УДК 616-053.32-053.36-07:314/316
https://doi.org/10.20538/1682-0363-2025-1-114-123

Perinatal and social predictors of early childhood health in preterm infants: multicenter cohort study results

Khodkevich P.E.[1,2], Fedorova O.S.[1], Kulikova K.V.[3], Deev I.A. [4]

[1] *Siberian State Medical University*
2, Moscow Trakt, Tomsk, 634050, Russian Federation

[2] *Children's Hospital No. 1*
4, Moscow Trakt, Tomsk, 634050, Russian Federation

[3] *I.D. Evtushenko Regional Perinatal Center*
96/1, I. Chernykh Str., Tomsk, 634063, Russian Federation

[4] *Pirogov Russian National Research Medical University*
1, Ostrovityanova Str., Moscow, 117997, Russian Federation

ABSTRACT

Aim. To identify perinatal and social predictors that determine the health of premature infants in early childhood, based on their birth weight.

Materials and methods. This publication is part of a cohort prospective observational study of premature infants that was initiated in Tomsk in 2014 (Deev I.A., Kulikova K.V., Kobyakova O.S. et al., 2016). The main group consisted of 226 premature infants: 78 infants with low birth weight (LBW), 76 – with very low birth weight (VLBW), and 72 – with extremely low birth weight (ELBW), while a control group included 76 term infants. The follow-up period was 3 years, with examinations conducted every 12 months.

Results. The study found that 57.1% (n = 36) of ELBW infants, 34.9% (n = 23) of VLBW infants, and 32.9% (n = 23) of LBW infants showed an "improvement" in their health during early childhood (transition from health groups IV and V to III, as well as transition from health group III to II at subsequent visits). The presence of siblings (for the main group OR = 2.6 [95% CI 1.3–5.3], p = 0.006, for children with ELBW OR = 8.4 [95% CI 1.0–69.6], p = 0.045) and the mother's higher education (for children with VLBW OR = 3.9 [95% CI 1.2–12.2], p = 0.018 and with LBW OR = 3.4 [95% CI 1.2–9.9], p = 0.025) were identified as predictors of a favorable clinical prognosis. Perinatal and social predictors associated with the development of pathological abnormalities included intrauterine growth retardation, intraventricular hemorrhage, severe anemia in the neonatal period, maternal obesity, maternal smoking, parental age over 35 years, and lack of higher education for the mother.

Conclusion. To implement a health-preserving strategy for the group of premature infants, especially those with ELBW, health improvement can be achieved by addressing controllable social factors.

Keywords: health, premature infants, social predictors

Conflict of interest. The authors declare the absence of obvious or potential conflicts of interest related to the publication of this article.

Source of financing. The authors state that they received no funding for the study.

Conformity with the principles of ethics. An informed consent for the child's participation in the study was signed by legal representatives. The study was approved by the local Ethics Committee at Siberian State Medical University (Protocol No.7937 of 28.10.2019).

For citation: Khodkevich P.E., Fedorova O.S., Kulikova K.V., Deev I.A. Perinatal and social predictors of early childhood health in preterm infants: multicenter cohort study results. *Bulletin of Siberian Medicine.* 2025;24(1):114–123. https://doi.org/10.20538/1682-0363-2025-1-114-123.

✉ *Khodkevich Polina E.,* pkhodkevich@mail.ru

Перинатальные и социальные предикторы, определяющие состояние здоровья недоношенных детей в раннем детском возрасте: результаты когортного многоцентрового исследования

Ходкевич П.Е.[1, 2], Федорова О.С.[1], Куликова К.В.[3], Деев И.А.[4]

[1] *Сибирский государственный медицинский университет (СибГМУ)*
Россия, 634050, г. Томск, Московский тракт, 2

[2] *Детская больница № 1*
Россия, 634050, г. Томск, Московский тракт, 4

[3] *Областной перинатальный центр (ОПЦ) им. И.Д. Евтушенко*
Россия, 634063, г. Томск, ул. Ивана Черных, 96/1

[4] *Российский национальный исследовательский медицинский университет (РНИМУ) им. Н.И. Пирогова*
Россия, 117997, г. Москва, ул. Островитянова, 1

РЕЗЮМЕ

Цель. Установить перинатальные и социальные предикторы, определяющие состояние здоровья недоношенных детей в раннем детском возрасте в зависимости от массы тела при рождении.

Материалы и методы. Публикация является частью когортного проспективного наблюдательного исследования недоношенных новорожденных, инициированного в г. Томске в 2014 г. (Деев И.А., Куликова К.В., Кобякова О.С. и др., 2016). Основную группу составили 226 недоношенных новорожденных (с низкой массой тела (НМТ) – 78, с очень низкой массой тела (ОНМТ) – 76, с экстремально низкой массой тела (ЭНМТ) – 72 ребенка), в группу контроля включены 76 здоровых младенцев. Период катамнестического наблюдения – 3 года, периодичность обследования – 12 мес.

