

## Clinical and diagnostic features in the study of the condition of the placentas of extremely premature newborns and disabling pathology at preschool age

### *Charakterystyka kliniczno-diagnostyczna łożysk noworodków urodzonych skrajnie przedwcześnie oraz wpływ stanu łożyska na występowanie niepełnosprawności w wieku przedszkolnym*

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**Key words:** premature babies, Neonate Post-discharge Follow-up Department, disability, long-term consequences.

**Słowa kluczowe:** wcześniaki, oddział obserwacji powypisowej wcześniaków, niepełnosprawność, następstwa odległe.

#### Abstract

**Introduction:** Premature newborns are a special category of children with inherent morpho-functional immaturity and specific pathological conditions that cause significant differences in the survival and morbidity, and the consequences of their care in comparison with children of other weight categories. The problems of premature babies are at the forefront of neonatal research and perinatal care.

**Aim of the research:** To establish an association between the formation of adverse consequences in preschool children born prematurely, with a body weight of less than 1500 g, and placental changes.

**Material and methods:** The study involved 220 preschool children born prematurely. The results of a pathomorphological study of the placentas of mothers of 220 children were analysed. The results distinguished 5 groups of mothers according to the classification of changes in the placenta. In the course of the study, this category of children was under observation of the doctors of the Prematurity and High-risk Neonate Post-discharge Follow-up Department, in order to regular assess their health. Clinical indicators such as body weight, height, head circumference, neurological and general cognitive development, and low-severity dysfunction, the post-discharge history including respiratory diseases, skeletal system problems, and haematological and metabolic disorders was analysed. Ophthalmological and audiological examinations were performed prospectively to assess vision and hearing. Patients were divided into 3 groups depending on the severity of the disabling pathology.

**Results:** An analysis of the clinical parameters of children with severe disability consequences was carried out; these were divided into 5 groups according to the changes found in their placentas. All the children involved in the study had a disease combination in the neonatal period that caused severe conditions. Pathological changes of the placenta significantly affected the course of the neonatal period. Thus, newborns with signs of inflammatory changes and immaturity were 10 times more likely to suffer generalized intrauterine infections and neonatal sepsis; they also significantly more frequently had intraventricular haemorrhages, periventricular leukomalacia, and bronchopulmonary dysplasia. The course of the neonatal period in groups of children with signs of premature aging of placenta and blood flow disorders was characterized by a low frequency of infections, but periventricular leukomalacia was diagnosed 5 times more often.

**Conclusions:** It was found that transplacental infection and pathological placenta immaturity had a negative impact on the health of children of groups III and IV, causing their birth 3 weeks prematurely, unlike the children in the comparison group. Newborns of groups III and IV needed resuscitation care in the delivery room 9 times more often, and the need for respiratory support was 10 times higher than in the comparison group, which predetermined a significantly longer duration of hospital stay for children of groups III and IV – on average 30–45 days longer compared to the newborns of group V.

#### Streszczenie

**Wprowadzenie:** Noworodki przedwcześnie urodzone stanowią szczególną grupę dzieci, u których stwierdza się niedojrzałość morfofunkcjonalną i swoiste stany patologiczne wywołujące istotne różnice pod względem przeżywalności, zachowalności i wymogów dotyczących opieki w porównaniu z dziećmi z innych kategorii masy ciała. Problemy związane z wcześniactwem są jednym z głównych kierunków badań dotyczących noworodków i opieki okołoporodowej.

**Cel pracy:** Ustalenie zależności między zmianami w łożysku w okresie ciąży a niekorzystnymi skutkami u dzieci w wieku przedszkolnym, które urodziły się przedwcześnie, z masą ciała poniżej 1500 g.

**Materiał i metody:** Do badania włączono 220 urodzonych przedwcześnie dzieci w wieku przedszkolnym. Przeanalizowano wyniki badań patomorfologicznych łożysk ich matek. Wyniki analizy pozwoliły na wyodrębnienie 5 grup matek według klasyfikacji zmian stwierdzonych w łożysku. W okresie badania dzieci z tej grupy pozostawały pod obserwacją lekarzy z oddziału obserwacji powypisowej wcześniaków i noworodków wysokiego ryzyka w celu regularnej oceny stanu ich zdrowia. Analizie poddano wskaźniki kliniczne obejmujące masę ciała, wzrost, obwód głowy, stan neurologiczny, ogólny rozwój poznawczy i występowanie zaburzeń o niewielkim nasileniu, a także historię chorób po wypisie, m.in. schorzeń układu oddechowego, nieprawidłowości układu szkieletowego, zaburzeń hematologicznych i metabolicznych. Prospektywnie przeprowadzono badania okulistyczne i audiologiczne w celu oceny wzroku i słuchu. Pacjentów podzielono na 3 grupy w zależności od stopnia nasilenia patologii powodującej niepełnosprawność.

