UDC 616.791-08:618.2
DOI https://doi.org/10.32782/2411-9164.22.1-6

MODERN PATHOPHYSIOLOGICAL MECHANISMS OF PRETERM LABOR DEVELOPMENT

Oliferuk Yu.S.[1], Tokar P.Yu.[2]

[1]*Chernivtsi Regional Perinatal Center, Chernivtsi, Ukraine*

[2]*Bukovinian State Medical University, Chernivtsi, Ukraine*

UDC 616.791-08:618.2
DOI https://doi.org/10.32782/2411-9164.22.1-6

MODERN PATHOPHYSIOLOGICAL MECHANISMS OF PRETERM LABOR DEVELOPMENT

Oliferuk Yu.S., Tokar P.Yu.

Preterm birth is one of the biggest problems of modern obstetrics, as it significantly affects the health of both the mother and the newborn. According to the World Health Organization, preterm birth is one of the leading causes of infant mortality in the world. The pathophysiology of preterm labor is a complex multifactorial process that includes the interaction of infectious and inflammatory reactions, hormonal disorders, genetic factors, and physiological changes in a woman's body. An important aspect is that urinary tract infections, urogenital infections, and inflammatory processes in the uterus can initiate the release of pro-inflammatory mediators such as interleukins and prostaglandins, which activate uterine contractions and lead to premature labor.

Hormonal disorders, in particular, a decrease in progesterone levels or disruption of its receptors, are an important factor in the development of this pathology. Genetic factors that determine individual predisposition to this pathology may also play a role in the development of preterm labor. In addition, impaired cervical integrity, such as cervical insufficiency or shortness, significantly increases the likelihood of preterm birth.

Socio-environmental factors, such as stress, poor nutrition, and environmental pollution, also play an important role in the occurrence of preterm birth. Since preterm birth is a complex and multifaceted process, research into the pathophysiology of this pathology is essential for the development of effective methods of diagnosis, treatment and prevention. To date, significant advances in the use of progesterone, prostaglandin inhibitors, and ultrasound diagnostics have reduced the risk of preterm birth, but further research remains important to improve treatment strategies and reduce the rate of premature mortality among newborns.

Key words: preterm birth, prevention, treatment, prognosis, placenta, pregnant women, newborns.

УДК 616.791-08:618.2
DOI https://doi.org/10.32782/2411-9164.22.1-6

СУЧАСНІ ПАТОФІЗІОЛОГІЧНІ МЕХАНІЗМИ РОЗВИТКУ ПЕРЕДЧАСНИХ ПОЛОГІВ

Оліферук Ю.С., Токар П.Ю.

Передчасні пологи є однією з найбільших проблем сучасного акушерства, оскільки вони суттєво впливають на здоров'я як матері, так і новонародженого. За даними Всесвітньої організації охорони здоров'я, передчасні пологи є однією з основних причин дитячої смертності у світі. Патофізіологія передчасних пологів є складним багатофакторним процесом, який включає взаємодію інфекційно-запальних реакцій, гормональних порушень, генетичних факторів та фізіологічних змін в організмі жінки. Важливим аспектом є те, що інфекції сечовивідних шляхів, урогенітальні інфекції, а також запальні процеси у матці можуть ініціювати вивільнення прозапальних медіаторів, таких як інтерлейкіни та простагландини, що активують скорочення матки та призводять до передчасних пологів.

Гормональні порушення, зокрема зниження рівня прогестерону або порушення його рецепторів, є важливим чинником у розвитку цієї патології. Також роль у розвитку передчасних пологів можуть відігравати генетичні чинники, які визначають індивідуальну схильність до цієї патології. Окрім того, порушення цілісності шийки матки, зокрема її недостатність або коротка довжина, значно підвищують імовірність розвитку передчасних пологів.

Соціально-екологічні чинники, такі як стрес, погане харчування та забруднення навколишнього середовища, також відіграють важливу роль у виникненні передчасних пологів. Оскільки передчасні пологи є складним і багатогранним процесом, дослідження патофізіології цієї патології має велике значення для розроблення ефективних методів діагностики, лікування та профілактики. Сьогодні значні досягнення у застосуванні прогестерону, інгібіторів простагландинів та ультразвукової діагностики дають змогу знизити ризик передчасних пологів, однак подальші дослідження залишаються важливими для вдосконалення лікувальних стратегій і зменшення рівня передчасної смертності серед новонароджених.