Результаты. Установлено, что 57,1% (n = 36) детей с ЭНМТ, 34,9% (n = 23) детей с ОНМТ и 32,9% (n = 23) детей с НМТ при рождении имели «улучшение» состояния здоровья (переход из IV и V групп здоровья в III, а также переход из III группы здоровья во II на последующих визитах) в раннем детском возрасте. Предикторами благоприятного клинического прогноза являлись наличие сибсов (для основной группы отношение шансов (ОШ) 2,6 [95%-й доверительный интервал (ДИ) 1,3–5,3], p = 0,006, для детей с ЭНМТ при рождении ОШ = 8,4 [95%-й ДИ 1,0–69,6], p = 0,045) и наличие высшего образования у матери (для детей с ОНМТ при рождении ОШ = 3,9 [95%-й ДИ 1,2–12,2], p = 0,018 и с НМТ при рождении ОШ = 3,4 [95%-й ДИ 1,2–9,9], p = 0,025). Также установлены перинатальные и социальные предикторы развития патологических отклонений по разным функциональным системам в зависимости от массы тела при рождении в раннем детском возрасте: задержка внутриутробного развития, внутрижелудочковое кровоизлияние, тяжелая анемия в неонатальном периоде, ожирение у матери, курение матери, возраст родителей более 35 лет, отсутствие высшего образования у матери.

Заключение. Таким образом, в целях реализации стратегии здоровьесбережения в группе недоношенных детей, особенно с ЭНМТ при рождении, улучшение состояния здоровья может быть достигнуто воздействием на управляемые социальные факторы.

Ключевые слова: здоровье, недоношенные дети, социальные предикторы

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

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

Соответствие принципам этики. Информированное согласие на участие ребенка в исследовании подписано законными представителями. Исследование одобрено локальным этическим комитетом СибГМУ (протокол № 7937 от 28.10.2019).

Для цитирования: Ходкевич П.Е., Федорова О.С., Куликова К.В., Деев И.А. Перинатальные и социальные предикторы, определяющие состояние здоровья недоношенных детей в раннем детском возрасте: результаты когортного многоцентрового исследования. *Бюллетень сибирской медицины.* 2025;24(1):114–123. https://doi.org/10.20538/1682-0363-2025-1-114-123.

INTRODUCTION

Health preservation strategy is a priority area of medicine. This approach promotes the need for pregravid preparation, since human health is largely determined by the course of the ante-, intra- and neonatal periods of life, and according to the theory of "fetal programming", is the result of a combination of the genetic program under the influence of perinatal factors [1–3]. Premature infants, especially those with very low birth weight (VLBW) and extremely low birth weight (ELBW), are particularly vulnerable to developing various diseases both in the neonatal period and later in life [4–7]. Several studies have identified laboratory, instrumental, and clinical predictors of an unfavorable clinical prognosis for premature infants in the neonatal period have been established [8, 9]. Additionally, some studies have examined perinatal risk factors for chronic health issues in children born with VLBW and ELBW. However, these studies are limited in number and often only focus on one aspect of the body's functioning [5]. At the same time, identifying predictors of a favorable clinical prognosis associated with a decrease in morbidity and the absence of chronic disease exacerbations can be an effective tool in strengthening the health of the population of premature infants.

Thus, we planned and conducted a study to determine perinatal and social predictors that influence the health of premature infants in early childhood, based on their birth weight.

MATERIALS AND METHODS

This study is part of a cohort prospective observational study of premature infants initiated in Tomsk in 2014 [10]. The study included data from 302 children born in 2014–2020 at the I.D. Evtushenko Regional Perinatal Center and the Tomsk Maternity Hospital No. 4. Once the legal representatives signed the informed consent for their child to participate in the study, the child was included in one of the observation groups. The study methodology, inclusion and exclusion criteria, results of the ethical review, study design, and clinical characteristics of the children during the neonatal period were previously published [7, 11]. Four in-person visits were conducted: visit 0 (during the neonatal period), visit 1 (at one year of age), visit 2 (at two years of age), and visit 3 (at three years of age).

This article presents an analysis of the anamnestic data of parents (socioeconomic status, education, health status, anthropometric data, presence of bad habits, and medication intake) and the health groups of the children according to the Order of the Ministry of Health of the Russian Federation dated December 30, 2003 No. 621 "On a comprehensive assessment of the health of children". Additionally, conclusions from narrow medical specialists and medical commissions based on medical documentation (forms 112/u) were used to established medically verified diagnoses (such as malnutrition, obesity, transient hypothyroidism, bronchopulmonary dysplasia, myopia, astigmatism, patent ductus arteriosus, psychomotor retardation, hearing loss, etc.). When assessing the health dynamics of the observed children, a comparison was made between the current visit and the previous visit. A favorable clinical outcome was recorded when a child was assigned to a more "favorable" health group (for example, transitioning from IV to III health group or from III to II health group) or maintained their I, II, or III health group without exacerbation or decompensation of chronic diseases. An unfavorable clinical outcome was recorded when a child was assigned to a less favorable health group (from I and II health groups to III group) or experienced decompensation or exacerbation of chronic diseases.

