JOURNAL OF MULTIDISCIPLINARY SCIENCES AND INNOVATIONS
VOLUME 5, ISSUE 02
MOPNTHLY JOURNALS
ISSN NUMBER: 2751-4390
IMPACT FACTOR: 9,08

PREDICTING THE DEVELOPMENT OF PRETERM LABOR IN MICROBIOTA CHANGES BASED ON INSULIN RESISTANCE

Temirova Dilnoza Olimjonovna
Asia International University

Annotation

Premature birth is the leading risk factor for neonatal mortality, accounting for 35% of the 3.1 million deaths annually.
Worldwide, more than 15 million babies are born too early, too small, every year, which is equivalent to one baby being born prematurely every 116 minutes.
Complications related to preterm birth are the leading cause of death in children under five years of age, with an estimated 900,000 global deaths in 2019. In our republic, the number of preterm births has increased by 15.4% in the last 3 years, with a total of 6,840 preterm births registered in 2019 and 10,873 in 2023, according to SIAT.

Keywords
preterm birth, intrauterine infection, cervical insufficiency, perinatal pathology, cytokines

Failure to carry a pregnancy to term is the gradual displacement of the fetal egg from the uterine wall and its exit from the uterine cavity as a result of increased uterine contraction activity. It is associated with the specificity of obstetric tactics and consequences in premature labor, taking into account the gestational age for the fetus,

It is advisable to distinguish 3 periods of such childbirth: 1. Premature birth at 22-27 weeks (fetal weight 500-1000 gr.) accounts for 5% of the total number of births. They occur mainly due to isthmic-cervical insufficiency, inflammation of the lower pole of the placenta and its premature rupture.

In this group, the outcome of labor is very poor for the fetus, with high perinatal morbidity and mortality. 2. Preterm births occurring at 28-33 weeks (fetal weight 1000-1800g) have different causes than very preterm births. Despite the immature fetal lungs, their maturation can be achieved with the use of glucocorticoids or other drugs.

The results of childbirth are better than in the previous 35 ` group. 3. The causes of premature births (fetal weight 1900-2500 g and more) occurring at 34-37 weeks of pregnancy are very diverse compared to the previous groups. Etiology: genital infantilism, endocrine diseases (thyrotoxicosis, diabetes mellitus), kidney, heart diseases, isthmic cervical insufficiency, multiple pregnancy, hypertensive syndromes, maternal age (x≤ 18, 35≥x), placenta previa, fetal malposition, intrauterine infections

The characteristics of the pregnancy process in women with preterm labor, the structure of uterine-vaginal infections, and complications of the early neonatal period of newborns were determined by the type of their occurrence (with intact membranes or with their premature rupture) with the development of spontaneous labor.

The latest version of the guidelines of the European Association of Perinatal Medicine emphasizes the important role of intrauterine infection in the development of preterm birth. The pathogen Streptococcus agalactiae (group B Streptococcus) is associated with complications such as cervical cancer, preterm birth, stillbirth and neonatal sepsis, but the mechanisms leading to these outcomes are not fully understood.

Based on the identified clinical and anamnestic factors associated with spontaneous pregnancy in obese patients (Certificate of State Registration of Database No. 2020621365 dated

08.05.2020), a prognostic model of the risk of spontaneous pregnancy for this category of pregnant women was developed for the first time.

New data on clinical and laboratory parameters specific to obese patients at risk of preterm birth within 48 hours were obtained.

The effect of cervical length on the timing of spontaneous preterm birth was determined for obese pregnant women at risk of preterm birth, and information was obtained on the test characteristics of transvaginal ultrasound cervicometry in relation to the prognosis of spontaneous preterm birth within 48 hours.

A new model was developed that allows determining the level of risk of spontaneous preterm birth in obese patients at risk of preterm birth to decide whether to prescribe tocolytic therapy to them.

The efficacy and safety of acute tocolysis with hexoprenaline and nifedipine in the treatment of risk of preterm birth in obese pregnant women for the first time were evaluated.

Despite extensive research on this condition, the incidence of MOT remains stable worldwide, with an increase in Africa and North America. The incidence of MOT in the United States is approximately 12-13% and in most developed countries in Europe is 5-9%.

Premature birth is part of the "major obstetric syndromes" that include paternal, maternal, fetal and epigenetic factors.

In recent years, the problem of very preterm and premature birth associated with cervical insufficiency has increased several times for local obstetricians due to the registration of perinatal deaths according to the new criteria for live births from 22 weeks of gestation.

Currently, there is increasing evidence of the role of intrauterine infection (IUI) in the genesis of spontaneous MOT.

Intrauterine infection, from the point of view of modern medicine, is defined as an infectious and inflammatory process localized in the uterus, between the maternal tissues and fetal membranes, directly in the amniotic fluid, in the umbilical cord. The latest version of the guidelines of the European Association of Perinatal Medicine emphasizes the significant role of intrauterine infection in the development of preterm birth.

The pathogen Streptococcus agalactiae (group B Streptococcus) is associated with complications such as cervical cancer, preterm birth, stillbirth and neonatal sepsis, but the mechanisms leading to these outcomes are not fully understood.

The presence of cytokine gene polymorphisms leads to increased production of these genes in the uteroplacental unit (UPU) during pregnancy, which leads to increased prostaglandin production and the onset of labor. A single patient may have gene polymorphisms of several cytokines.