**Wyniki:** U dzieci z ciężkimi następstwami w postaci niepełnosprawności przeprowadzono analizę parametrów klinicznych; podzielono je na 5 grup w zależności od zmian stwierdzonych w łożysku. U wszystkich dzieci włączonych do badania w okresie noworodkowym występowały mnogie choroby wywołujące ciężkie stany. Zmiany patologiczne w obrębie łożyska w znamienny sposób wpływały na przebieg okresu noworodkowego. Noworodki z objawami zapalnymi i niedojrzałością organizmu były 10-krotnie bardziej narażone na uogólnione zakażenia wewnątrzmaciczne i posocznice noworodków. Ponadto znamiennie częściej występowały u nich krwotoki śródkomorowe, leukomalacja okołokomorowa i dysplazja oskrzelowo-płucna. Przebieg okresu noworodkowego u dzieci z objawami przedwczesnego starzenia się łożyska i zaburzeniami przepływu krwi charakteryzował się niską częstością występowania zakażeń, natomiast leukomalację okołokomorową rozpoznawano 5-krotnie częściej.

**Wnioski:** Wykazano, że zakażenie przezłożyskowe i patologiczna niedojrzałość łożyska miały niekorzystny wpływ na stan zdrowia dzieci z grup III i IV, wywołując poród o 3 tygodnie wcześniej niż u dzieci z grupy porównawczej (grupy V). Noworodki z grup III i IV wymagały opieki resuscytacyjnej na sali porodowej 9-krotnie częściej, a potrzeba wspomaganie oddechowego była 10-krotnie większa niż w grupie porównawczej. Czynniki te wpłynęły na znamiennie dłuższy okres hospitalizacji dzieci z grup III i IV – o średnio 30–45 dni w porównaniu z noworodkami z grupy V.

## Introduction

Premature newborns are a special category of children with inherent morpho-functional immaturity and specific pathological conditions that cause significant differences in the survival and morbidity, and the consequences of their baby care in comparison with children of other weight categories [1, 2].

The problem of preterm birth is not confined to low-income countries [3–5]. Annually, about 15 million babies are born prematurely, and this figure is increasing [6]. According to literature sources, it can be argued that the problems of premature babies come to the fore in the field of neonatological research and perinatal care [7, 8].

Understanding placental changes is extremely important for elucidating the mechanisms of influencing the developing foetus and the formation of adverse consequences in subsequent age periods, but the features of the placenta are still poorly understood [9–11]. The development of technologies for premature baby care has led to a significant decrease in the mortality rate of this newborn category. The introduction of modern methods of intensive care, respiratory support, and resuscitation of newborns, including the use of modern respiratory equipment, the use of non-invasive diagnostic measures, and modern drug therapy, can save the lives of the youngest patients [12–14]. At the same time, there is an increase in morbidity rates among premature infants due to pathologies associated with morpho-functional immaturity [15, 16]. This specific group of pathologies includes the development of bronchopulmonary dysplasia (Bpd), periventricular leukomalacia (PVL), retinopathy of

prematurity (ROP), anaemia of prematurity, postnatal growth, and development delay, which significantly worsen the child's condition not only in the neonatal period but also in subsequent childhood periods, causing the formation of disabling consequences [2, 7]. The mortality among premature newborns in Ukraine is dominated by sepsis (which accounts for almost 40%), intraventricular haemorrhages (IVH), infections specific to the perinatal period, congenital malformations, respiratory distress syndrome (RDS), and necrotic enterocolitis (NEC). Data from the conducted studies indicate that the morbidity and mortality rates of this category of infants is up to 20 times higher than that among children born with normal weight [17, 18].

In the structure of long-term consequences, the frequency of neurological, general cognitive development and low-severity dysfunction, require further improvement of diagnostic methods and timely correction for better developmental prognosis [19, 20].