Statistical analysis was performed using the Statistica for Windows, 13.0 software package. Quantitative data were described using the arithmetic mean and standard deviation (M±SD). For qualitative data, the absolute value and percentage were determined. The Mann-Whitney U-test was used to assess the differences in quantitative data. The Pearson $\chi 2$ test (with Yates' correction for values less than 10) was used to compare the frequencies of qualitative features. The difference in values was considered statistically significant at $p < 0.05$.

RESULTS

The study included the main group of 226 premature infants (low birth weight (LBW) – 78 children, VLBW – 76 children, and ELBW – 72 children), and a control group of 76 healthy infants. At the beginning of the study, the main group consisted of 123 boys (54%) and 103 girls (46%), while the control group had 57 boys (75%) and 19 girls (25%). There were statistically significant differences in anthropometric parameters and gender between the main and control groups, but the groups of premature infants were comparable in terms of gender [7].

When the children were divided into health groups based on their birth weight, it was found that at the visit 0, health group II was predominant among premature infants with LBW (n = 46, 58.9%) than among those with VLBW (n = 24, 31.6%, p < 0.001). In the ELBW group, children with health groups III–IV were more common than in the other groups. Throughout the observation period, children with a birth weight of less than 1,000 grams were less likely to be in health group II than children in other observation groups, and more often belonged to regular health check-up groups III–IV compared to children with LBW and VLBW (Table 1).

Table 1

Distribution of children by health groups based on their birth weight and age, % (n)

Age	Health group	LBW	VLBW	ELBW	Control group
Visit 0	I	0 (0)	0 (0)	0 (0)	67.1 (51)
	II	58.9 (46)	31.6* (24)	0 (0)	32.9 (25)
	III	37.1 (29)	61.8* (47)	45.8 (33)	0 (0)
	IV	1.3 (1)	5.3 (4)	37.5** (27)	0 (0)
	V	2.6 (2)	1.3 (1)	16.7** (12)	0 (0)
Visit 1	I	7.1 (5)	1.5 (1)	0 (0)	57.1** (40)
	II	58.6 (41)	33.3 (22)	7.9$^{\#}$ (5)	31.8 (20)
	III	28.6 (20)	53.0$^{\#\#}$ (35)	55.6$^{\#\#}$ (35)	4.8 (3)
	IV	5.7 (4)	12.2 (8)	33.3$^{\#}$ (21)	0 (0)
	V	0 (0)	0 (0)	3.2 (2)	0 (0)
Visit 2	I	9.8 (4)	5.6 (2)	0 (0)	8.3 (1)
	II	53.7 (22)	41.7 (15)	20.5$^{\#\#}$ (9)	83.3 (10)
	III	26.8 (11)	30.6 (11)	43.2 (19)	8.3 (1)
	IV	9.8 (4)	19.4 (7)	36.4* (16)	0 (0)
	V	0 (0)	2.8 (1)	0 (0)	0 (0)
Visit 3	I	10.5 (4)	8.6 (3)	0 (0)	8.3 (1)
	II	60.5 (23)	45.7 (16)	27.3$^{\#\#}$ (12)	75.0 (9)
	III	21.1 (8)	31.4 (11)	47.7* (21)	16.7 (2)
	IV	5.3 (2)	14.3 (5)	22.7 (10)	0 (0)
	V	0 (0)	0 (0)	2.3 (1)	0 (0)

* p < 0.05 when compared with the LBW group (Pearson χ2 test); ** p < 0.05 when compared with the LBW and VLBW groups (Pearson χ2 test); $^{\#}$ – p < 0.05 when compared with the LBW, VLBW, and control groups (Pearson χ2 test); $^{\#\#}$ p < 0.05 when compared with the LBW and control groups (Pearson χ2 test).

The study also analyzed the prevalence of pathological deviations in the main functional systems of the body. It was found that at the age of one year, children with VLBW (n = 9, 13.6%, p = 0.017) and ELBW (n = 18, 28.6%, p < 0.001) were more likely to have malnutrition than children in the control group (n = 1, 1.6%). At the age of two and three years, statistically significant differences in the presence of malnutrition between premature infants based on birth weight were not found. This deviation was not recorded at visits 2 and 3 (Table 2) among children in the control group.

The study also found that children with ELBW were more likely to have abnormalities in the nervous system (such as delayed psychomotor development, movement disorder syndrome, hypertension syndrome, and cerebral palsy) than children in other groups at the age of one and two years. At the age of three, there were no differences in the prevalence of neurological pathology between the groups.

Children with ELBW were also more likely to have endocrine pathology (mainly transient hypothyroidism) throughout the observation period compared to children in other groups (Table 2).

When analyzing data on the presence of visual organ deviations, children with ELBW (n = 31, 49.2%) were more likely to have ophthalmic pathology (such as retinopathy of prematurity, severe myopia, astigmatism, and others) at the first visit compared to children with LBW (n = 9, 12.9%, p < 0.001) and VLBW (n = 7, 10.6%, p < 0.001). At the age of two, no differences were found between the groups. At visit 3, ophthalmic pathology was statistically significantly more common among

children with ELBW (n = 12, 27.3%) than among children with LBW at birth (n = 2, 5.3%, p = 0.019).