Ключові слова: передчасні пологи, профілактика, лікування, прогнозування, плацента, вагітні, новонароджені.

Introduction. Preterm birth is one of the main causes of high morbidity and mortality among newborns. They occur before 37 weeks of pregnancy and are accompanied by numerous complications for both mother and child. The consequences for newborns include respiratory, neurological, and traumatic disorders that can have long-term consequences for their development. Understanding the pathophysiological mechanisms of preterm birth is important for timely diagnosis, prevention, and development of new therapeutic approaches [2].

The process of preterm labor is complex and multifactorial, involving a variety of mechanisms. One of the main causes is an infectious and inflammatory process that stimulates the release of proinflammatory mediators that initiate uterine contractions. Infections, in particular urogenital infections, are an important cause of preterm labor, as microorganisms can activate inflammatory reactions in the body [3].

Hormonal disorders play an important role in the development of preterm labor. A decrease in the level of progesterone, which maintains pregnancy, can lead to the

initiation of labor. Disorders of endocrine regulation, such as increased levels of stress hormones, also contribute to the early onset of labor. In addition, genetic factors may play a role, including the presence of mutations in genes that regulate inflammation or hormones [3].

The mechanisms of preterm labor may also be related to uterine integrity disorders, such as a short cervix or malformations. Social and environmental factors, such as stress, environmental pollution, and lifestyle, are also important and can increase the risk of preterm birth.

Understanding these mechanisms allows us to develop new strategies for the prevention and treatment of preterm birth. This includes drug therapy and lifestyle changes aimed at reducing the risk. A comprehensive approach to this problem is key to improving pregnancy outcomes and maternal and child health [4].

Objective. To study modern pathophysiological mechanisms of preterm labor.

Materials and methods. The literature was searched through scientific databases such as PubMed, Google Scholar, and Scopus using keywords related to the pathophysiological mechanisms of preterm birth, infectious factors, hormonal disorders, and genetic markers.

Results. Preterm births are one of the biggest problems in obstetrics and neonatology, as they significantly increase the risk of serious complications in newborns and pregnant women. They occur before the 37th week of pregnancy and have serious consequences for both the mother's health and the child's health. Today, preterm birth is one of the main causes of high mortality and morbidity among newborns. According to WHO estimates, about 15 million births worldwide occur prematurely, and this is one of the main medical problems that requires more detailed study. Since the development of preterm birth is a complex and multifactorial process, the study of the pathophysiological mechanisms underlying this phenomenon is of great importance for improving diagnostic, treatment and prevention methods [1, 3].

The process of preterm labor is the result of a complex interaction between several underlying mechanisms that can be individualized for each pregnancy. The pathophysiology of preterm labor involves numerous biological, hormonal, and mechanical processes that lead to the early onset of labor. Although there are various theories regarding the pathogenesis of this pathology, the most recognized are those that imply the influence of infections, hormonal disorders, genetic factors, and cervical integrity disorders [2, 3].

One of the main causes of preterm labor is infectious and inflammatory processes that activate inflammatory mediators in the body. In particular, urinary tract infections, urogenital infections, and other bacterial, viral, and fungal infections can stimulate the activation of mechanisms that initiate labor. Infection in a woman's body leads to the release of pro-inflammatory cytokines, such as interleukins, prostaglandins, and tumor necrosis factors (TNF), which stimulate uterine contractions. Microorganisms can enter the uterus through the blood or lymphatic pathways or through infection through the cervix. In addition, inflammation can reduce progesterone levels, which is the main hormone that supports pregnancy [4, 5].

Studies show that when a bacterial infection is present in the mother's body, not only local inflammatory reactions in the uterus are activated, but also general systemic inflammatory reactions, which can cause premature birth. For example, an infection with bacteria such as Chlamydia trachomatis, Mycoplasma genitalium, or Ureaplasma

urealyticum is associated with an increased risk of preterm labor. The release of prostaglandins as a result of an infectious process can cause myometrial contraction and subsequent labor [6].

