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Disorders in the Mother-Placenta-Fetus System and their Role in the Development of Fetal Growth Restriction Syndrome

Aslonova M. J.
Bukhara State Medical Institute Department of Obstetrics and Gynecology. Uzbekistan, the city of Bukhara

Abstract
The article presents the effectiveness of doppler imaging for assessing blood flow in large vessels, including the umbilical, uterine artery and middle cerebral artery. 90 women were examined in the second trimester, and 45 women showed signs of fetoplacental insufficiency, such as fetal growth restriction syndrome at 28-34 weeks. The study of utero-placental-fetal blood flow allows timely detection of early signs of a violation in the fetoplacental system and its timely correction.

Keywords: Fetal growth restriction syndrome, dopplerometry, middle cerebral artery, umbilical artery.

Introduction

Today, fetal growth restriction syndrome (FGRS) is one of the most important problems of modern obstetrics, which plays an important role in the manifestation of perinatal diseases andfatal outcomes. Fetal growth restriction syndrome occurs with a frequency of 5 to 22% among full-term infants and 18 to 24% among premature infants. According to the World Health Organization, "...the incidence of fetal growth retardation syndrome in Central Asia is 31.1%, in the USA - 10-15%, in Russia - 2.4-17%...". It is often believed that nonвынашивание-gestation and fetal growth restriction syndrome are associated with the presence of common pathogenetic mechanisms in development). [2,4,7,10,13].

A number of studies are being conducted around the world regarding forecasting issues, to identify its causes and the consequences that come from it, as well. Aspects for identifying the causes of FGRS –rearly detection of them, using highly sensitive laboratory tests for both diagnosis , and screening. Therefore, early diagnosis and treatment of fetal growth restriction syndrome, especially the development of prevention methods for specialists in this field, remains poorly understood and controversial [1,3,7,10,15]. Fetal growth restriction syndrome is an important risk factor for neonatal and post-neonatal death. The mortality rate of children with this pathology is 3-10 times higher than in newborns with normal development, which increases the risk of stillbirth in young children by 8 times. Epidemiological studies confirm that a number of changes in the blood coagulation system, such as maternal thrombophilia in 40-75% of cases, lead to the development of pathogenetic mechanisms of pregnancy aggravation, including fetal loss syndrome in 39.1% of casesплода, 11,5 % , retrochorial hematoma in 11.5 %, premature

detachment of the normally located placenta in 13.6%, complications in the form of thromboembolism during pregnancy and the postpartum period). [8,12,14,17].

Purpose of the study:

To develop criteria for predicting the development of fetal growth restriction syndrome based on the determination of ultrasound and doppler markers.

Materials and methods

In order to solve the identified problems, 120 pregnant women with a gestation period of 24-36 weeks were examined. All examined women were divided into 2 groups: the main group, 90 pregnant women, with FGRS, the control group consisted of, and 30 pregnant women with a physiological course of the antenatal period.

During the study, on the basis of the research department of the Bukhara State Medical Institute, the Bukhara Regional Screening Center, the Department of Obstetrics and Gynecology and the research was conducted in the Bukhara city maternity complex. Metody (ultrasound and doppler) in the regional screening center, as well as maternity hospitals and private clinics in Bukhara.

Results

The average age of pregnant women in the main groupe was 26.78 ± 0.63 years, in the control group-26.20 ± 0.9 years (ranged from 19 to 37 years) ($p < 0.05$).

Analysis of the obtained data on the place of residence of pregnant women showed that 46 patients (51.1%) of the main group live in cities (mainly urbane), 44 (48.9%) - in rural areas. In the control group, data close to the above were obtained: 16 womenли lived in the city (53.3%); in rural areas – 14 (46.7%).

The reproductive function of pregnant women included in the study was evaluated taking into account the number of pregnancies in the anamnesis and their outcome. When analyzing the ratio of pregnancies with FGRS during pregnancy, it was found that this pathology significantly develops in women who had multiple pregnancy (16% vs. 1% in the control group, $p<0.05$).