The main lung pathology among premature infants included in the study throughout the entire observation period was bronchopulmonary dysplasia (BPD). Children with ELBW were more likely to have this diagnosis than premature infants of other groups throughout early childhood (Table 2). At the age of one year, according to the results of the study, 26 children (37.1%) with LBW, 29 children (43.9%) with VLBW, and 21 children (33.3%) with ELBW had anemia of varying severity, which was more common than that in the control group – 4 (6.4%, $p < 0.001$).

When studying the prevalence of cardiovascular diseases (congenital heart defects, except for patent ductus arteriosus, arrhythmia), gastrointestinal tract (chronic constipation, biliary tract diseases, functional bowel disorders, etc.), and genitourinary system (hypospadias, congenital kidney defects, spermatic cord cysts, labia minora adhesions, etc.), no statistically significant differences were found between the groups in early childhood [7].

At the end of the follow-up, 27.3% (n = 12) of children with ELBW had a disabling disease, which was significantly more common than among children with LBW (n = 2, 5.3%, p = 0.019) and VLBW (n = 1, 2.9%, p = 0.010). According to our study, having a birth weight of less than 1,000 grams increased the odds of having a disability at the age of three by 9 times compared to premature infants with birth weights between 1,000 and 2,500 grams (OR = 8.8 [95% CI 2.3–3.2], $p < 0.001$). No child in the control group had a disabling disease.

Table 2

Structure of pathological abnormalities in children based on their birth weight in early childhood

Pathological deviations	Main group		LBW		VLBW		ELBW		Control group	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
1 year										
Malnutrition	34#	17.1	7	10	9#	13.6	18#	28.6	1	1.6
Pathology of the cardiovascular system	42	21.1	15	21.4	12	18.2	15	23.8	0	0
Pathology of the nervous system	48	24.1	15#	21.4	12	18.2	21#	33.3	4	6.4
Endocrine pathology	104	52.3	15	21.4	37*	56.1	52**	82.5	3	4.8
Ophthalmic pathology	47#	23.6	9	12.9	7	10.6	31**	49.2	6	9.5
Lung pathology	38	19.1	1	1.4	4	6.1	33***	52.4	0	0
Pathology of the genitourinary system	27	13.6	10	14.3	12	18.2	5	7.9	0	0
Gastrointestinal tract pathology	10	5.0	3	4.3	3	4.6	4	6.4	0	0
Anemia	76#	38.2	26#	37.1	29#	43.9	21#	33.3	4	6.4
2 years										
Malnutrition	20	16.5	5	12.2	3	8.3	12	27.3	0	0
Pathology of the cardiovascular system	16	13.2	5	12.2	2	5.6	9	20.5	0	0
Pathology of the nervous system	48	39.7	11	26.8	12	33.3	25***	56.8	0	0
Endocrine pathology	51	42.2	7	17.1	13	36.1	31**	70.5	2	16.7
Ophthalmic pathology	21	17.4	4	9.8	3	8.3	14	31.8	1	8.3
Lung pathology	16	13.2	0	0	4	11.1	12	27.3	0	0
Pathology of the genitourinary system	9	7.4	2	4.9	4	11.1	3	6.8	1	8.3
Gastrointestinal tract pathology	22	18.2	7	17.1	7	19.4	8	18.2	1	8.3
3 years										
Malnutrition	8	6.8	0	0	4	11.4	4	9.1	0	0
Pathology of the cardiovascular system	11	9.4	2	5.3	3	8.6	6	13.6	0	0
Pathology of the nervous system	40	34.2	10	26.3	10	28.6	20	45.5	3	25.0
Endocrine pathology	40	34.2	7	18.4	10	28.7	24**	54.6	2	16.7
Ophthalmic pathology	18	15.4	2	5.3	4	11.4	12*	27.3	0	0
Lung pathology	5	4.3	0	0	1	2.9	4	9.1	0	0
Pathology of the genitourinary system	10	8.6	3	7.9	4	11.4	3	6.8	3	25.0
Gastrointestinal tract pathology	17	14.5	6	15.8	4	11.4	7	15.9	1	8.3

# $p < 0.05$ relative to the control group (Pearson $\chi 2$ test); * $p < 0.05$ relative to the LBW group and the control group (Pearson $\chi 2$ test); ** $p < 0.05$ relative to the control group, LBW and VLBW groups (Pearson $\chi 2$ test); *** $p < 0.05$ relative to the LBW and VLBW groups at birth (Pearson $\chi 2$ test).

Social predictors of a favorable clinical prognosis for premature infants in early childhood

During the follow-up, some children were a posteriori assigned to a group of infants with improved health. This group consisted of children who moved to a more favorable health group during subsequent visits, for example, from IV to III health group, from III to II health group. It was found that 57.1% (n = 36) of children with ELBW, 34.9% (n = 23) of children with VLBW, and 32.9% (n = 23) of children with LBW at birth had improved health in early childhood.

An analysis of possible social predictors (such as age, anthropometric data, education and social status of parents, income, presence of bad habits, and chronic diseases) of a favorable clinical prognosis (assignment to a more favorable health group at subsequent visits or maintenance of I, II or III health group in the absence of exacerbation and decompensation of chronic diseases) for premature infants included in the study was conducted during the follow-up period (Fig).