We were interested in studying the combination of polymorphisms in several cytokine genes and their effect on the occurrence and course of preterm labor. We hypothesized that

• a combination of polymorphisms in several cytokine genes in a single patient may lead to increased production of several pro-inflammatory cytokines.

This may be the cause of a more active inflammatory process in the IMC, and as a result, early termination of pregnancy and resistance to tocolytic therapy.

For the first time, a comprehensive study of the main links in the pathogenesis of spontaneous preterm birth was conducted to develop an algorithm for pre-pregnancy preparation, prevention, pregnancy management and delivery tactics for women at risk of preterm birth. Polymorphisms of the cytokine genes IL-1@-3953C/T, IL-IIIa VNTR (intron 2) and IL-4 VNTR (intron 3) were found to be risk factors for preterm birth. The combination of polymorphisms of several cytokine genes statistically significantly increases the risk of preterm birth, especially preterm and very preterm birth.

Clinical, anamnestic, prenatal and intrapartum risk factors for pathological blood loss (PBL) and massive blood loss (MBL) in preterm labor were identified for the first time. For the first time, the structure of the causes of PBL and MBL in preterm labor was established, and the causes of PBL and MBL in preterm labor were identified. The relationship between the amniotic fluid index (AFI), the resistance index of the uterine arteries (RI) in the postpartum period, the duration of the anechoic period (AP) and the risk of postpartum hemorrhage (PPH) PR was shown. For the first time, it was found that GK in preterm labor was associated with a low level of progesterone receptor expression (less than 24%) in the myometrium and decidual tissues, which is associated with longer controlled balloon tamponade of the uterus (CBT), subinvolution of the uterus after delivery and low uterine artery indices in the postpartum period.

Several polymorphisms have been identified in the SEPS1 gene, which are largely unstudied. The SEPS1 G-105A (rs28665122) polymorphism has been shown to be associated with an increased risk of preterm birth in Chinese women.

The prevalence of polymorphisms in this gene has not been studied in Russia, so it should be taken into account that the implementation of genetic determinants may vary significantly depending on ethnic origin and differences in the influence of environmental factors.

Samples for microscopic examination were taken from the urethra, cervical canal, and posterior vaginal fornix. Bacterioscopy was performed with a light microscope using an immersion system.

The quantitative and qualitative composition of the microflora of the lower reproductive system was determined using bacteriological studies.

All patients underwent ultrasound fetometry. Using ultrasound, the structure and location of the placenta, the amount of amniotic fluid, and fetometric parameters were determined.

The causes of premature birth are diverse. These include infections, iatrogenic and idiopathic factors, cervical insufficiency, and uterine malformations.

Bleeding during pregnancy, multiple pregnancy, polyhydramnios, placental insufficiency with fetal growth retardation syndrome. Studying risk factors for premature birth will help develop more effective programs for its prediction and prevention.

Another method of prediction is to study the dynamics of changes in the concentration of placental proteins during pregnancy, namely placental-specific α-microglobulin - PAMG-1

However, the diagnostic value of determining PAMG-1 in the blood of pregnant women with inflammatory diseases of the reproductive system remains unclear. Prenatal preparation in patients with pelvic inflammatory disease allows to reduce the risk of miscarriage, reduce the risk of preterm birth, and prevent endothelial dysfunction of the fetoplacental complex.

It is important to predict preterm birth in women with cervical insufficiency. Since cervical length itself is a proven risk factor for preterm birth, it cannot be used as a predictor of early pregnancy loss in patients with cervical insufficiency.

In this regard, there is a need to develop other prognostic markers of preterm birth in patients with cervical insufficiency.

Among the causes of premature birth, intrauterine infection occupies a leading place, for the implementation of which the ascending route of infection is considered to be the priority, therefore, the study of the inflammatory and dysbiotic state of the vagina and cervix in pregnant women with cervical insufficiency is of great interest. The data show that changes in innate immune parameters in endocervical secretions are associated with the intra-amniotic infectious and inflammatory state, and the local inflammatory process at the level of the lower genital tract is associated with the development of cervical insufficiency.

Scientists around the world have conducted a number of studies on the prediction of preterm birth. The role of several factors in the occurrence of preterm birth has been studied and substantiated. These include premature rupture of the membranes, isthmic-cervical insufficiency, the SEPS1 G-105A (rs28665122) gene polymorphism, the role of intrauterine infection (IUI), the importance of cytokine gene polymorphisms, uterine-vaginal infections, obese pregnant women, and the importance of systemic immune-inflammatory reactions in the occurrence of preterm birth. Unlike these scientists, we set ourselves the goal of studying microbiota changes based on insulin resistance in predicting preterm birth. In this regard, we planned to conduct a survey among women who had preterm birth. We want to identify women with insulin resistance among the women who participated in the survey and study their vaginal microflora and intestinal microflora. The goal of our study is to prove the role of microbiota changes based on insulin resistance in the occurrence of preterm birth and to put it into practice.

Because nowadays, perinatal pathologies and infant mortality are often observed in babies born prematurely. Women also experience a number of obstetric pathologies. Preventing preterm birth creates the basis for maintaining the health of mothers and children.

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