In the study of obstetric history of women with a history of FGRS, miscarriage (10% vs. 1% in the control group, $p<0.05$), preterm birth (11.6% vs. 3.3% in the control group, $p <0.05$) and FGRS (22% vs. 1% in the control group, $p<0.05$) previous pregnancies were reliably recorded. The study groups were similar in other indicators of obstetric history.

Analysis of the structure of gynecological diseases in the examined women showed that in the main group, pelvic and genital inflammatory diseases (endometritis, colpitis)were common respectively, in 34 (37.8%) and uterine fibroids in 14 (15.5%) women.

The medical history of the examined women showed the presence of various somatic diseases. Somatic diseases such as anemia (95%), varicose veins (30%), urinary tract infections (4%), and chronic arterial hypertension (13%) were detected more frequently in the main group than in the control group ($p<0.05$).

Thus, when studying the medical history of the examined patients, the most important risk factors for the development of FGRS in pregnant women are a burdened history of obstetrics and gynecology, as well as a high frequency of somatic pathology.

Ultrasound examination was mainly performed in 90 pregnant women of the main group, who

were divided into 3 subgroups depending on the level of FGRS.

Using ultrasound fetometry, we observed the development of the fetus and determined its size in 4 weeks from the 28th week. The data obtained during fetometryare shown in Table 1.

Table 1 Comparison of fetometric parameters (mm) in the examined women

Pregnancy period	Indicator	Main group			Control group, n = 30
		I degree, n = 34	II degree, n = 42	III degree, n = 14	
28	BPR	69,75±0,1,8767,5,1,87^	±2,3461,75^	±0,05**	70,85±3,06
	CH	256,75±4,72^	243,1,15±2,14***	236,8383±0,04** *	264.05±5.13
	CA	226,0±2,05***	219,0±2,24***	209,6,6±0,6***	236,95±1,07
	LF	52,6,6±1,3951,0^	±0,53*	48,3,3±0,3***	53,65±1,22
32	BPR	79,21±2,77^	77,21±1,474^	75,45,45±0,7,78*	80.20±2.08
	CH	GAS 293,00±5,829^	290,12,12±2,5,592^	288,23,23±3,02297,45^	±3,62
	CA	level 261,65,65±3,2727***	259,21±3,92***	251,06,06±4,14***	278,40±1,84
	LF	62,15,15±1,6760,68,67^	±1,0958,68^	58±1,5*	63,00±1,26
36	BPR	85.90±1.49849^	82.14,14±1,3535***	81,75,75±1,29***	87,61±0,8585
	CH	318,0±2,493^	309,9,9±3,84***	301,11±2,2***	320,48±1,2
	CA	level 297,21±2,12***	289,13,13±2,86**	281,61,61±3,83***	319,70±2,31
	LF	67.58±1.226^	66,1,18±0,64***	65,12,12±0,64***	69,87±0,7979

Note:- P0. 05; *- P0. 05; **-P0. 01; ***-P0. 001; significance of differences in indicators in patients of the compared group with the control group

As can be seen from Table 1, significant differences were found between the values of abdominal circumference (CA) and femoral bone length (LF) in fetal women of the main and control groups during the entire third trimester of pregnancy. Thus, the value of CA in the fetus of the main group of pregnant women was 5.5% lower than in the fetus of the control group at 28 weeks, by 7% - at 32 weeks and by 11% - at 36 weeks. -legal age.

LF values in fetuses of the main group of pregnant women were 5% lower than in fetuses of the 28-week control group, 4 % — in 32-week — olds, and 3%-in 36-week-olds. Then we compared the estimated fetal weight in pregnant women of the main and control groups, which was calculated on the basis of ultrasound fetometry data.

This analysis showed that 63 (70%) out of 90 patients in the main group had fetal hypotrophy detected by ultrasound fetometry: 29 (32%) had a symmetrical shape, and 61 (68%) had an asymmetric shape.

