

### SCIENTIFIC REVIEWS AND LECTURES

# Modern View on the Causes of Preterm Delivery

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### **ABSTRACT**

Among the most important problems of modern practice of obstetrics, one of the most acute problems is premature birth. After all prematurity is the leading cause of perinatal morbidity, mortality and disability of children. The article presents an overview of current research done in the world to outline the causes of premature birth.

**Keywords:** preterm labor, amniotic fluid, morbidity, infant mortality.

# INTRODUCTION

Since 2012, according to WHO recommendations, Russia has moved to a new standard of live births and the problem of premature birth has become one of the most important in the medical and social aspects. According to the latest definition of the World Health Organization considered premature births that occurred in the period from 22 to 37 weeks, the fruit of 500 or more grams. The intensive care unit of the country joined the very preterm babies with extremely low birth weight, require enormous resources on nursing, treatment and further rehabilitation. Children's health as the future of the nation, is an important matter for each state and only the prediction of preterm birth and a rational choice of tactics in complicated pregnancy and childbirth can positively affect the outcome.

The share of premature babies up to 70% of early neonatal and infant mortality rates of 65-75%. Still births in preterm labor in 8-13 times more than the timely delivery. [3] The incidence of preterm birth, according to local experts, ranging from 10 to 12%. [1] According to various reports of foreign authors their frequency varies from 5 to 18 % in different countries. In the US, approximately 12% of all live births are born prematurely, of which 25-50% subsequently suffer neurological disorders, 70% and 36% of neonatal infant mortality is due to premature birth. [12] A retrospective analysis of the infant mortality rate is extremely preterm infants in Sweden, showed considerable variations between different medical institutions and directly dependent on the level of medical care. [9] In France and the United States among infants born alive at less than 34 weeks of pregnancy, higher mortality was revealed in born with stunted growth. [6] By the same the conclusion reached by Japanese scientists, where the extremely preterm children with growth retardation are marked as the most prone excl risks of mortality and diseases, such as chronic lung disease, retinopathy of prematurity, sepsis, necrotizing enterocolitis. [11]

In Russia, in 2013, put into practice a clinical protocol for the prevention and management of preterm labor, which are defined and announced numerous risk factors, such as complications of obstetric and gynecological history, low socio-economic standard of living, drug addiction and smoking, multiple or induced pregnancy, cervico-vaginal infection, severe extragenital pathology and others. [2] But in spite of all the work being done, the number of premature births in Russia is growing, as well as throughout the world.

Studying the numerous recent studies in the field of premature birth, it becomes clear that the search for solutions to this problem took a planetary scale, and can take a lot of time. Indeed, despite the recent advances in obstetric and neonatal service, the number of premature births in the world is increasing. [19] The reason for this multifactorial etiology of preterm labor, where about half of the cases is idiopathic. Idiopathy - from the greek idios - own, pathos - disease, the origin of which is difficult to understand. Spontaneous preterm delivery occurred against a background of complete well-being, the search for new encounters predictors, multiple duplication of studies in different countries, the use of a non-invasive and invasive methods, conducting experiments using animals as a model.

In this respect, scientists have placed great hope in the discovery of new biochemical markers that act as a reliable predictor of preterm birth that will allow time to conduct targeted therapies and medical interventions to improve outcomes for the fetus and the mother. All human body fluids, including the amniotic fluid, urine, saliva, cervical fluid and blood are a rich source of various proteins, various pathophysiological biomarkers suspected pregnancy disorders, including premature birth. This is especially true for the prediction of preterm delivery and intraamniotic infection. [13] One of these biomarkers may perform proteins detected during pregnancy in human cervix-vaginal fluid (CVF cervical-vaginal fluid proteins), which are a reflection of the local biochemical environment of the vagina condition, cervix and adjacent overlying fetal membranes. The prognostic significance of these proteins has become even more promising with the opening of their resistance to vaginal flora and semen. Research and search for these proteins goes on, some of them have already been successfully isolated and demonstrated the relationship with premature birth. [10] A thorough study of the composition of cervico-vaginal fluid (CVF cervical-vaginal fluid) revealed high levels of interleukin-6 in cases of subclinical chorioamnionitis at the whole sac. Production and implementation of rapid test on cervicovaginal interleukin-6 may be useful in the diagnosis of chorioamnionitis most likely to justify amniocentesis or transfer the pregnant woman on a higher level of care. [8]

