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**ТИББИЁТДА ЯНГИ КУН
НОВЫЙ ДЕНЬ В МЕДИЦИНЕ
NEW DAY IN MEDICINE**

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EARLY PREDICTION OF INTRAUTERINE GROWTH RESTRICTION SYNDROME IN PREGNANT WOMEN

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✓ Resume

The aim of the study: prediction of developing fetal growth retardation syndrome. Materials and methods of research: a retrospective analysis of the medical history of the Bukhara city maternity complex for the period 2018-2020 was carried out, as well as a prospective examination of 60 pregnant women in the 2nd and 3rd trimester of gestation. The main group consisted of 30 pregnant women at risk of developing FGRS at 28-38 weeks, the control group consisted of 30 conditionally healthy pregnant women at the time of the examination. Clinical, laboratory and instrumental studies were carried out in all pregnant women to evaluate the fetoplacental system. The results of the study: according to our study the women of main group has more outweigh anamnesis and the results of ultrasound dopplerometry showed more pathological conditions in the fetoplacental system rather than in control group. Conclusion: we can predict FGRS in pregnant women according to risk factors and ultrasound dopplerometry.

Key words: intrauterine growth restriction syndrome, ultrasound examination, Doppler velocimetry, fetoplacental insufficiency.

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Tadqiqot maqsadi: homila o'sishdan ortda qolish sindromining rivojlanishini erta bashorat qilish. Tadqiqot materiallari va usullari: Buxoro shahar tug'ruq majmuasining 2018-2020 yillardagi 30ta kasallik tarixini retrospektiv tahlil qilish, shuningdek, homiladorlikning 2 va 3trimestridagi homilador ayollarni istiqbolli tekshirish o'tkazildi. Asosiy guruh 28-38 xaftada homila o'sishdan ortda qolish sindromining rivojlanish xavfi bo'lgan 30ta homilador ayoldan iborat edi, nazorat guruhi 30ta shartli sog'lom homilador ayollardan iborat edi. Fetoplacental tizimni baholash uchun barcha homilador ayollarda klinik, laboratoriya va instrumental tadqiqotlar o'tkazildi. Tadqiqot natijalari: bizning tadqiqotimizga ko'ra, asosiy guruh ayollari ko'proq og'ir anamnezga ega va ularda ultratovushli dopplerometriya natijalari fetoplacental tizimda ko'proq patologik sharoitlarni ko'rsatdi. Xulosa: ayolning risk omillari hamda ultratovushli dopplerometriya homila o'sishdan ortda qolish sindromini bashoratlashda qollash mumkin.

Kalit so'zlar: homila o'sishdan ortda qolish sindromi, ultratovush tekshiruvi, Doppler velosimetriya, fetoplacental etishmovchilik.

РАННЕЕ ПРОГНОЗИРОВАНИЕ СИНДРОМА ОТСТАВАНИЯ РОСТА ПЛОДА У БЕРЕМЕННЫХ ЖЕНЩИН

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✓ **Резюме**

Цель исследования: раннее прогнозирование развития синдрома задержки роста плода. **Материалы и методы исследования:** проведен ретроспективный анализ истории болезни Бухарского городского родильного комплекса за период 2018-2020 годов, а также проспективное обследование 60 беременных женщин во 2-м и 3-м триместре беременности. Основную группу составили 30 беременных женщин с риском развития СОРП на сроке 28-38 недель, контрольную группу составили 30 условно здоровых беременных на момент обследования. Всем беременным были проведены клинические, лабораторные и инструментальные исследования для оценки состояния фетоплацентарной системы. **Результаты исследования:** согласно нашему исследованию, женщины основной группы имели больший анамнез избыточного веса, а результаты ультразвуковой доплерометрии показали больше патологических состояний в фетоплацентарной системе, чем в контрольной группе. **Заключение:** СОРП можно прогнозировать исходя от риска факторов и ультразвуковой доплерометрии.

Ключевые слова: синдром задержки внутриутробного роста, ультразвуковое исследование, доплерография, фетоплацентарная недостаточность.

