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Research Article

Preterm birth: current opportunities for prediction and prevention

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ABSTRACT

BACKGROUND: The need for resuscitation at birth depends on the gestational age — the shorter the gestational age, the more often resuscitation is required.

AIM: to determine risk factors and possible methods for preventing preterm birth.

MATERIALS AND METHODS: A retrospective analysis of medical documentation data was carried out on 12,342 women whose delivery was carried out at the Perinatal Center of the Pediatric University. The main group included 680 patients whose pregnancy ended with delivery at 22 weeks — 36 weeks 6 days, the control group included 11,662 patients whose pregnancy ended with term birth.

RESULTS: When analyzing anamnestic factors, it was found that the age of the patients at the time of registration for pregnancy in the main group was statistically significantly higher, height was statistically significantly lower, the serial number of both pregnancy and childbirth was statistically significantly higher, VI or more pregnancies, IV or more births, obesity, arterial hypertension, and a burdened obstetric history (miscarriage, premature birth) are statistically significantly more common than in the control group. In the main group of symptoms, the following are most often noted: pregnancy resulting from the use of assisted reproductive technologies, moderate and severe preeclampsia, isthmic-cervical insufficiency, abnormal indicators of the umbilical cord artery, breech presentation of the fetus. Meconium staining of amniotic fluid was 2 times more common in full-term pregnancies.

CONCLUSIONS: Ascending infection of the placenta, mycoplasma, herpetic and chlamydial choriodecidualitis, sub- and decompensated chronic placental insufficiency were statistically significantly more common in premature births. Based on discriminant analysis, a model for predicting the risk of preterm birth was built.

Keywords: pregnancy; premature birth; gestational age; chlamydia trachomatis; pre-eclampsia; placenta.

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Научная статья

Факторы риска и пути предотвращения преждевременных родов

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АННОТАЦИЯ

Актуальность. Необходимость в проведении реанимационных мероприятий при рождении зависит от гестационного срока — чем меньше срок гестации, тем чаще требуется реанимационное пособие.

Цель — определение факторов риска и возможных методов профилактики преждевременных родов.

Материалы и методы. Проведен ретроспективный анализ данных медицинской документации 12 342 женщин, родоразрешение которых проводилось в Перинатальном центре Педиатрического университета. В основную группу вошли 680 пациенток, беременность которых закончилась родоразрешением в сроке 22 нед. – 36 нед. 6 дней, в контрольную — 11 662 пациентки, беременность которых закончилась срочными родами.

Результаты. При анализе анамнестических факторов установлено, что возраст пациенток на момент постановки на учет по беременности в основной группе статистически значимо выше, рост — статистически значимо ниже, порядковый номер беременности и родов статистически значимо больше (VI и более по счету беременность, IV и более по счету роды), ожирение, артериальная гипертензия и отягощенный акушерский анамнез (невынашивание беременности, преждевременные роды) встречаются статистически значимо чаще, чем в контрольной. В основной группе статистически значимо чаще были отмечены: беременности, наступившие в результате применения вспомогательных репродуктивных технологий, умеренная и тяжелая преэклампсия, истмико-цервикальная недостаточность, нарушение параметров кровотока в артерии пуповины, тазовое предлежание плода. Мекониальная окраска околоплодных вод встречалась в 2 раза чаще при доношенной беременности.

Выводы. Восходящее инфицирование последа, микоплазменный, герпетический и хламидийный хориодецидуит, суб- и декомпенсированная хроническая плацентарная недостаточность встречались при преждевременных родах статистически значимо чаще. На основании дискриминантного анализа построена модель прогнозирования риска преждевременных родов.

Ключевые слова: беременность; преждевременные роды; срок гестации; хламидийная инфекция; преэклампсия; плацента.

Как цитировать

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BACKGROUND

Reducing perinatal mortality is crucial in modern medicine [2, 6, 7, 11]. Early neonatal death (in the first 168 h of extrauterine life) is commonly caused by neonatal asphyxia (ICD10: P21) [3, 10, 15, 16].

An Apgar score of 8–10 indicates that the newborn is in good health. A score between 4 and 7 at 1 min after birth shows moderate hypoxia, which is characterized by partial centralization of blood flow to varying degrees, accompanied by impaired function of organ systems, particularly the central nervous system. Severe hypoxia (Apgar score of 0–3 at the end of the first minute) is marked by impaired organ and system function and requires a comprehensive resuscitation approach¹.

In preterm infants, a low Apgar score is not typically associated with asphyxia. The need for resuscitation at birth depends on gestational age: the shorter the period of gestation, the more frequently resuscitation may be required². [8, 12].