A statistically significant predictor associated with improved health status of premature infants in early childhood, according to the results of our study, was the presence of siblings. The probability of a positive clinical prognosis increased 3-fold among children in the main group (OR = 2.6 [95% CI 1.3–5.3], p = 0.006) and 8-fold among children with ELBW at birth (OR = 8.4 [95% CI 1.0–69.6], p = 0.045). At the same time, according to the logistic regression model, with each subsequent child born in the family, the probability of a favorable clinical prognosis for premature infants increased (OR = 14.2 [95% CI 1.7–118.8], p = 0.007).

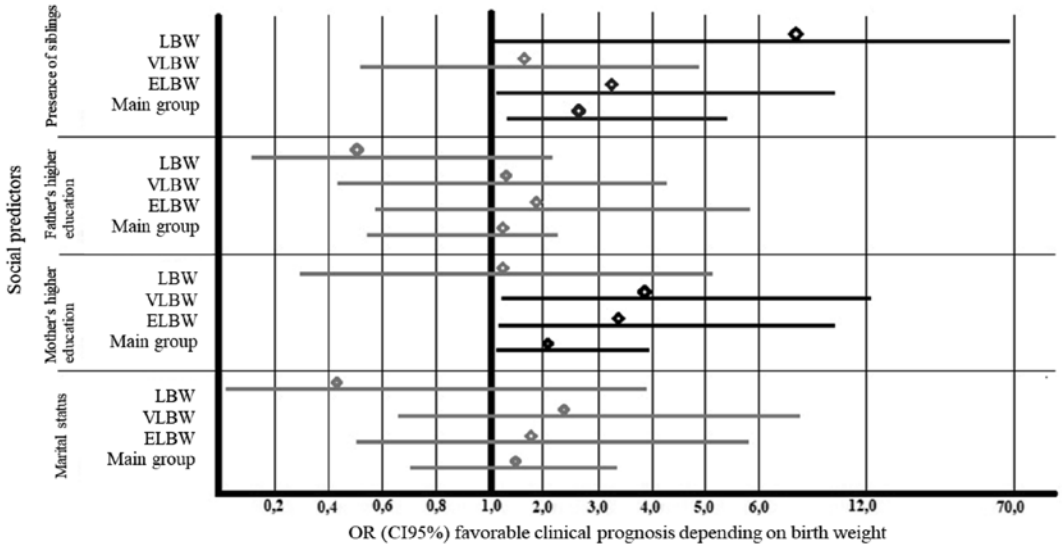

Fig. Social predictors of a favorable clinical prognosis: ** for premature infants in early childhood based on their birth weight. * higher education; ** assignment to a more favorable health group (e.g. transition from IV to III health group, from III to II health group) at subsequent visits or maintenance of I, II or III health group in the absence of exacerbation and decompensation of chronic diseases.

According to the results of the study, a positive predictor of the health status of children in the main group was the presence of higher education for the mother. This factor statistically significantly increased the chance of a favorable clinical prognosis in premature infants with VLBW at birth by 4 times (OR = 3.9 [95% CI 1.2–12.2], p = 0.018) and with LBW at birth by 3 times (OR = 3.4 [95% CI 1.2–9.9], p = 0.025).

The data analysis using the logistic regression method revealed that a decrease in the number of cigarettes consumed per day by the father was associated with a favorable clinical prognosis of premature infants in the groups with LBW (OR = 0.1 [95% CI 0.0–0.6], p = 0.012) and ELBW (OR = 0.001 [95% CI 0.0–0.9], p = 0.009).

Perinatal predictors determining the health status for premature infants in early childhood

The study analyzed the contribution of several perinatal factors (such as anthropometric data at birth, gestational age, presence of intrauterine growth

retardation, intraventricular hemorrhage, severe asphyxia and seizures in the neonatal period, presence of lateral ventricular dilation, invasive ventilation, and infectious diseases in the neonatal period). A number of predictors associated with an increased likelihood of developing pathological abnormalities in individual functional systems and individual nosological units depending on birth weight at the age of one, two, and three years were identified.

According to the results of the study, one of the significant perinatal factors worsening the prognosis for several systems among premature infants of all groups was severe anemia requiring blood transfusion in the early neonatal period. The presence of this deviation increased the probability of nervous system pathology (OR = 6.2 [95% CI 1.4–25.5], p = 0.008) and ophthalmic pathology (OR = 5.5 [95% CI 1.1–28.9], p = 0.029) by 6 times at the age of one year among children with LBW at birth. It also increased the probability of having 4 or more pathological deviations in different functional systems of the body among children with VLBW at birth by 4 times at the age of one year (OR = 4.3 [95% CI 1.3–13.9], p = 0.012) and the probability of having neurological pathology by 5 times at the age of two years (OR = 4.7 [95% CI 1.1–22.7], p = 0.043).

The study established that for premature infants with low birth weight (LBW) who experienced intraventricular hemorrhages (IVH) and intrauterine growth retardation (IUGR) were more likely to develop pathological abnormalities in multiple functional systems during early childhood.