Relevance

Fetal growth restriction syndrome (FGRS) refers to the discrepancy between the fetal body weight and the average body weight for this period of pregnancy. The main number of newborns who have undergone to intrauterine growth restriction syndrome is found in Asia, followed by Africa and Latin America [12]. According to M. And Yu. Ismatova (2017) conducted by retrospective and prospective analysis in the perinatal center of Bukhara in 2014, it was determined that among 3,476 urgent deliveries, 73 women had FGRS (5.1%). [10]. The most common cause leading to fetal development disorders in utero is placental insufficiency. Utero-placental blood flow, necessary for optimal supply of nutrients and oxygen to the growing organism, reaches the interstitial space along the spiral arteries. Histological and morphological changes in these arteries are closely related to the stage of trophoblast invasion [1,2,13]. It is believed that uteroplacental insufficiency is caused by anomalies of placentation, more precisely, disorders that occur at the stage of trophoblast invasion. The reactions of the vessels of the terminal villi have compensatory reserves, with their depletion there are no opportunities for the development of an additional vascular network, all this is the beginning of involutive-dystrophic changes with the formation of uteroplacental insufficiency and fetal growth retardation, antenatal fetal loss, premature detachment of the normally and low-lying placenta [8,14]. Chronic inflammatory diseases of the urinary tract and female genital organs can lead to endothelial dysfunction due to the formation of cytokines and protein synthesis disorders. And as a result, these processes can lead to hypercoagulation and the development of FGRS [3,15]. Prediction of fetal growth retardation based on clinical and anamnestic data. Fetal growth retardation is a multifactorial disease [10,11]. In addition to ultrasound diagnostics, Dopplerometry is also an important diagnostic method. To date, a safe, highly diagnostic, rapidly conducted and economically affordable Doppler examination is the main method for assessing the state of uteroplacental circulation and fetal hemodynamics [11,9].

Dopplerometry displays the main changes in the mother-placenta-fetus system. Violation of hemodynamics is the leading cause of fetal disorders [12,8,14]. In recent decades, genes predicting disorders in the fetoplacental system in pregnant women have been studied. These include genes (IL10, IL6, IL6R) that regulate immune responses in the placenta and during implantation, (VEGFA) transformation of the vascular network in the placenta, regulating metabolic function in the placenta (PPARG, IGF II, PLA 1, PLA2), as well as genes that lead to disruption in the blood clotting system during implantation and placentation (F2, F5, FGB, ITGA2, ITGB3, SERPINE1) [4,5,6].

The aim of the study: prediction of developing fetal growth retardation syndrome.

Materials and methods

To solve the tasks, carried out a retrospective analysis of the medical history of the Bukhara city maternity complex for the period 2018-2020 was carried out, as well as a prospective examination of 60 pregnant women in the 2nd and 3rd trimester of gestation. The main group consisted of 30 pregnant

women at risk of developing FGRS at 28-38 weeks, the control group consisted of 30 conditionally healthy pregnant women at the time of the examination.

Result and discussions

According to the retrospective analysis, the average age of pregnant women in the retrospective analysis with FGRS was 28.5 ± 5.12 years (between 21 to 36 years). When analyzing the parity of the retrospective group, there were many patients with the first pregnancy and the first birth, 19 (63.3%) and 18 (63%), respectively, but the number of patients with repeated pregnancy, 11 (36.6%) and multiparous also prevailed: 7 (23.3%). According to retrospective studies, it was revealed that in pregnant women with FGRS, the anamnesis was burdened with various somatic diseases, the analysis of which showed sufficient variability in the frequency of various nosological forms. Anemia was most often noted (90% or more in both groups), ARVI was noted in 43% and varicose veins in 30%, which may be a full risk for the development of FGRS. When studying the obstetric history of women, it was noted that patients with FGRS had a history of hypertensive conditions 33.3% of cases ($p < 0.05$).

We also studied the gynecological history of the examined women. According to retrospective data, many pregnant women were previously observed and treated for various gynecological diseases. As follows from the diagrams presented, inflammatory diseases of the uterine appendages and ectopia of the cervix were most often detected. A high level of inflammatory diseases of the genital organs was observed in all groups, and in women with varicose veins more often than in patients with isolated dilation of the venous vessels of the pelvis. Thus, chronic inflammatory processes of the uterus and appendages in the anamnesis were detected in 37.8% of women. Thus, a retrospective study of the medical history of the examined patients showed that the most significant risk factors for the development of FGRS in pregnant women were burdened obstetric and gynecological anamnesis; parity of pregnancy and childbirth, as well as an increased frequency of somatic pathology.

According to the retrospective analysis, we transformed the main group of women with a burdened somatic, obstetric and gynecological history, which serves as a risk factor for the development of FGRS, and conducted further studies (clinical, laboratory and instrumental) to assess the fetoplacental system. With the help of fetometry ultrasound, we observed the development of the fetus and determined its size from 20 weeks. The data obtained during fetometry are shown in Table 1.

Ultrasound examinations in dynamics were performed in 60 pregnant women of the main and control groups. Significant differences throughout the third trimester of pregnancy were revealed between the values of AC and FL in fetuses of patients of the main and control groups. Thus, the values of AC in the fetuses of pregnant women of the main group were lower than in the fetuses of patients of the control group at 36 weeks - by 7% and at 40 weeks - by 8%. The FL values in the fetuses of pregnant women of the main group were less than in the fetuses of patients of the control group at 36 weeks - by 3% and at 40 weeks - by 4%.

