



INTERCONNECTION OF BIOCHEMICAL AND HEMODYNAMIC INDICATORS IN PREMATURE LABOR

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Abstract

Premature labor (PL) continues to be at the epicenter of attention of obstetricians and gynecologists around the world. The nature of the relationship between the synthesis of placenta-specific proteins and uterine hemodynamics in threatening preterm labor was studied. The study included 150 women with a clinic of threatened preterm birth with gestational terms from 22 to 36.6 weeks (main group), who were treated in the Perinatal Center and City Maternity Complex in Bukhara. The control group consisted of 50 pregnant women with the physiological course of gestation at the same time. The revealed character of correlations between the content of gravidar proteins and the parameter of uterine hemodynamics in threatening preterm labor indicates the presence of progressive disorders in the mother-placenta-fetus system. The results of the study dictate the need for further study of the pathogenetic mechanisms of miscarriage in order to improve the existing principles of treatment.

Keywords: premature birth, risk factors, PAMG1, hemodynamic parameters.

ВЗАИМОСВЯЗЬ БИОХИМИЧЕСКИХ И ГЕМОДИНАМИЧЕСКИХ ПОКАЗАТЕЛЕЙ ПРИ ПРЕЖДЕВРЕМЕННЫХ РОДАХ

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Резюме

Преждевременные роды (ПР) продолжают оставаться в эпицентре внимания акушеров-гинекологов всех стран мира. Изучен характер взаимосвязи синтеза плацентоспецифических протеинов и маточной гемодинамики при угрожающих преждевременных родах. В исследование включены 150 женщин с клиникой угрожающих преждевременных родов при сроках гестации от 22 до 36,6 недель (основная группа), находившихся на лечении в Перинатальном центре и городском родильном комплексе города Бухары. Контрольную группу составили 50 беременных с физиологическим течением гестации аналогичных сроков. Выявленный характер корреляционных связей между содержанием гравидарных белков и параметром маточной гемодинамики при угрожающих преждевременных родах свидетельствует о наличии прогрессирующих



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нарушений в системе «мать-плацента-плод». Результаты проведенного исследования диктуют необходимость дальнейшего изучения патогенетических механизмов невынашивания беременности для совершенствования существующих принципов лечения.

Ключевые слова: преждевременные роды, факторы риска, ПАМГ1, гемодинамические параметры.

ERTA TUG'RUQDAGI BIOKIMYOVYIY VA GEMODINAMIK KO'RSATGICHLARNING O'ZARO BOGLIQLIGI.

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Annotation

Erta tug'ruq (ET) dunyo bo'ylab akusher-ginekologlarning diqqat markazida bo'lib kelmoqda. Platsentaga xos bo'lgan oqsillarni sintezi va bachadon gemodinamikasi bilan muddatdan oldingi tug'ruq paytida bog'liqlikning tabiat o'rganildi. Tadqiqotga Buxoro shahridagi perinatal markaz va shahar tug'ruq kompleksida davolangan 22-36,6 haftalik (asosiy guruh) gestatsion muddat bilan erta tug'ilish klinikasi bo'lgan 150 nafar ayol jalg qilingan. Nazorat guruhi analogik 22-36,6 haftalik fiziologik homiladorlikni o'tayotgan 50 ta ayoldan iborat. Erta tug'ruq paytida tahdid soluvchi gravidar oqsillari va bachadon gemodinamikasi parametri o'rtasidagi o'zaro bog'liqlikning aniqlangan xarakteri ona-platsenta-homila tizimida progressiv kasalliklarning mavjudligini ko'rsatadi. Tadqiqot natijalari davolashning mavjud tamoyillarini takomillashtirish uchun homiladorlikning muddatiga yetmasligining patogenetik mexanizmlarini yanada o'rganish zarurligini belgilab beradi.

Kalit so'zlar: erta tug'ilish, xavf omillari, PAMG1, gemodinamik ko'rsatkichlar.