Studies on the molecular mechanisms underlying spontaneous preterm birth showed that DNA methylation change of fetal umbilical cord can be used as a marker. DNA samples of



umbilical cord blood obtained by cordocentesis, are an easy source of material for research. Violation of methylation plot strand of DNA coding for myosin light chain 4 is a reliable prognostic factor for idiopathic preterm labor. [18]

By etiological factors could be considered a higher risk of preterm birth for various environmental variables, such as air pollution, increased noise and high air temperature in the big city on the example of Madrid. A retrospective analysis of all cases of premature birth in Madrid showed a slight increase in the number of spontaneous preterm birth in the daytime, in 14chasov 30min, in the period of maximum increase of noise, smoke and temperature. [17]

The American College of Obstetricians and Gynecologists Research revealed several controversial facts. Studies have shown that there is no clear connection between proven cervical shortening and binding premature termination of pregnancy. Careful assessment of multiple risk factors in women, in order to avoid unnecessary hospitalizations and possible iatrogenic effects, in particular the use of corticosteroids, cervical shortening is practical and prognostic significance only in conjunction with a test for fetal fibronectin. [7] The quantitative analysis on fetal fibronectin in the period from 18 to 21 weeks of gestation is valuable in predicting spontaneous preterm labor very early. Various concentrations allow you to choose one or the other tactics pregnant. [14] Alternatively, the risk threshold is 10 ng/mL or less, and the concentration of 200 ng / ml indicates an increased risk of spontaneous preterm birth, which is especially important for asymptomatic women with a short cervix [15].

Research scientists in Pakistan have revealed that one of the leading risk factors for preterm birth was iron deficiency anemia in pregnant women. During pregnancy, there are high demands to the woman's body on the synthesis and patients with iron deficiency anemia have been compromised by a high risk of birth weight infants, preterm birth and perinatal mortality [5].

Careful examination of medical history of patients with preterm labor revealed a greater likelihood of preterm birth in women who themselves were born from spontaneous preterm birth [16].

Thus, premature birth is an actual problem of modern health care. The number of premature births has no tendency to decrease, and late diagnosis leads to large economic and social costs to society due to the high risk of morbidity and disability in children. Joint research scientists in the world in search of reliable predictors will improve preterm birth outcomes for mother and child. And it is to this issue, I want to quote from Socrates: "The more I learn, the more I realize that I know nothing ...».

