of the circulatory system (2.27%). In the main group in the 1st trimester of pregnancy, UARP and ultrasound markers of chromosomal abnormalities were detected in 16.3% of cases. In 83.2% of patients, isolated UAIA or ultrasound of chromosomal abnormalities were diagnosed, in 16.7% the changes were combined. The most frequently detected VUA 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 in the 1st trimester of pregnancy in relation to chromosomal diseases was noted in 16.7% of cases. The highest sensitivity of ultrasound was noted in relation to such anomalies as cystic hygroma of the neck and hydrocephalus (75%).

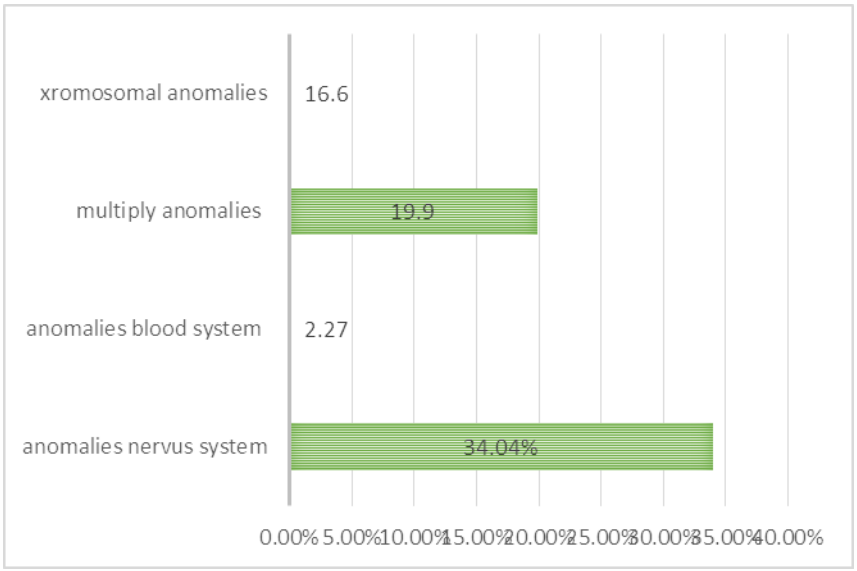

Figure 1 - Results of screening analyzes of the occurrence of IUA

Conclusions:

Summing up the results of our study, we can conclude that in the structure of UAIV detected perinatally, UAIV of the nervous system (34.4%), multiple malformations (19.9%) and congenital

malformations of the circulatory system (2.27%) predominate. In UAVR of the nervous system, the highest sensitivity and specificity has an increase in AFP, as well as ultrasound markers detected in the 1st trimester; with multiple UARP - a decrease in PAPP and ultrasound markers in the 2nd trimester, with UAVR 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.

The predictors of the presence of a fetus in a pregnant UA are a history of congenital malformations, abnormalities according to ultrasound data in the 1st and 2nd trimester, changes in PAPP-A, and the woman's age from 16 to 24 years.

The method of rational formation of risk groups among pregnant women proposed in the article will increase the level of timely diagnosis of congenital anomalies and reduce perinatal and infant mortality in the Bukhara region.

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