Relevance

Premature birth remains one of the urgent problems of modern obstetrics, as it determines the level of perinatal mortality and morbidity [1,3,5,7]. Of no small importance are the psycho-social, economic, demographic aspects of the problem of undermaturity, as well as the frequency of this pathology, which has not been has a downward trend. All this indicates the need for a comprehensive study problems of premature birth, the search for new approaches to forecasting. Since it is PR that make an unfavorable contribution to the statistics of perinatal morbidity and mortality [2, 4, 6,8,10]. Literary sources claim that despite





the advances in modern medicine, the incidence of PR remains in the range of 25 to 30%. At the same time, the rate of early neonatal mortality among premature newborns is 60-70%, and the incidence exceeds 50% [3]. Special attention should be paid to the problems of nursing premature babies born with extremely low body weight [1,5,7,9.].

Among the risk factors for PD, a significant role belongs to infectious pathogens, inflammatory processes, dysfunction of the immune and endocrine systems [11.12.13.14.]. There is an opinion about the important role of genetic mutations in the pathogenesis of PR. However, to date, a single mechanism for implementing the PR has not been defined. And the PRs themselves are considered a polyetiological clinical syndrome, which is characterized by a chronic course, with the obligatory participation of the fruit factor and environmental factors in the pathogenesis. At the same time, some scientists associate the occurrence of clinical symptoms of various forms of miscarriage with the development of placental insufficiency [15, 16,17.]

Purpose of the Study

To study the nature of the relationship between the synthesis of placenta-specific proteins and uterine hemodynamics in threatening preterm labor.

Material and Methods

The study included 150 women with a clinic of threatened preterm birth with gestational age from 22 to 36.6 weeks (main group), who were treated at the Perinatal Center and the city maternity complex of the city of Bukhara. The control group consisted of 50 pregnant women with the physiological course of gestation at the same time.

Examination of pregnant women was carried out in accordance with Order No. 572n. Doppler ultrasound examination (US) was performed on a HITACHI-5500 apparatus using broadband, ultra-high-density convex probes 3.5-5.0 MHz and cavity probes 5.0-7.5 MHz. Additionally, in terms of diagnostic measures, the content of placenta-specific alpha-1-microglobulin (PAMG-1) in the blood serum of pregnant women was studied by the method of enzyme-linked immunosorbent assay (ELISA) using diagnostic kits (Russia). The results were recorded using an enzyme immunoassay analyzer (Stat fax, USA). Statistical processing was performed using the software package "Excel MS Office Professional" and "Statistica 6.0", with the derivation of $M + m$, percent, logarithmic means (x) with a 95% confidence interval and the reliability of differences according to Student's t-test and Fisher's exact test (R). The relationship between the studied parameters was established on the basis of correlation analysis





using nonparametric methods for testing statistical hypotheses. Correlation was assessed by Spearman's rank correlation coefficients (R).

Research Results and their Discussion

The age of pregnant women ranged from 19 to 36 years, while the average age in both groups was comparable (Table 1).

A detailed study of the obstetric and gynecological history showed that 56% of women in the main ($n = 84$) and 53.1% of the control ($n = 26$) groups had their first birth. At the same time, out of 72 multiparous patients of the main group, every second previous pregnancy ended in preterm labor ($n = 39$; 54.2%). The frequency of undergone abortions in the main group was 14 times higher than the control indicator (Table 1). And various forms of miscarriage in the first half of gestation and ectopic pregnancy were traced in the anamnesis only in the main group. Among gynecological diseases in the group of pregnant women with the threat of premature birth, inflammatory processes of the genital organs, menstrual irregularities and cervical pathology were significantly more often detected (Table 1). The results obtained coincide with the opinion of many scientists about the significant importance of a history of premature birth, as well as gynecological diseases in the pathogenesis of pregnancy failure.