To optimize the antenatal diagnosis of FGRS in the fetus, we developed ultrasound markers, and then evaluated their effectiveness in the diagnosis of:

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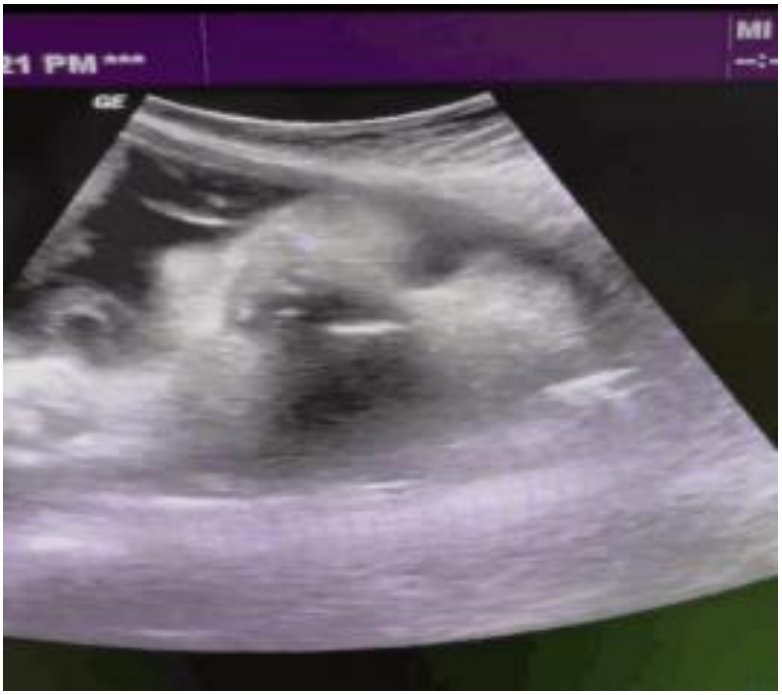


2. Pregnant N. (birth history No. 1890). Diagnosis: Pregnancy II 33.4 weeks. FGRSII II degree. Circulatorye blood circulation disorders of the fetoplacental system are 2b degrees. The buccal coefficient is 8 mm.

The frequency of detection by ultrasound markers in the clinical groups was as follows (Table 2). A head index <71% indicated a dolichocephalic shape of the fetal head and was found in 9 (10%) cases in the main groups, while a head index >87% was found only in 9 (10%) cases in the main groups. brachycephalic shape of the fetal head. Therefore, these indicators are not effective for FGRS. In addition, in the control group, more than 87% were detected in 2 (6.7%) cases and less than 71% in 1 (3.3%) case, which can be explained by the constitutional specifics of the skull configuration in fetuses.