#### LIST OF REFERENCES

- 1. Ajlamazjan Je. K. V. I. Kulakov V. E. Radzinskij G. M. Savel'eva. Akusherstvo. Nacional'noe rukovodstvo [Obstetrics. National leadership]. Moscow: GeOTAR-Media, 2015, 250 -258 p.
- 2. Klinicheskij rotocol MZ RF «Prezhdevremennye rody» ot 17.12.201Zg №15-4/10/2- 9480 [The Russian Ministry of Health Clinical Protocol "Premature birth" from 17.12.2013. №15-4 / 10 / 2- 9480]
- 3. Sidel'nikova V.M. Antonov A.G. Prezhdevremennye rody. Nedonoshennyj rebenok [Premature birth. Premature baby]. Moscow: GeOTAR, Media 2006, 448 p.
- 4. A core outcome set for evaluation of interventions to prevent preterm birth. / Van 't Hooft, Janneke MD; Duffy, James M. N. MD; Daly, Mandy MSc et al. // Obstetrics & Gynecology: January 2016 Volume 127 Issue 49–58. 1 Doi: 10.1097/AOG.0000000000001195.
- 5. Anemic patients; relationship of frequency and severity of iron deficiency anemia with preterm labor and eventual perinatal outcome. / Majeed, Tayyaba, Adnan, Rabia, Mahmood, Zahid et al. // Professional Medical Journal. 2015, Vol. 22 Issue 12, p1550-1554. 5p. 6 Charts.
- Cause of preterm birth as a prognostic factor for mortality. / Delorme, Pierre MD; Goffinet, François MD, PhD; Ancel, Pierre-Yves MD, PhD et al. // Obstetrics & Gynecology: January 2016 – Volume 127 – Issue 1 – p 40–48. Doi: 10.1097/AOG.00000000001179
- 7. Corticosteroid use in the face of threatened preterm labor. / Cabbad, Michael Frederick MD; De Los Heros, Daniel MD; Baltajian, Kedak Zovac MD et al. // Obstetrics & Gynecology: May 2015. Doi: 10.1097/AOG.0000463737.77543.37. Sunday, May 3, 2015
- 8. Detection of microbial invasion of the amniotic cavity by analysis of cervicovaginal proteins in women with preterm labor and intact membranes. / Combs CA; Garite TJ; Lapidus JA et al. // American Journal Of Obstetrics And Gynecology 2015 Apr; Vol. 212 (4), pp. 482.e1-482.e12. Date of Electronic Publication: 2015 Feb 14.
- Express study shows significant regional differences in 1-year outcome of 9. extremely preterm infants in Sweden. / Serenius, Fredrik Sjörs, Gunnar Blennow, Mats et al. // Acta Paediatrica. Jan2014, Vol. 103 Issue 1, p27-37. 11p.
- Human cervicovaginal fluid biomarkers to predict term and preterm labor. / Yujing J. Heng, Stella Liong, Permezel, Michael et al. // Frontiers in Physiology. May2015, Vol. 6, p1-18. 18p.



- 11. Itabashi, Kazuo. / Mortality and morbidity risks vary with birth weight standard deviation score in growth restricted extremely preterm infants. / Itabashi, Kazuo, Kusuda, Satoshi. // Early Human Development. Jan2016, Vol. 92, p7-11. 5p.
- Obstetrics & Gynecology. 127(1):190-191, January 2016. Practice Bulletin No. 159 Summary management of preterm labor.
- Predicting preterm labour: current status and future prospects. / Georgiou, Harry 13. M., Di Quinzio, Megan K. W., Permezel, Michael et al.// Disease Markers. 6/15/2015, Vol. 2015, p1-9.9p
- 14. Quantitative fetal fibronectin at 18 weeks of gestation to predict preterm birth in asymptomatic high-risk women. / Hezelgrave, Natasha L. BSc; Abbott, Danielle S. BSc; Radford, Samara K. BSc et al. // Obstetrics & Gynecology: February 2016 – Volume 127 – Issue 2 – p 255– 263. Doi: 10.1097/AOG.0000000000001240
- 15. Quantitative fetal fibronectin to predict preterm birth in asymptomatic women at high risk. / Abbott, Danielle S. MBBS; Hezelgrave, Natasha L. MBBS; Seed, Paul T. MSc et al. // Obstetrics & Gynecology: May 2015 - Volume 125 - Issue 5 - p 1168-1176. Doi: 10.1097/AOG.00000000000000754
- Risk for preterm and very preterm delivery in women who were born preterm. 16. Boivin, Ariane PhD; Luo, Zhong-Cheng MD, PhD; Audibert, François MD, MSc et al. // Obstetrics & Gynecology: May 2015 - Volume 125 - Issue 5 - p 1177-1184. Doi: 10.1097/AOG.00000000000000813
- 17. Short term effect of air pollution, noise and heat waves on preterm births in Madrid (Spain). / Arroyo, Virginia, Díaz, Julio, Ortiz, Cristina et al // Environmental Research. Feb2016, Vol. 145, p162-168. 7p.
- 18. The idiopathic preterm delivery methylation profile in umbilical cord blood DNA. / Fernando, Febilla, Keijser, Remco, Henneman, Peter et al. // BMC Genomics. 9/30/2015, Vol. 16 Issue 1, p1-12. 12p.
- 19. Transplacental transfer of azithromycin and its use for eradicating intra-amniotic ureaplasma infection in a primate model. / Acosta, Edward P., Grigsby, Peta L., Larson, Kajal B. et al. // Journal of Infectious Diseases. Mar2014, Vol. 209 Issue 6, p898-904. 7p.



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