Table 1. Features of the obstetric and gynecological history in the groups of women examined

The investigated indicator	Main group (n=150)		Control group (n=50)	
	N	%	n	%
Average age	44,5±3,6		43,6±4,1	
Childbirth	72	47,9±1,3	23	46,9±1,2
Abortions	64	42,7±1,1*	1	3,1±0,3
Spontaneous miscarriage	9	6,3±0,5	0	0
Non-developing pregnancy	20	13,5±0,7	0	0
Ectopic pregnancy	8	5,2±0,4	0	0
Infertility	30	19,8±0,9	0	0
Inflammatory diseases of the genital organs	59	39,6±1,2	0	0
Menstrual irregularities	39	26,1±1,1	3	6,3±0,4
Uterine fibroids	9	6,3±0,5	0	0
Genital endometriosis	5	3,12±0,3	0	0
Endocervicitis / cervical erosion	81	54,2±1,5	1	3,1±0,3

Note: hereinafter * - reliability of differences with the control group ($P < 0.05$).



The analysis of extragenital pathology in the main group revealed a high proportion of diseases of the urinary system in the form of pyelonephritis and cystitis (up to 41.2%) (Fig. 1). The incidence of chronic gastritis and pancreatitis in women in the main group was 5 times higher than in the control group, and endocrinopathies (diffuse enlargement of the thyroid gland without dysfunction) and obesity were diagnosed in the main group 2-3 times more often.

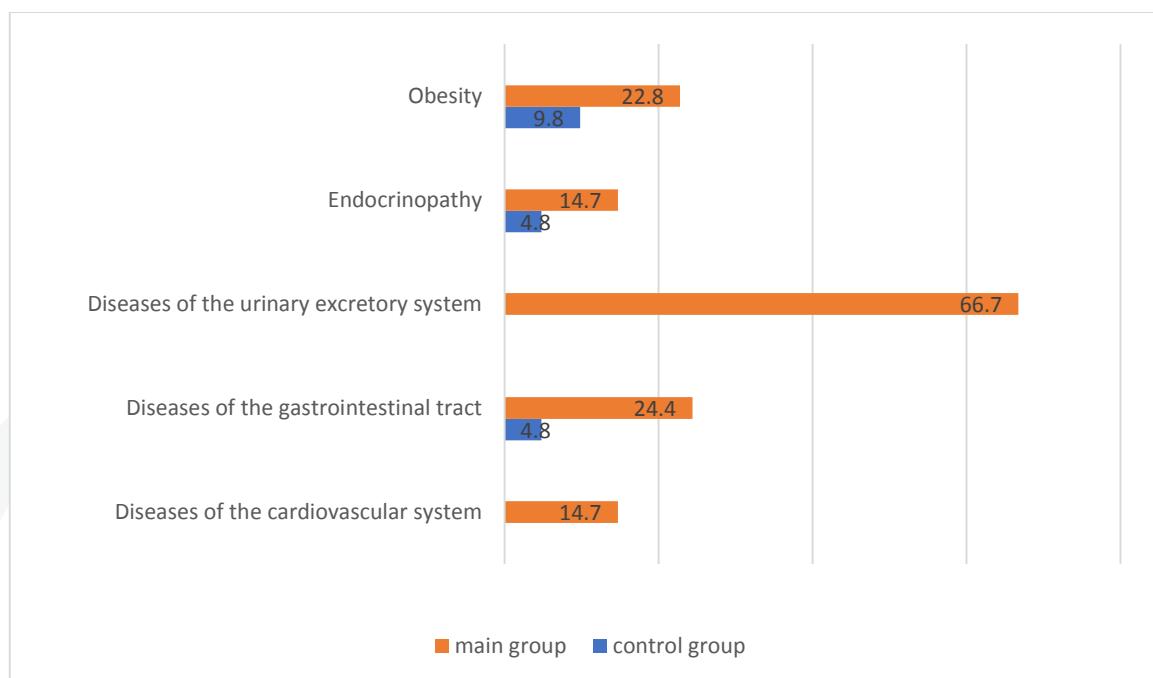


Fig. 1. Somatic diseases in groups.