This study aimed to identify risk factors of and possible preventive methods for preterm birth.

MATERIALS AND METHODS

The medical records of 12,342 women who gave birth at the Perinatal Center of St. Petersburg State Pediatric Medical University (a level IIIB obstetric facility) was retrospectively analyzed. The main group included 680 patients whose pregnancies resulted in delivery between 22 weeks and 36 weeks and 6 days of gestation, and the control group included 11,662 patients who had term births. Retrospective analysis was performed based on the individual card of the pregnant and postpartum woman (form no. 111/u), anamnesis (form no. 096/u), anamnesis on the newborn development (form no. 097/u), and postpartum examination protocol.

When analyzing the individual card of a pregnant and postpartum woman (form no. 111/u), the following data were assessed:

1. Passport part of the card: age at the time of registration of pregnancy, educational level (primary, secondary, higher), marriage registration in the registry office, and availability of a permanent place of work/study

2. Somatic anamnesis: diseases and surgeries, presence of somatic pathology, hemocontact infections, and bad habits

3. Gynecologic history: age of menarche, age of sexual debut, presence of gynecologic diseases, gynecologic surgeries, and genital infections

4. Reproductive anamnesis: serial number of the given pregnancy and delivery, presence of aggravated obstetric anamnesis (abortions before the first delivery, two or more abortions before repeated deliveries, ectopic and undeveloped pregnancies, spontaneous miscarriages, preterm births, complicated pregnancies and deliveries, birth of children with developmental anomalies, perinatal losses), and operative delivery

5. Primary examination data: anthropometry (height, weight, body mass index) and pelviometry

6. Examination results: clinical and biochemical blood tests; coagulogram; urinalysis; smears for biocenosis and oncology; examination for hemocontact infections; bacteriologic tests of pharyngeal and nasal secretions; cervical smear; blood group and Rh factor determination; anti-RH antibody titer assessment (in Rh-negative pregnant women); sexually transmitted infection and TORCH-complex infection (*Toxoplasma gondii*, *Cytomegalovirus*, *Rubella virus*, and *Human herpesvirus 1, 2*) screening; examination by a general practitioner, dentist, ophthalmologist, and ENT doctor; triple screening ultrasound; biochemical markers of chromosomal anomalies (RARP-A and beta-hCG, alpha-fetoprotein and hCG); and additional tests as indicated.

7. Identified features and pathologic conditions during pregnancy: early toxicosis; abnormal weight gain; pregnancy edema; hypertension; proteinuria; preeclampsia; genital tract inflammatory diseases; threatened abortion; chronic placental insufficiency; fetal growth retardation; isthmio-cervical insufficiency; application of various methods of its correction; acute diseases suffered during pregnancy; and exacerbation of chronic diseases, traumas, and toxic lesions

When analyzing the history of childbirth (form no. 096/u), the gestational age at the time of delivery, use of surgical aids, macroscopic and histological examination data of the afterbirth (normal structure; ascending infection of stages I, II, and III; hematogenous infection; and compensated, subcompensated, and decompensated chronic placental insufficiency) were evaluated.

RESULTS

The medical history data of the study patients were analyzed to determine the risk factors for preterm birth (Table 1).

Analysis of the anamnestic factors showed that the age of the patients at the time of pregnancy registration in the main group was significantly higher. Moreover, the height was statistically significantly lower. The number of pregnancies and childbirths was also higher (with six or more pregnancies and four or more births). Furthermore, obesity, hypertension, and a burdened obstetric history (including miscarriages and preterm births) were significantly more common in this group.

¹ Resuscitation and stabilization of newborn in the delivery room. Methodological letter of the Ministry of Health of the Russian Federation from 04.03.2020.

² Ibid.

Table 1. Social status, somatic and obstetric-gynecological anamnesis of patients in the main and control groups

Таблица 1. Социальный статус, соматический и акушерско-гинекологический анамнез пациенток основной и контрольной групп