IVH increased the likelihood of developing transient hypothyroidism among premature infants with LBW by 4 times at the age of one year (OR = 4.1 [95% CI 1.0–16.0], p = 0.034) and by 10 times at the age of two years (OR=10.3 [95% CI 1.7–64.0], p = 0.020), as well as anemia at one year by 11 times (OR = 11.1 [95% CI 2.2–56.9], $p < 0.001$). Premature infants with a birth weight of 1,500 to 2,500 grams with IUGR were statistically significantly more likely to have malnutrition at the age of one year (OR = 5.1 [95% CI 1.0–25.8], p = 0.033) and psychomotor developmental delay (OR = 16.0 [95% CI 1.6–155.0], p = 0.003). IUGR also increased the likelihood of a neurological diagnosis among children with LBW by 9 times at the age of three years (OR=8.7 [95% CI 1.3–58.9], p = 0.014).

When analyzing the results of instrumental studies among premature infants in the studied cohort, it was revealed that a significant predictor of nervous system pathology in early childhood was dilation of the lateral ventricles, as identified by neurosonography (NSG) during infancy (from 1 to 12 months of age), even without the development of hydrocephalus and hypertension syndrome. This deviation increased the likelihood of a neurological diagnosis among children with LBW by 5 times at the age of one year (OR = 5.0 [95% CI 1.2–20.5], p = 0.017) and two years (OR = 5.4 [95% CI 1.1–26.5], p = 0.028). Additionally, dilation of the lateral ventricles according to neurosonography results increased the chance of persistent transient hypothyroidism among children with ELBW by 5 times (OR = 4.6 [95% CI 1.1–20.2, p = 0.034) at the age of two years.

Social predictors determining the health status of premature infants in early childhood

The study analyzed a number of socioeconomic risk factors (such as age, anthropometric data, education and social status of parents, bad habits, chronic diseases, and income of parents) and identified several predictors associated with an increased likelihood of developing pathological abnormalities in individual functional systems among premature infants.

When analyzing the anthropometric data of parents, it was found that one of the significant predictors of nervous system pathology among premature infants in all groups included in the study was the mother's body mass index (BMI) > 25. At the age of one year, among premature infants with ELBW at birth, whose mothers had a BMI over 25 at the beginning of pregnancy. There was a statistically significant increase in the occurrence of a combination of four or more pathological deviations in different functional systems (OR = 3.8 [95% CI 1.1–13.3]), p = 0.047), psychomotor developmental delay (OR = 3.7 [95% CI 1.0–13.1]), p = 0.037), visual pathology (OR = 6.6 [95% CI 1.8–23.2]), p = 0.002), and the course of bronchopulmonary dysplasia (BPD) (OR = 5.4 [95% CI 1.5–19.0]), p = 0.013). At the age of two years, among premature infants, regardless of birth weight, whose mothers had a BMI over 25, there was a statistically significant increase in delayed speech development (OR = 2.5 [95% CI 1.0–5.9], p = 0.041). This predictor was also associated with the likelihood of a longer course of transient hypothyroidism at the age of two years among children with LBW (OR = 9.7 [95% CI 1.1–89.9]), p = 0.022).

The study established that one of the significant factors in maternal history, as a predictor of an unfavorable clinical prognosis for the group of children with a birth weight of less than 1,000 grams, is maternal smoking before and during pregnancy. This bad habit in the mother increased the likelihood of BPD persistence by 5 times (OR = 4.7 [95% CI 1.5–15.3], p = 0.007), visual pathology (OR = 4.1 [95% CI 1.3–12.6], p = 0.013), and the development of anemia at the age of one year (OR = 3.5 [95% CI 1.2–10.7], p = 0.023) by 4 times among premature infants with ELBW at birth.

Another significant social predictor of the development of pathological deviations in premature infants with a birth weight of less than 1,500 grams, according to the results of our study, was the mother's lack of higher education. Children with VLBW, whose mothers did not receive a higher education before the child's birth, were significantly more likely to have BPD at the age of one year (OR = 5.4 [95% CI 1.8–15.8]), p = 0.002). The lack of mother's higher education increased the likelihood of a neurological diagnosis in a child with VLBW at the age of two years by 6 times (OR = 6.1 [95% CI 1.2–30.1]), p = 0.021) and a combination of four or more pathological deviations among children with VLBW at the age of three years by 4 times (OR = 4.2 [95% CI 1.2–15.4], p = 0.026).

One more significant factor in parental anamnestic data associated with the clinical prognosis of premature infants in the study sample was age over 35 years. This predictor, both on the mother's and father's side, increased the likelihood of transient hypothyroidism among children with LBW at the age of two and three years.

DISCUSSION

The study found that children born with ELBW have different health statuses and are more likely to have pathological abnormalities in their nervous, endocrine, respiratory, and visual systems compared to premature infants with a birth weight of over 1,000 grams. This is consistent with previous studies [12, 13].