Literature sources also confirm the connection between the low index of somatic health of pregnant women and the development of placental dysfunction, which directly affects the course and outcomes of the gestational process.

When assessing the characteristics of the course of pregnancy before the inclusion of pregnant women in a prospective study, a high incidence of complications of gestation in the study group was revealed (Fig. 2). Toxicosis of the first half of pregnancy in patients of the main group was 3 times more frequent in comparison with the control group, the proportion of threatening termination at different periods of gestation was 14 times higher than the control values. Various disorders of the uteroplacental-fetal blood flow (UFBF), fetal growth retardation and pathology of the amniotic fluid (oligohydramnios and polyhydramnios) were traced only in the main group. In addition, colpitis and acute respiratory viral infections (ARVI) were diagnosed only in this group during pregnancy (Fig. 2).

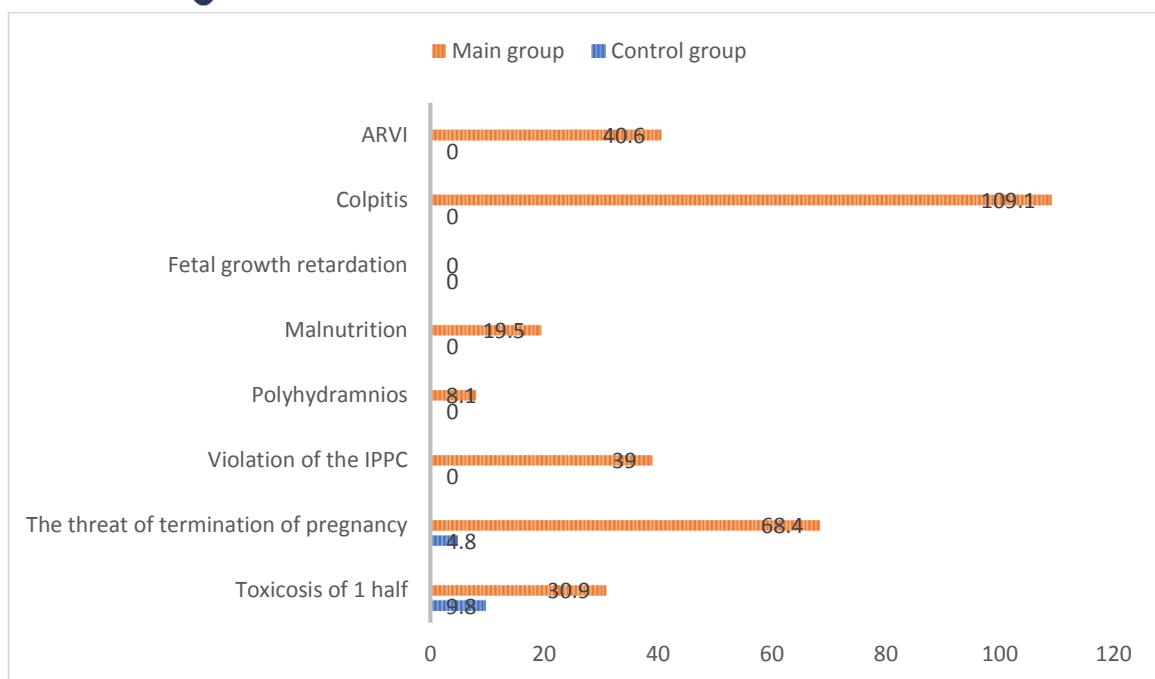


Fig. 2. Features of the course and complications of pregnancy in groups.