Indicator / Показатель	Main group (preterm birth) / Основная группа (преждевременные роды) (n = 680)	Control group (term delivery) / Контрольная группа (срочные роды) (n = 11662)	Statistical significance / Статистическая значимость
Patient age / Возраст пациенток, лет	32.033 ± 5.59 (16–58)	31.237 ± 6.28 (12–54)	p = 0.008
Education / Образование			
• initial / начальное	55 (8.1%)	490 (4.2%)	χ ² = 4.66; p = 0.098
• average / среднее	267 (39.2%)	4408 (37.8%)	
• higher / высшее	358 (52.7%)	6764(58.0%)	
Officially employed / Официально трудоустроены	535 (78.7%)	9330(80.0%)	χ ² = 0.17; p = 0.677
Negative Rh factor / Отрицательный резус-фактор	133 (19.6%)	1879 (16.1%)	χ ² = 5.64; p = 0.046
Patient height, cm / Рост пациенток, см	163.78 ± 6.39 (135–182)	165.63 ± 6.12 (141–184)	p < 0.000
Weight of patients before pregnancy, kg / Масса пациенток до беременности, кг	71.50 ± 14.223 (43.7–130.4)	71.87 ± 15.123 (41.7–160.0)	p = 0.706
Body mass index / Индекс массы тела	26.61 ± 4.968 (16.22–51.58)	26.163 ± 5.094 (15.43–52.25)	p = 0.175
Chronic pyelonephritis / Хронический пиелонефрит	54 (7.9%)	1003 (8.6%)	χ ² = 0.41; p = 0.523
Obesity / Ожирение	25 (3.7%)	248 (2.1%)	χ ² = 4.19; p = 0.035
Arterial hypertension Hypertonic disease / Артериальная гипертензия и гипертоническая болезнь	26 (4.0%)	245 (2.1%)	χ ² = 1.81; p = 0.178
Complicated obstetric history / Отягощенный акушерский анамнез	147 (21.6%)	1399 (12.0%)	χ ² = 54.09; p < 0.000
Ordinal number of pregnancy / Порядковый номер беременности	2.57 ± 1.67 (1–11)	2.11 ± 1.32 (1–12)	p < 0.000
Ordinal number of births / Порядковый номер родов	1.69 ± 0.82 (1–7)	1.57 ± 0.73 (1–8)	p < 0.000
Sixth or more pregnancy / Шестая и более по счету беременность	41 (6.0%)	277 (2.4%)	χ ² = 33.79; p < 0.000
Fourth or more births / Четвертые и более по счету роды	18 (2.6%)	175 (1.5%)	χ ² = 5.46; p = 0.02

Table 2 presents the abnormalities in the course of pregnancy, labor, and neonatal condition.

Gestational diabetes mellitus and anemia, changes in the amount of amniotic fluid (low and high water content), and fetal growth retardation (based on fetometry) occurred with equal frequency in the study groups (differences were not significant). The following were significantly more frequent in the main group: pregnancies resulting from in vitro fertilization and intracytoplasmic sperm injection; hypertensive disorders in pregnancy, especially moderate (2 times more frequent) and severe (7 times more frequent) preeclampsia; isthmic-cervical insufficiency; circulatory insufficiency (based on ultrasound);

fetal breech presentation (2.5 times more often); premature detachment of the normally located placenta; premature water shedding; and surgical abdominal delivery. Meconium staining of amniotic fluid was 2 times more common in preterm pregnancies (differences are significant).

Table 3 displays the structure of the afterbirth in the main and control groups.

No significant differences were found in the occurrence of ureaplasma or RNA viral chorioamnionitis. Afterbirth ascending infections with mycoplasmas, herpes viruses, and chlamydia were significantly more common in cases of preterm birth. Most preterm births led to

Table 2. Features of the course of pregnancy, childbirth and the condition of newborns in patients of the main and control groups**Таблица 2.** Особенности течения беременности, родов и состояния новорожденных у пациенток основной и контрольной групп