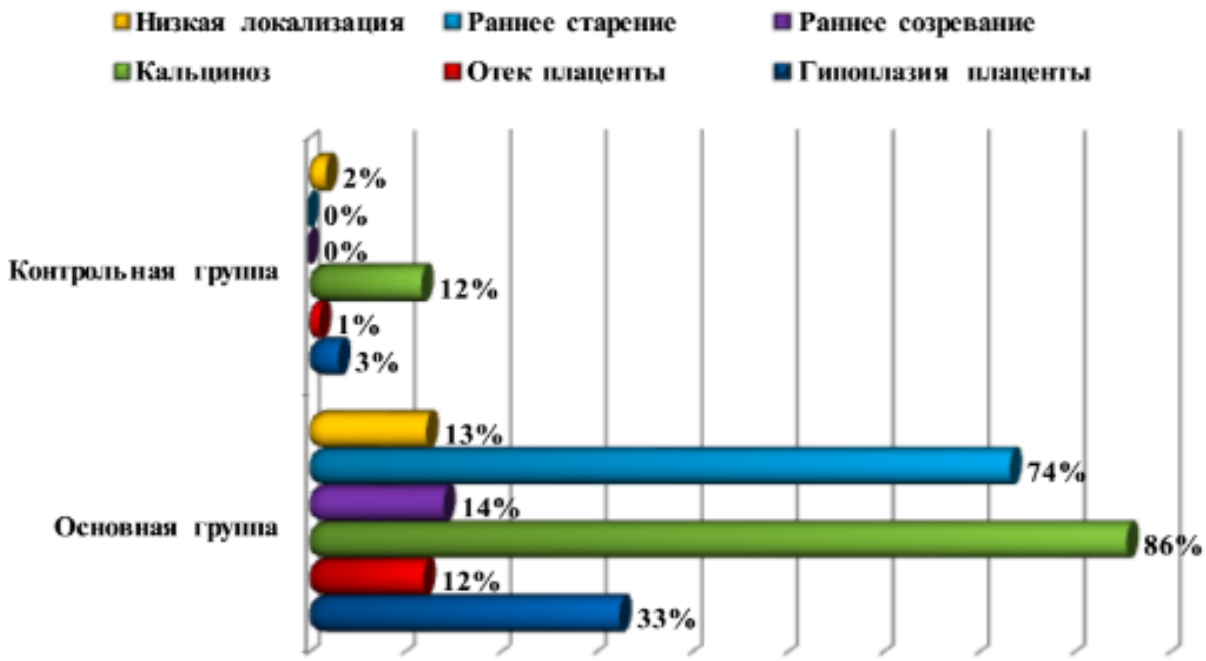
Table 2. Ultrasound markers in the study groups

№	Indicator no	Main group						Control group, n = 30	
		I degree, n = 34		II degree, n = 42		III degree, n = 14			
		Abs.	%	Abs.	%	Abs.	%	Abs.	%
1.	**Buccal index <10 mm**	8	23,5%	30	71,4%	14	100%	0	0
2.	**Cephalic Index <71%**	1	2,9%	5	12%	3	21,4%	1	3,3%
3.	**Cephalic Index> 87%**	1	2,9%	4	9,5%	4	28,5%	2	6,7%

The main groups showed an increase in the number of ultrasound markers with an increase in the severity of FGRS, as well as an increase in the number of pregnant women with different ultrasound markers. This is largely due to the fact that the buccal index is less than 10 mm (in

pregnant women with grade I FGRS - 8 (23.5%), grade II - 30 (71.4%), and in the group with grade III FGRS - 100% of pregnant women). A decrease in the buccal index is associated with immaturity of subcutaneous fat in fetuses with FGRS, and placental hypoplasia is associated with placental insufficiency.

Ultrasound specificity of the placenta in the analyzed small groups is shown in Figure 3.



Pic. 1. Data of ultrasound placentography in examined pregnant women

Lack of water was detected in 3 (8.8%) pregnant women with grade I, 10 (23.8%) pregnant women with grade II, and 6 (42.8%) pregnant women with grade III. The amniotic fluid index (AFI) was moderate: from 5 to 8 cm in grade I, from 2 to 5 cm in grade II, and less than 2 cm in grade III. In group I, it was moderate from 5 to 8 cm, in group II from 2 to 5 cm, in group III it was less than 2 cm.

In the main groups, placental calcifications were observed in 32 pregnant women (35.6%). At the same time, the level of placental maturation was corresponding in all pregnant women with FGRS of the first degree, in pregnant women with FGRS of the third degree-in half of all cases, its premature "aging" was noted, and in pregnant women with FGRS of the second degree - 14 (33.4%) did not meet the deadline, and in 11 (78.6%) there were cases of premature "aging" and in 3 (21.4%) cases - morphofunctional insufficiency. In most cases, a combination of several exographic features was observed. In the individual analysis, changes in placental thickness, placental cysts, premature maturation and "aging" were observed in 10 cases (71.4%) in a small group with grade III FGRS. as well as a combination of exographic signs such as calcification. Of 42 women with grade II FGRS, 36 pregnant women (85.7%) were characterized by a combination of symptoms such as premature maturation and "aging", calcification, low and placental density.