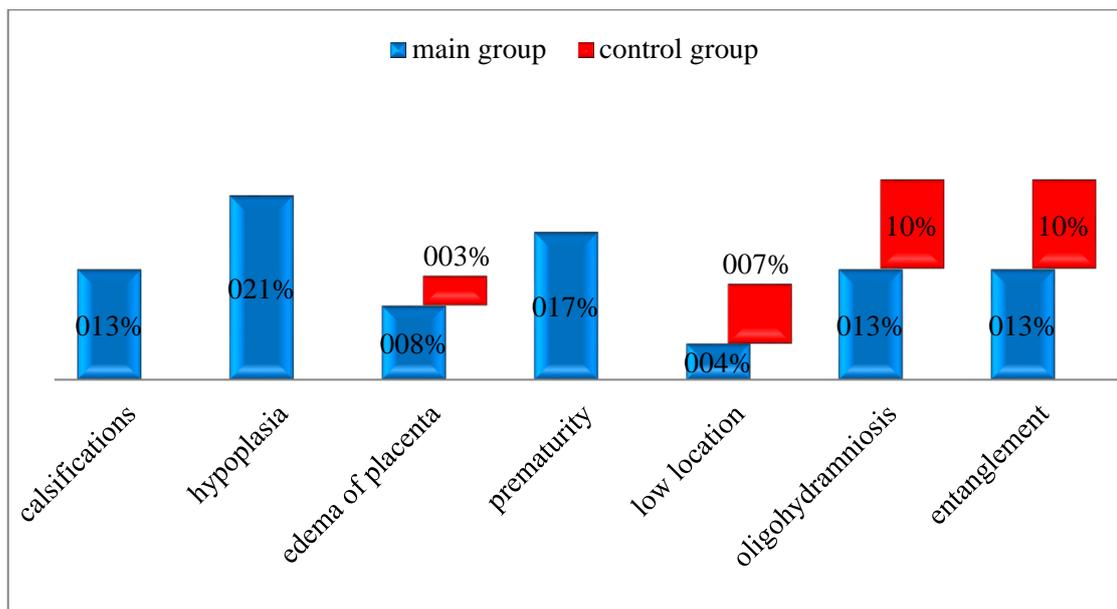
Table № 1. Comparison of fetometric indicators of examined women (mm).

Week of gestation	Indications	Main group, n=30	Control group, n=30
36	BPD	$82,14 \pm 1,20$	$87,61 \pm 0,66$
	HC	$309,9 \pm 2,65$	$320,48 \pm 2,02$
	AC	$289,13 \pm 5,73^*$	$319,70 \pm 3,04$
	FL	$66,18 \pm 1,07^*$	$69,87 \pm 0,58$
40	BPD	$87,03 \pm 0,86$	$90,55 \pm 0,88$
	HC	$329,0 \pm 2,03$	$338,0 \pm 1,73$
	AC	$315,33 \pm 1,45^{**}$	$343,27 \pm 2,90$
	FL	$71,0 \pm 1,15^*$	$73,82 \pm 0,55$

Note : * $p < 0,05$, ** $p < 0,001$ relative to the control group

Ultrasound placentography was performed in pregnant women with a high risk of developing fetal growth restriction syndrome (the main group). At the same time, the following markers of fetoplacental insufficiency were identified during ultrasound and Doppler examination: (73.5%) combinations of premature maturation and "aging" (16.7), calcification (12.5%) and placental

hypoplasia (20.8%) were most characteristic. At this time, women in the control group showed signs such as lack of water (10%) and umbilical cord entanglement (10%) (pic 1).



Pic .1. Ultrasound placentography of examined pregnant women

Nevertheless, it is obvious that the most significant echographic signs for FGRS is the thickness of the placenta. Of the 30 patients of the main group, hemodynamic disorders of placental circulation at the time of the study were absent in 5 (16.7%) pregnant women of the main group, however, the fetuses of these patients had hypotrophy according to ultrasound fetometry. Hemodynamic disorders of the I degree were found in 10 (33.3%) patients, of which fetal hypotrophy was noted in 2 (20%) patients; II degree – in 12 (40%), of which fetal hypotrophy was noted in 4 (33.3%) patients; III degree - in 3 (10%), of which 2 fetuses have hypotrophy (66.7%). In the dynamics of pregnancy, simultaneously with fetometry, all patients underwent Dopplerometric studies of blood flow in the main arteries of the functional mother-placenta-fetus system (uterine arteries, umbilical cord arteries and the middle cerebral artery of the fetus), as well as Dopplerometric assessment.