Indicator / Показатель	Main group (preterm birth) / Основная группа (преждевременные роды) (n = 680)	Control group (term delivery) / Контрольная группа (срочные роды) (n = 11662)	Statistical significance / Статистическая значимость
Extra corporal fertilization / Экстракорпоральное оплодотворение	52 (7.7%)	595 (5.1%)	$\chi^2 = 4.54$; $p = 0.033$
ICSI / ИКСИ	29 (4.2%)	280 (2.4%)	$\chi^2 = 5.01$; $p = 0.024$
Gestational arterial hypertension / Гестационная артериальная гипертензия			
• absent / нет	605 (89.0%)	9831 (84.3%)	
• arterial hypertension / артериальная гипертензия	38 (5.5%)	1668 (14.3%)	$\chi^2 = 66.77$; $p < 0.000$
• moderate preeclampsia / умеренная преэклампсия	15 (2.2%)	105 (0.9%)	
• severe preeclampsia / тяжелая преэклампсия	22 (3.3%)	58 (0.5%)	
Gestational diabetes mellitus / Гестационный сахарный диабет	37 (5.5%)	956 (8.2%)	$\chi^2 = 3.42$; $p = 0.064$
Gestational anemia / Гестационная анемия	54 (7.9%)	1295 (11.1%)	$\chi^2 = 3.56$; $p = 0.059$
Isthmic cervical insufficiency / Истмико-цервикальная недостаточность	12 (1.7%)	35 (0.3%)	$\chi^2 = 21.10$; $p < 0.000$
Polyhydramnios / Многоводие	15 (2.2%)	268 (2.3%)	$\chi^2 = 0.00$; $p = 0.969$
Oligohydramnios / Маловодие	7 (1.0%)	257 (2.2%)	$\chi^2 = 2.71$; $p = 0.099$
Impaired blood flow in the umbilical cord artery / Нарушение кровотока в артерии пуповины	18 (2.7%)	50 (0.4%)	$\chi^2 = 49.50$; $p < 0.000$
Fetal growth restriction / Задержка роста плода	17 (2.5%)	152 (1.3%)	$\chi^2 = 3.23$; $p = 0.072$
Premature rupture of amniotic fluid / Преждевременное излитие околоплодных вод	586 (86.1%)	7005 (60.1%)	$\chi^2 = 214.57$; $p < 0.000$
Premature abruption of a normally located placenta / Преждевременная отслойка нормально расположенной плаценты	15 (2.2%)	89 (0.8%)	$\chi^2 = 9.75$; $p = 0.002$
Transverse/oblique fetus position / Поперечное/косое положение плода	4 (0.6%)	23 (0.2%)	$\chi^2 = 2.29$; $p = 0.130$
Breech presentation / Тазовое предлежание	16 (2.4%)	116 (1.0%)	$\chi^2 = 12.34$; $p < 0.000$
C-section / Кесарево сечение	500 (73.6%)	4980 (42.7%)	$\chi^2 = 244.95$; $p < 0.000$
Perineotomy / Перинеотомия	38 (5.6%)	1563 (13.4%)	$\chi^2 = 41.07$; $p < 0.000$
Amniotomy / Амниотомия	5 (0.76%)	198 (1.7%)	$\chi^2 = 3.48$; $p = 0.062$
Manual uterine cavity examination / Ручное обследование полости матки	13 (1.9%)	222(1.9%)	$\chi^2 = 0.01$; $p = 0.944$
Meconium amniotic fluid staining / Мекониальная окраска околоплодных вод	27 (3.9%)	840 (7.2%)	$\chi^2 = 9.79$; $p = 0.002$

Table 3. Features of the structure of the placenta in the studied groups**Таблица 3.** Особенности строения плацента в исследуемых группах

Indicator / Показатель	Main group (preterm birth) / Основная группа (преждевременные роды) (n = 680)	Control group (term delivery) / Контрольная группа (срочные роды) (n = 11662)	Statistical significance / Статистическая значимость
Ascending placenta infection / Восходящее инфицирование плаценты	323 (47.0%)	4432 (38.0%)	$\chi^2 = 22.42$; $p < 0.000$
Chlamydial choriodecidualitis / Хламидийный хориодецидуит	48 (7.1%)	660 (5.7%)	$\chi^2 = 4.69$; $p = 0.020$
Mycoplasma choriodecidualitis / Микоплазменный хориодецидуит	209 (30.7%)	3587 (29.0%)	$\chi^2 = 11.35$; $p = 0.001$
Ureaplasma choriodecidualitis / Уреаплазменный хориодецидуит	71 (10.4%)	1255 (10.8%)	$\chi^2 = 0.05$; $p = 0.828$
RNA viral choriodecidualitis / РНК-вирусный хориодецидуит	166 (24.4%)	2902 (24.9%)	$\chi^2 = 0.32$; $p = 0.858$
Herpetic choriodecidualitis / Герпетический хориодецидуит	350 (51.4%)	5311 (45.5%)	$\chi^2 = 9.33$; $p = 0.002$
Chronic placental insufficiency / Хроническая плацентарная недостаточность			
• compensated / компенсированная	45 (6.6%)	1761 (15.1%)	$\chi^2 = 43.75$; $p < 0.000$
• sub- and decompensated / суб- и декомпенсированная	232 (34.1%)	1376 (11.8%)	$\chi^2 = 226.06$; $p < 0.000$
Normal structure of the placenta / Нормальное строение плаценты	6 (0.9%)	211 (1.8%)	$\chi^2 = 2.52$; $p = 0.112$

pregnancies complicated by subcompensated and decompensated chronic placental insufficiency.

Based on the analysis, a criteria for predicting the risk of preterm birth was developed, which enables prompt preventive measures and choice of hospital, considering the increased risk of early delivery.