The results of a complex ultrasound scan in pregnant women with a clinic of threatening termination made it possible to visualize signs of premature maturation of the placenta in 62.5% of women ($n = 94$), IGR - in 27.1% ($n = 41$), polyhydramnios - in 4.2% ($n = 6$), lack of water - 19.8% ($n = 30$). In addition, according to cervicometry data, a significant shortening of the average value of the cervical length in the study group (24.5 ± 1.7 mm) was established in comparison with the control data (43.6 ± 1.2 mm) ($P < 0.05$). Moreover, in every third patient of the main group ($n = 50$; 33.3%), the length of the cervix was less than 20 mm. At the same time, we did not find any pronounced disorders of the uteroplacental and fetal-placental blood flow in pregnant women of the main group. However, a comparative analysis of the qualitative parameters of Doppler measurements in the uterine arteries showed a slight decrease in the indices of peripheral vascular resistance against the background of a slight increase in the velocities of systolic and diastolic blood flow, in the absence of significant differences in the parameters between the groups (Table 2). The data obtained are consistent with the opinion of other researchers about the importance of an increase in the velocities of arterial and venous blood flow against the background of a decrease in peripheral resistance of the uterine vessels with coordinated uterine contractions in the last two weeks of gestation, as well as with the appearance of clinical symptoms of premature termination of pregnancy.



Table 2. Results of dopplerometry of the uterine arteries in groups

The investigated indicator		Main group (n=150)	Control group (n=50)
СДО	22-31 weeks	1,82±0,3	1,85±0,3
	32-36 weeks	1,67±0,3	1,74±0,2
ПИ	22-31 weeks	1,04±0,2	1,1±0,3
	32-36 weeks	0,9±0,3	0,91±0,3
ИР	22-31 weeks	0,43±0,3	0,46±0,2
	32-36 weeks	0,42±0,3	0,43±0,2

The study of specific proteins of the "pregnancy zone" indicated a violation of the protein-synthetic function of the uteroplacental complex with the threat of premature birth (Table 3).

Table 3. Results of the study of placenta-specific protein

The investigated indicator		Main group (n=96)	Main group (n=32)
PAMG-1	22-31 weeks	157,4±8,2*	78,3±4,2
	32-36 weeks	185,3±9,6*	92,2±5,8

The content of PAMG-1 in the blood serum of pregnant women significantly increased 2 times ($P <0.05$) in the main group in relation to the same parameters in the control group ($P <0.05$). An increase in PAMG-1 is considered by many scientists to be a manifestation of the maladaptive nature of the "mother-placenta-fetus" system with the dominance of programs aimed at suppressing or stopping the further development of pregnancy.

To obtain specific mathematical and logical dependencies that establish relationships between the studied values, we calculated the correlation coefficients that allow us to determine the effect of placental dysfunction on the state of uterine hemodynamics in threatening preterm labor. Taking into account the unidirectionality of the revealed changes in the qualitative parameters of uterine hemodynamics in pregnant women of the main group, to calculate the correlation coefficients, we used the mean value of IR in the right and left uterine arteries in both groups. In the physiological course of pregnancy, no significant relationships were found: there was a weak positive relationship between IR and the level of PAMG-1 ($r = 0.146$; $P > 0.2$). When a clinic of threatening termination of pregnancy appeared, an increase in the connection with a change in the signs of the correlation between the parameter of uterine hemodynamics and the intensity of synthesis of placenta-specific protein was observed. According to the results of the correlation analysis, a significant negative relationship with the PAMG-1 level was established ($r = -0.621$; $P <0.05$).





Conclusion

The revealed character of correlations between the content of the gravidar protein PAMG1 and the parameter of uterine hemodynamics in threatening preterm labor indicates the presence of progressive disorders in the mother-placenta-fetus system: maladjustment of the uteroplacental complex in the form of activation from the maternal part and inhibition of the protein-synthetic function of its fetus component is accompanied by a decrease in resistance to uterine blood flow, which contributes to increased vascularization of the cervix and its structural changes, increasing the risk of premature birth. The results of the study dictate the need for further study of the pathogenetic mechanisms of miscarriage in order to improve the existing principles of treatment.

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