During dopplerometry of fetoplacental complex vessels, it was revealed that patients of the main group had various degrees of hemodynamic disorders in the arteries of the functional mother-placenta-fetus system, we analyzed their occurrence. During all the studied periods, the values of SDR, IR, and PI in the uterine arteries of the patients of the main group were significantly higher than those in pregnant women of the control group (tab.2). In the patients of the main group, the indicators of vascular resistance in the uterine arteries and umbilical cord arteries were higher than in pregnant women of the control group. Dopplerometric parameters of blood flow in the middle cerebral artery of pregnant fetuses of the main group were lower than similar parameters in pregnant women of the control group.

Table No. 2. Dopplerometric indicators of blood flow in uterine arteries in patients of the main group and the comparison group in the third trimester of pregnancy

Weeks of gestation	Indications	Group of patients	
		Control group, n=30	Main group, n=30
36	SDR	1,86±0,03	2,49±0,21**
	IR	0,46±0,01	0,57±0,02**
	PI	0,66±0,02	1,03±0,20**
40	SDR	1,93±0,07	2,07±0,14
	IR	0,47±0,02	0,51±0,03
	PI	0,67±0,05	0,73±0,09

Note: *p<0.05, **p<0.001 relative to the control group

Thus, in the main group, the speed of blood flow in the venous duct decreases, and the speed of reverse blood flow during atrial contraction in the inferior vena cava increases. At the same time, in the umbilical cord vein, the nature of the blood flow spectrum becomes "pulsating". This indicates the centralization of blood circulation in the fetus

Risk factors associated with fetal FGRS do not always lead to a pronounced violation of the state of the regulatory systems of the fetal body, and, therefore, may not significantly affect the outcome of pregnancy

Conclusion

According to a retrospective analysis, the most significant risk factors for the development of fetal growth restriction syndrome in pregnant women include anemia in 95% of cases, ARVI was noted in 43%, varicose veins in 30% of cases, chronic hypertension in 33% of cases, urinary tract infections in 4% of cases ($p>0.05$). At the same time, it was noted that in the burdened obstetric and gynecological history, the leading positions were occupied by such complications as: threatening miscarriages in 23.3% of cases ($p<0.05$), amniotic fluid discharge in 16.7% of cases ($p<0.05$) and antenatal fetal death in previous pregnancies in 10% of pregnant women ($p<0.05$), chronic inflammatory processes of the uterus and appendages in the anamnesis were detected in 34 (37.8%) women

In pregnant women with a high risk of developing fetal growth restriction syndrome, the following markers of fetoplacental insufficiency were identified during ultrasound and Doppler examination: For pregnant women of the main group (73.5%), combinations of premature maturation and "aging" (16.7), calcification (12.5%) and placental hypoplasia (20.8%) were most characteristic. At this time, women in the control group showed signs such as lack of water (10%) and umbilical cord entanglement (10%).

Of the 30 patients of the main group, hemodynamic disorders of placental circulation at the time of the study were absent in 5 (16.7%) pregnant women of the main group, however, the fetuses of these patients had hypotrophy according to ultrasound fetometry. Hemodynamic disorders of the I degree were found in 10 (33.3%) patients, of which fetal hypotrophy was noted in 2 (20%) patients; II degree – in 12 (40%), of which fetal hypotrophy was noted in 4 (33.3%) patients; III degree - in 3 (10%), of which 2 fetuses have hypotrophy (66.7%).

Thus, the values of AC in the fetuses of pregnant women of the main group were lower than in the fetuses of patients of the control group at 36 weeks - by 7% and at 40 weeks - by 8%. The values FL in the fetuses of pregnant women of the main group were less than in the fetuses of patients of the control group at 36 weeks - by 3% and at 40 weeks - by 4%.

Next, we compared the estimated fetal weights in pregnant women, as this analysis showed, fetal hypotrophy was detected in 6 (20%) of 30 pregnant women of the main group during ultrasound fetometry: 5 (16.7%) of them had a symmetrical shape, 1 (3.3%) had an asymmetric shape. Thus, different degrees of hemodynamic disorders of placental circulation were observed in fetuses of patients of the main group with the same frequency. In the patients of the main group in the uterine arteries and umbilical cord arteries, vascular resistance indicators were higher than in pregnant women of the control group. Dopplerometric parameters of blood flow in the middle cerebral artery of pregnant fetuses of the main group were less than similar parameters in pregnant women of the control group.

The outcome of pregnancy and childbirth in pregnant women with FGRS is determined by the time of onset of the disease, the severity of structural disorders in the placenta, the state of the adaptive and compensatory mechanisms of the mother-placenta-fetus system. In this regard, a comprehensive study of the functional state of the mother-placenta-fetus system using ultrasound fetometry and placentometry, ultrasound examination of amniotic fluid, Doppler examination of uteroplacental and fetoplacental blood circulation is of particular importance to optimize the choice of delivery method

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