From the abovementioned data, six criteria (severe preeclampsia, umbilical artery Doppler flow abnormalities, gestational age of 6 or more, isthmic-cervical insufficiency, Rh-negative, and ultrasound low birth weight) that had a significant association with preterm birth were selected (Table 4). A prognostic system with the six criteria was developed using the discriminant analysis method to identify the high risk group for preterm birth, and a classification matrix was constructed (Table 5). In the control group, the proposed model provided a 99.4% accuracy of the predicted outcome compared with the actual result (the specificity of the prognosis). In the main group, the accuracy of the prediction was 73.6% compared with the real outcome (sensitivity of the prognosis).

The model has high prognostic significance and predicts early abortion with high sensitivity and specificity (93.8% model efficiency). Additionally, current regulatory documents [8, 9] focus on the prediction and timely diagnosis of conditions such as severe preeclampsia and isthmic-cervical insufficiency, and the present study

confirmed their significant role in pregnancy termination. However, several other factors that predispose to early abortion have been identified: Rh-negative blood, six or more pregnancies, the presence of circulatory insufficiency, and low water supply according to ultrasound. Women exhibiting these risk factors should be considered at high risk for preterm birth and treated as patients with a comparable risk based on the results of the biochemical screening during the first trimester of pregnancy, with appropriate preventive diagnostic measures being taken.

The presence of Rh-negative blood was significantly more common among pregnant women in the main group, both with and without antibody titers. Some studies reported that women with Rh-negative blood are significantly more likely to have perinatal losses in both preterm and term births [1, 4, 13, 17]. This pattern may be explained by genetic characteristics [5, 14].

The factors that increase the risk of preterm birth were identified: severe preeclampsia, low water supply and disturbance of blood flow parameters in the umbilical artery, six and more pregnancies, isthmic-cervical insufficiency, and negative Rh factor in the mother. These indicators were used to identify the group at high risk for preterm birth. Ascending infection of the afterbirth, mycoplasma, herpetic and chlamydial choriodecidualitis and combined infection in afterbirth with several pathogens

Table 4. Statistical significance of parameters that increase the risk of preterm birth**Таблица 4.** Статистическая значимость параметров, повышающих риск преждевременных родов

Indicator / Показатель	Main group (preterm birth) / Основная группа (преждевременные роды) (n = 680)	Control group (term delivery) / Контрольная группа (срочные роды) (n = 11662)	Statistical significance / Статистическая значимость
Severe preeclampsia / Тяжелая преэклампсия	22 (3.3%)	58 (0.5%)	0.000000
Violation of blood flow parameters in the umbilical cord artery / Нарушение параметров кровотока в артерии пуповины	18 (2.7%)	50 (0.4%)	0.000000
VI or more serial number of pregnancy / VI и более порядковый номер беременности	31 (4.6%)	277 (2.4%)	0.000000
Isthmic-cervical insufficiency / Истмико-цервикальная недостаточность	12 (1.7%)	35 (0.3%)	0.000255
Negative Rh factor / Отрицательный резус-фактор	133 (19.6%)	1879 (16.1%)	0.005812
Oligohydramnios / Маловодие	7 (1.0%)	257 (2.2%)	0.021670

Table 5. Classification matrix for predicting the birth of a premature baby**Таблица 5.** Классификационная матрица методики прогнозирования рождения недоношенного ребенка

Outcome / Исход	%	Term (predicted) / Доношенный (прогнозируемый)	Premature (predicted) / Недоношенный (прогнозируемый)
Full-term baby (real result) / Доношенный ребенок (реальный результат)	99.39	5347	133
Premature baby (real result) / Недоношенный ребенок (реальный результат)	73.61	321	12
Total / Всего	93.80	5668	145

were significantly more frequent in preterm births. Data obtained confirm the need for additional examination of pregnant women at high risk for preterm birth and, if necessary, prescription of etiotropic therapy.

CONCLUSIONS

In conclusion, severe preeclampsia, isthmic-cervical insufficiency, Rh-negative blood and six or more pregnancies, blood flow abnormalities in the umbilical artery, and low water according to ultrasound increase the risk of premature termination of pregnancy. Women with these factors should be placed on the same level of care as those at similar risk according to biochemical screening in the first trimester of pregnancy. Moreover, all women at high risk for early termination of pregnancy (including patients at high risk according to biochemical screening in the first trimester of pregnancy) should undergo additional screening for infectious agents, namely, *Chlamydia trachomatis*, Human herpesvirus, and *Mycoplasma genitalium*/*Mycoplasma hominis* and cervical canal culture for flora and sensitivity to antibacterial drugs to determine pathogenic and opportunistic microflora.

ADDITIONAL INFORMATION

Authors' contribution. All authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published, and agree to be accountable for all aspects of the study.

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Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

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