Hormonal balance plays an important role in maintaining the normal development of pregnancy. Progesterone is one of the main hormones that prevents premature birth. It keeps the uterus calm during pregnancy by inhibiting its contractions. A decrease in progesterone levels or disruption of its receptors can lead to activation of labor activity. In addition to progesterone, other hormones, such as estrogens, oxytocin, and cortisol, are important and also play a role in the initiation of labor [7].

In particular, low levels of progesterone or a deficiency of progesterone receptors can contribute to the premature onset of labor. It is known that progesterone acts through receptors located on uterine cells, and if the receptors do not function properly, even with high progesterone levels, this can lead to uterine contractions. At the same time, the level of stress hormones, such as cortisol, can change depending on a woman's emotional state. Elevated cortisol levels can affect uterine function and initiate the onset of labor [8].

Genetic factors may play a significant role in the development of preterm labor, although this issue remains poorly understood. According to some studies, the presence of certain genetic mutations or polymorphisms can increase the likelihood of preterm birth. For example, polymorphisms in genes that regulate the synthesis of proinflammatory cytokines or hormone receptors may affect the body's ability to respond to infections or other factors that stimulate labor [5, 9].

There are studies that show that the presence of certain genetic variants in the mother or in the child may be associated with an increased risk of preterm labor. For example, mutations in the genes encoding cytokines can lead to an increased inflammatory response, which is an important mechanism for initiating labor [4, 7].

Cervical abnormalities are another factor that increases the risk of preterm labor. Insufficiency of the cervix or its short length can lead to premature cervical dilatation and the onset of labor. The causes of such disorders can be both congenital anomalies and cervical injuries, for example, after previous births or surgical interventions [8].

Cervical insufficiency may be associated with an increased risk of preterm labor, as cervical dilatation is the first step in the onset of labor. Assessment of cervical length using ultrasound methods is an important part of monitoring pregnant women at risk of preterm labor.

Social and environmental factors that can influence the development of preterm labor are equally important. Stress, environmental pollution, poor nutrition, drug or alcohol use, and low socioeconomic status are risk factors for the development of this pathology. Psychological stress can directly affect hormonal balance and increase the level of stress hormones such as cortisol, which in turn can stimulate labor activity [9].

Understanding the pathophysiological mechanisms of preterm labor is important for developing new approaches to the treatment and prevention of this pathology. Modern methods of prediction, including the use of biomarkers, ultrasound and hormonal tests, allow us to identify women at high risk of preterm birth in the early stages of pregnancy. This allows for timely treatment, which includes the use of progesterone drugs, prostaglandin inhibitors, and special therapeutic strategies aimed at strengthening the cervix or reducing inflammatory reactions [9, 10].

In general, many mechanisms of preterm birth remain unknown, and modern research is revealing new opportunities for early detection, prevention and treatment of this pathology [10].

Conclusions. Preterm labor is a complex and multifactorial process that includes infectious and inflammatory reactions, hormonal disorders, genetic factors, and cervical abnormalities. Important aspects include the influence of environmental and social factors, such as stress and poor living conditions, which can also increase the risk. Modern methods of diagnosis and treatment, including the use of progesterone and prostaglandin inhibitors, can significantly reduce the likelihood of preterm birth and improve pregnancy outcomes. Further research in this area will contribute to the development of new strategies for the prevention and treatment of preterm birth.