However, the most important echographic marker of grade II-III FGRS was placental thickness. Thus, placental hypoplasia was 1.4 times more common in patients with severe FGRS than in subgroups I and II. On the contrary, the placental size thickening was 2.3-2.5 times greater in

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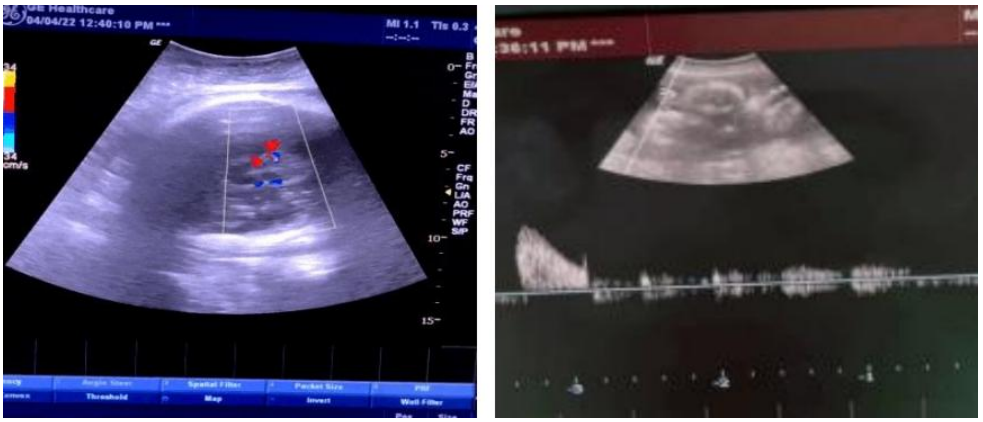
grade II–III FGRS than in group I and control. This may be due to the peculiarities of the formation of placental compensatory mechanisms.

Simultaneously with fetometry in pregnancy dynamics, all patients underwent doppler studies of blood flow in the main arteries of the mother-placenta-fetus functional system (uterine artery, umbilical artery and fetal midbrain), as well as Doppler evaluation.

In the main group of women, we analyzed their occurrence due to the fact that hemodynamic disorders in the arteries of the functional mother-placenta-fetus system were observed at different levels. Of the 39 pregnant women of the main group, 12 (13.3%) had no hemodynamic disorders of placental circulation at the time of the study, but according to ultrasound fetometry, hypotrophy was noted in the fetuses of these patients. Grade I hemodynamic disorders were observed in 34 (43.6%) patients, including fetal hypotrophy in 11 (32.4%) patients. Grade II hemodynamic disorders were detected in 21 (26.9%), of which fetal hypotrophy was noted in 10 (47.6%), grade III hemodynamic disorders were detected in 11 (14.1%), of which fetal hypotrophy was detected in 8 (72.7%), acute circulatory disorders-in 12 (15.4%), of which 10 (83.3%) patients had atrophy(Fig. 4).

We started our analysis of the results of a placental blood flow doppler study by comparing vascular resistance indicators in the main arteries.



Ris. 4. Hemodynamic disorders of the fetoplacental complex (UA, PA) on Doppler analysis

According to the results of a Doppler study of blood flow in the uterine arteries in pregnant women examined in the third trimester, the values of systole of diastolic ratio (SDR), resistance index (IR), pulsation index (PI) in the uterine arteries of the main group of patients in all the studied periods were significantly higher compared to these values in pregnant women of the control group.

In the main group, 6 pregnant women had severe violations of fetal blood flow in the period from 32 to 36 weeks of gestation. In these disorders, the SDR in the umbilical artery has no mathematical significance, and since the IR is always equal, only PI is shown. In the main group, the average PI of the umbilical artery was 2.16 ± 0.15 ($p < 0.05$) in patients with acute fetal blood flow disorders. According to Doppler measurements in the umbilical arteries of patients in the main group, SDR was 42-61%, IR - 16-39%, and PI - 33-98% higher than in pregnant women in the control group.