These pathological deviations that occur in the neonatal period largely determine the health status of premature infants at an older age. According to our study results, significant perinatal risk factors for the development of diseases of the nervous system, visual pathology, anemia, persistence of pulmonary pathology in premature infants depending on birth weight in early childhood include IUGR, IVH, severe anemia in the neonatal period, and dilation of the lateral ventricles. According to A.I. Safina et al. (2020) and A.K. Mironova et al. (2023), predictors of the development of disabling conditions in early childhood include gestational age less than 28 weeks, extremely low birth weight, oxygen dependence for more than 28 days after birth, grade 3 intraventricular hemorrhage, and periventricular leukomalacia [5, 13, 14].

A long-term cohort study by Yu.E. Shmatova et al. (2022) examined risk factors for children's health from the mother before and during pregnancy and found that maternal age over 40, smoking, single mother status, and mother's thyroid pathology can worsen the clinical prognosis in healthy full-term children in early childhood and primary school age [15]. During our study, for the first time in Russia, we obtained the data on the role of socioeconomic predictors associated with the clinical prognosis of premature infants based on birth weight. We found that the age of the parents over 35 years, the mother's BMI over 25, the level of mother's education, and parental smoking affect the health of premature infants throughout early childhood. A number of international studies have noted that maternal obesity affects the perinatal development of the brain in premature infants according to diffusion tensor imaging, which may be a pathogenetic rationale for the indirect effect of maternal obesity on the neuropsychic development of children [16, 17]. J.T. Bangma et al. (2020) in a systematic review found that maternal obesity and low socioeconomic status increase neonatal systemic inflammation and disrupt placental programming, which further worsens the health prognosis of premature infants with ELBW [18]. Our results can be used to carry out preventive measures among women planning pregnancy, pregravid preparation, as well as to create an individual plan for regular health check-up of premature infants whose mothers have these risk factors [19].

As a result of our study, it was established for the first time that the mother's higher education and the presence of siblings were significant predictors of a favorable clinical prognosis for premature infants, especially with ELBW, during a three-year follow-up. It was also established that the more children in the family, the greater the likelihood of improving the health of the premature infant in early childhood.

This fact may be associated with a fact that woman with higher education and experience raising her own children is more aware of the importance and possibility of regular health check-up and rehabilitation measures.

CONCLUSION

The conducted cohort prospective observational study of premature infants has provided unique data on the health status of children during the follow-up period. The study has also allowed us to identify key perinatal and social predictors of prognosis.

To implement a health-preserving strategy for the group of premature infants, it is crucial to improve not only the methods of nursing and neonatal care, but also to promote the principles of pre-conception preparation. This includes increasing awareness among the female population of childbearing age about the need to quit smoking, prevent and treat obesity, promote higher education among women, and support large families.