BIBLIOGRAPHY

1. Токар П.Ю., Каліновська І.В. Дисбаланс гормонів фетоплацентарного комплексу як фактор розвитку передчасних пологів. Буковинський медичний вісник, 2023, 27.3 (107): 10–14.
2. Токар П.Ю. Сучасні уявлення про етіопатогенез, прогнозування та профілактику передчасних пологів (огляд літератури). Клінічна анатомія та оперативна хірургія, 2024, 23.2: 97–107.
3. Токар П.Ю. The progins variant of the pgr gene and placental endocrine function at risk of preterm labor: a pilot study. Буковинський медичний вісник, 2024, 28.3 (111): 69–75.
4. Токар П.Ю. Histochemical and immunohistochemical features of differentiated trophoblast in chorionic villi of the placenta in preterm labor. Неонатологія, хірургія та перинатальна медицина, 2024, 14.1 (51): 84–90.
5. Adu-Bonsaffoh Kwame, Bayor Fidelis. Pathophysiological mechanisms of maternal pro-inflammatory mediators in preterm labour. Journal of Physiology and Pathophysiology, 2022, 13.1: 1–16.
6. Dauengauer-Kirlienė S., et al. Causes of preterm birth: genetic factors in preterm birth and preterm infant phenotypes. Journal of Obstetrics and Gynaecology Research, 2023, 49.3: 781–793.
7. Pisacreta E., Mannella P. Molecular and endocrine mechanisms involved in preterm birth. Gynecological Endocrinology, 2022, 38.5: 368–378.
8. Giouleka S., et al. Preterm labor: a comprehensive review of guidelines on diagnosis, management, prediction and prevention. Obstetrical & gynecological survey, 2022, 77.5: 302–317.
9. Phillippe M. Telomeres, oxidative stress, and timing for spontaneous term and preterm labor. American Journal of Obstetrics and Gynecology, 2022, 227.2: 148–162.
10. Jaiman S., et al. The role of the placenta in spontaneous preterm labor and delivery with intact membranes. Journal of perinatal medicine, 2022, 50.5: 553–566.

REFERENCES

1. Tokar, P.Yu., & Kalinovska, I.V. (2023). Dysbalans hormoniv fetoplatsentarnoho kompleksu yak faktor rozvytku peredchasnykh polohiv [Hormonal Imbalance of the Fetoplacental Complex as a Factor in the Development of Preterm Labor]. *Bukovynskyi Medychnyi Visnyk – Bukovinian Medical Herald*, 27(3)(107), 10–14. [in Ukrainian]
2. Tokar, P.Yu. (2024). Suchasni uyavlennia pro etiolohiiu, patohenez, prohnozuvannia ta profilaktyku peredchasnykh polohiv (ohliad literatury) [Modern Concepts of Etiology, Pathogenesis, Prediction, and Prevention of Preterm Labor (Literature Review)]. *Klinichna Anatomiia ta Operatyvna Khirurhiia – Clinical Anatomy and Operative Surgery*, 23(2), 97–107. [in Ukrainian]

3. Tokar, P.Yu. (2024). The progins variant of the PGR gene and placental endocrine function at risk of preterm labor: A pilot study. *Bukovynskyi Medychnyi Visnyk – Bukovinian Medical Herald*, 28(3)(111), 69–75. [in Ukrainian]
4. Tokar, P.Yu. (2024). Histochemical and immunohistochemical features of differentiated trophoblast in chorionic villi of the placenta in preterm labor. *Neonatolohiia, Khirurhiia ta Perynatalna Medytsyna – Neonatology, Surgery and Perinatal Medicine*, 14(1)(51), 84–90. [in Ukrainian]
5. Adu-Bonsaffoh, K., & Bayor, F. (2022). Pathophysiological mechanisms of maternal pro-inflammatory mediators in preterm labour. *Journal of Physiology and Pathophysiology,* 13(1), 1–16. https://doi.org/10.5897/JPAP2022.0001
6. Dauengauer-Kirlienė, S., et al. (2023). Causes of preterm birth: Genetic factors in preterm birth and preterm infant phenotypes. *Journal of Obstetrics and Gynaecology Research*, 49(3), 781–793. https://doi.org/10.1111/jog.15243
7. Pisacreta, E., & Mannella, P. (2022). Molecular and endocrine mechanisms involved in preterm birth. *Gynecological Endocrinology*, 38(5), 368–378. https://doi.org/10.1080/09513590.2022.2043127
8. Giouleka, S., et al. (2022). Preterm labor: A comprehensive review of guidelines on diagnosis, management, prediction and prevention. *Obstetrical & Gynecological Survey*, 77(5), 302–317. https://doi.org/10.1097/OGX.0000000000001007
9. Phillippe, M. (2022). Telomeres, oxidative stress, and timing for spontaneous term and preterm labor. *American Journal of Obstetrics and Gynecology*, 227(2), 148–162. https://doi.org/10.1016/j.ajog.2022.05.031
10. Jaiman, S., et al. (2022). The role of the placenta in spontaneous preterm labor and delivery with intact membranes. *Journal of Perinatal Medicine*, 50(5), 553–566. https://doi.org/10.1515/jpm-2022-0023