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Doppler blood flow in the middle cerebral artery in the fetus of the examined pregnant women showed a significant decrease in these indicators compared to the control group in the main group of women (Table 3).

Table 3 Doppler parameters in the middle cerebral artery of the fetus in the main and control groups

Pregnancy period	Indicator	Patient group	
		Control group	Main group
28	SDR	6.57±0.42	5.06±0.3232**
	IR	0.84±0.03	0.80±0.03PI^
	PI	2.0±0.15,15	1.54±0.0707**
32	SDR	7.81±0.2323	4.68±0.2828***
	IR	0.85±0.01	0.78±0.03*
	PI	2.07±0.0909	1.68±0.0909**
36	SDR	5.33±0.2424	4.87±0.22***IR***
	IR	0.79±0.02	0.78±0.02***PI***
	PI	1.76±0.07	1.70±0.0808^

Note:- P0. 05; *- P0. 05; **-P0. 01; ***-P0. 001; significance of differences in indicators in patients of the compared group with the control group

To identify signs of centralization of fetal-placental blood flow, we calculated the cerebral-placental ratio (CPR), which is a division of the resistance index values in the fetal midbrain artery and the umbilical artery.

CPR = RI (middle cerebral artery) / RI (umbilical artery)

CPR values differed at all time periods calculated based on the results of the study of fetal-placental circulation in the main group of patients and in the control group of patients. So, at 32 weeks in the fetus of the main group of patients, its decrease was revealed by 13%, at 36 weeks-by 15%.

Thus, different indicators of placental circulation-from the first to the acute level-were observed with the same frequency in fetuses of the main group of pregnant women. In the main group of pregnant women, the indicators of vascular resistance in the uterine arteries and umbilical cord arteries were higher compared to pregnant women in the control group. Doppler parameters of blood flow in the middle cerebral artery in the fetus of pregnant women in the main group were lower than in the control group.

The results of the hemastasiogram are presented in Table 4, which clearly shows a significant increase in the main indicators such as fibrinogen a, D-dimer, APTT (Table 4).

Tableica 4. Clinical and laboratory data of pregnant women with SORP

Indicator	Main group (n = 90)	Control group (n = 30)
Ppothrombin index, %	76,2±4,4**	95,6±1,88
Fibrinogen value , g / l	5.2±0.12,12**	3.1±0.0909
Activated partial thromboplastin time (APTT)	22.1±3.2*	25.8±1.11
D-dimer, ng/ ml	1170.2±58.4**	639.5±23
Ferritin, ng/ ml	66.6±5.84**	87.6±2.02
S-reagent protein, mg / l	12.1±0.6**	5.7±0.72

Note: *- P0. 05; **- P0. 001; significance of differences in indicators in patients of the compared group with the control group

With elevated fibrinogen and APTT values, we decided to assess the degree of D-dimer hemastasis disorder, which is the mostreliable indicator.

D-dimer was also high in women with FGRS, especially in those who had a complicated course - hypertensive disorders, preeclampsia of varying degrees, exacerbation of extragenital pathology, with varicose veins ofvarious localization. Out of 90pregnant catso, we tested the D-dimer with a double analysis of fibrinogen over 5 g/l, and the results did not always show violations in the last marker. From this, it should be noted that with low rates offibrinosis not with SORP, we still recommend that the degree ofhemostasis disturbance shouldbe evaluated with a D-dimer, which is the most sensitive and specific for such complications.

Thus, the study ofthe hemostatic system revealed some deviations: pregnant women with FGRS had a violation of the blood clotting process. Changes in the hemostatic system were significantly higher ($P<0.05$). An increase in the level of fibrinogen, c-reactive protein has a clinical effect. In severe cases, the level of D dimer increases significantly, which is a potential risk factor and grounds for an unfavorable prognosis.

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