REFERENCES

1. Sandakova E.A., Zhukovskaya I.G. Fetal programming. *Medical alphabet.* 2019;2(14):17–20. DOI: 10.33667/2078-5631-2019-2-14(389)-17-20.
2. Azarova E.V., Kosmovich T.V., Dimova S.G., Vyalkova A.A. Modern aspects of early neonatal adaptation (survey of the literature). *Orenburg Medical Bulletin.* 2019;3(2(10):59–67.
3. Kovtun O.P., Tsyvyan P.B., Solovyova O.E. Perinatal programming and cardiomyocyte aging. *Russian Bulletin of Perinatology and Pediatrics*. 2017;62(1):33–39. (In Russ). DOI: 10.21508/1027-4065-2017-62-1-33-39.
4. Kumar V.H.S. Cardiovascular morbidities in adults born preterm: getting to the heart of the matter! *Children (Basel).* 2022;9(12):1843. DOI: 10.3390/children9121843.
5. Safina A.I., Volyanyuk E.V. Long-term neuropsychiatric outcomes of deeply premature infants, prospects for diagnosis and correction. *Russian Bulletin of Perinatology and Pediatrics.* (In Russ). 2020;65(5):227–231. (In Russ). DOI: 10.21508/1027-4065-2020-65-5-227-231.
6. Volyanyuk E.V. Results of monitoring of morbidity and developmental outcomes by 3 years of age in premature infants born with extremely low body weight. *Practical Medicine*. 2019;17(5):175–179. DOI: 10.32000/2072-1757-2019-5-175-179.
7. Khodkevich P.E., Kulikova K.V., Fedorova O.S., Deev I.A., Kulikov E.S. Early childhood cardiological profile of premature infants with a birth weight below 2500 gram. *Pediatria n.a. G.N. Speransky*. 2024;103(1):30–38. (In Russ). DOI: 10.24110/0031-403X-2024-103-1-30-38.
8. Furman E.G., Nikolenko A.V., Kulizhnikov G.V. Clinical and laboratory predictors of unfavorable outcome in extremely premature infants. *Doctor.Ru.* 2020;19(10):10–15. (In Russ). DOI: 10.31550/1727-2378-2020-19-10-10-15.
9. Mustafin T.A., Karpova A.L., Mostovoy A.V., Kolesnikov A.N. Clinical and laboratory indicators of lethal outcome in premature newborns with body weight less than 1500 grams. *Neonatology: News Opinions, Training.* 2021;9(3):9–15. (In Russ). DOI: 10.33029/2308-2402-2021-9-3-9-15.
10. Deev I.A., Kulikova K.V., Kobyakova O.S., Kulikov E.S., Holopov A.V., Stepanov I.A. et al. Cinical characteristics of newborn with different birth weight (results of a multicenter cohort study). *Pediatrician.* 2016;7 (4):67–76. (In Russ). DOI: 10.17816/PED7467-76.
11. Khodkevich P.E., Kulikova K.V., Deev I.A., Fedorova O.S., Kulikov E.S.Vaccination of premature infants: real clinical practice. *Infection. Diseases.* 2022;20(3):50–58. (In Russ). DOI: 10.20953/1729-9225-2022-3-50-58.
12. Mironova A.K., Pykov M.I., Vatolin K.V., Osmanov I.M. Integrated approach of follow-up observation of children under 3 years old born with very low and extremely low body weight. *Russian Bulletin of Perinatology and Pediatrics*. 2020;65(1):122–127. (In Russ). DOI: 10.21508/1027-4065-2020-65-1-122-127.
13. Volyanyuk E.V., Safina A.I., Vakhitov Kh.M., Filatov V.S., Sharipova O.V.. Characteristic features of health indicators of premature children during the early childhood depending on the time of gestation at birth. *Pediatria n.a. G.N. Speransky.* (In Russ). 2022;101(1):121–127.
14. Mironova A.K. Health status of children born with very low and extremely low body weight, and differentiated system of providing them with medical care at an early age: Diss. ... Doctor of Medicine. Moscow; 2023. (In Russ). URL: https://www.elibrary.ru/item.asp?id=59961452. Available: 12.09.2024.
15. Shmatova Yu.E., Razvarina I.N., Gordievskaya A.N. Maternal risk factors for a child's health prior to and during pregnancy (results of long-term cohort monitoring in Vologda region). *Health Risk Analysis.* (In Russ). 2022;3:143–159. DOI: 10.21668/health.risk/2022.3.14.eng.
16. Parsaei M., Hashemi S.M., Moghaddam H.S., Peterson B.S. A systematic review of MRI studies on the effects of maternal obesity on offspring brain structure and function. *J. Neurosci. Res.* 2024;102(7):e25368. DOI: 10.1002/jnr.25368.
17. Lee J.Y., Lee H.J., Jang Y.H., Kim H., Im K., Yang S. et al. Maternal pre-pregnancy obesity affects the uncinate fasciculus white matter tract in preterm infants. *Front. Pediatr.* 2023;11:1225960. DOI: 10.3389/fped.2023.1225960.
18. Bangma J.T., Hartwell H., Santos H.P. Jr., O'Shea T.M., Fry R.C. Placental programming, perinatal inflammation, and neurodevelopment impairment among those born extremely preterm. *Pediatr. Res.* 2021;89(2):326–335. DOI: 10.1038/s41390-020-01236-1.
19. Petrov U.A., Berezovskaya K.E., Kupina A.D. Principles of compliance with premature training as a method of perspective medicine. *Health & Education Millennium.* 2019;21(5):17–22. (In Russ). DOI: 10.26787/nydha-2226-7425-2019-21-5.

Authors' contribution

Fedorova O.S. – conception and design, study coordination, drafting of the manuscript, critical revision of the manuscript for important intellectual content, and final approval of the manuscript for publication. Deev I.A. – conception and design, study coordination, drafting of the manuscript, and final approval of the manuscript for publication. Kulikova K.V. – database compilation, face-to-face visits, obtaining and interpreting clinical data, critical revision of the manuscript for important intellectual content, and final approval of the manuscript for publication. Khodkevich P.E. – literature analysis, database compilation, face-to-face visits, obtaining and interpreting clinical data, statistical processing of study results, and final approval of the manuscript for publication.

Authors' information

Khodkevich Polina E. – Neonatologist, Neonatal Pathology Department, Children's Hospital No. 1; Assistant Professor of the Intermediate-Level Pediatrics Division with a Pediatric Diseases Course, General Medicine Department, Siberian State Medical University, Tomsk, pkhodkevich@mail.ru, http://orcid.org/0000-0001-7639-1747.

Fedorova Olga S. – Dr. Sci. (Med.), Vice-Rector for Postgraduate Education and Research, Head of the Intermediate-Level Pediatrics Division with a Pediatric Diseases Course, General Medicine Department, Siberian State Medical University, Tomsk, olga.sergeevna.fedorova@gmail.com, https://orcid.org//0000-0002-7130-9609.

Kulikova Kristina V. – Cand. Sci. (Med.), Head of the Neonatal Intensive Care Unit, I.D.Evtushenko Regional Perinatal Center, Tomsk, kristina.v.kulikova@gmail.com, http://orcid.org/0000-0001-8926-5918.

Deev Ivan A. – Dr. Sci. (Med.), Professor of the Department of Management, Healthcare Economics and Health Insurance, Pirogov Russian National Research Medical University, Moscow, ivandeyev@yandex.ru, http://orcid.org/0000-0002-4449-4810.

(✉) **Khodkevich Polina E.,** pkhodkevich@mail.ru

Received 11.11.2024;
approved after peer review 18.11.2024;
accepted 28.11.2024