Because the generally accepted methods of the Prematurity and High-Risk Neonate Post-discharge Follow-up Department standard approach to managing children of different risk groups hinders full implementation of all the necessary medical, diagnostic, and rehabilitation measures, it is important to organize follow-up of this category of children [21, 22].

Follow-up of babies in developed countries has been conducted since the late 1970s, which today makes it possible to trace and assess the consequences of premature birth over 35 years in medical, social, and economic aspects [1]. World studies show that long-term consequences and the decrease in the quali-

ty of life of prematurely born children are determined by the chronic pathology developing as a result of diseases that occur in the first months of life, intensive care, and iatrogenic factors. The following triple factors have been recognized as unfavourable developmental consequences: cerebral palsy, bilateral blindness, and deafness. The main factors of death risk or side effects in children were Bpd, CNS damage, and severe retinopathy of prematurity [20].

Although numerous tools have been developed over the past 3 decades to predict long-term adverse outcomes in pre-term infants as well as new methods for determining the extent of disorders, no study has provided a comprehensive overview of these tools as well as their strong and weak points [23].

### Aim of the research

To establish a link between the formation of adverse consequences in preschool children born prematurely, with a body weight of less than 1500 g, and the placental changes.

### Material and methods

The study involved 220 preschool children born prematurely. The inclusion criterion was a birth weight of less than 1500 g. The exclusion criteria from the study were congenital malformations and genetic syndromes. These children were treated in the Department of Anaesthesiology and Neonatal Intensive Care Unit (NICU), and then – in the Special Neonatal Unit for Premature Newborns (SNUPN) of the Vinnytsia Regional Children's Clinical Hospital in the period 2012–2018.

An analysis of the results of pathomorphological examination of the placentas of mothers of 220 children was carried out on the basis of the Vinnytsia Regional Pathoanatomical Bureau in accordance with the protocol of pathoanatomical examination of the afterbirth (Form No. 013-1/O). Its results enabled us to distinguish 5 groups of mothers according to the classification of changes in the placenta [24, 25].

Group I included women in labour ( $n = 52$ ), in whose placenta dystrophic changes were diagnosed, microscopically manifested in the form of fibrinoid deposition, desulfurization, and changes in the Nitabuch and Langhans layers. The fibrinoid is a key structural placental component, the amount of which increases in accordance with the duration of pregnancy and reaches 10% of the placental area during timely delivery, but according to the results of our study, its percentage was above 25%. These changes are pathognomonic in relation to premature aging of the placenta.

Group II included women ( $n = 30$ ) whose placenta, umbilical cord, and afterbirth membranes presented circulatory disorders. Most often, hyperaemia, thrombosis, and heart attacks were observed at different

stages of development. Thrombosis was present both in the maternal part (interstitial space, basal plate vessels) and in the foetal vascular system, and was characterized by variability: from fresh blood clots – dark red, with a shiny surface and clear borders, to old ones – yellow, with a layered structure. Macroscopically, areas of necrosis were better visualized from the maternal surface in the form of clearly limited, dense foci of white or yellow colour. Microscopy showed necrotic villi surrounded by clotted blood in the area of heart attacks.

Group III consisted of women ( $n = 37$ ) whose placentas had the equivalent of intrauterine infection and, as a result of inflammatory changes, leukocyte infiltration in the placenta (placentitis), membranes (membranitis), umbilical cord (funiculitis), as well as their varieties (chorionitis, amnionitis, chorioamnionitis, vasculitis, intervenillesitis, deciduitis). Inflammation developed due to the penetration of the infectious agent in ascending, haematogenic, or (very rarely) descending ways. In the ascending route (through the cervical canal to the amnion) the after-birth showed the following: inflammation of the placental and parietal amnion, chorion, and leukocyte infiltration of the interstitial space, decidua membrane, and umbilical cord. The haematogenic route of infection (through the spiral arteries of the placental membrane, which comes off, or through the endometrial vessels) was accompanied by inflammation of the villi (villitis), the location of infiltrates in the interstitial space, basal deciduitis, and inflammation of the umbilical cord vessels. Localization of the inflammatory process in the descending pathway (from foci located outside the uterus) depended on placenta attachment to the opening of the fallopian tube. The analysis revealed that both placental and parietal chorioamnionitis were the most common.

Group IV included women in labour ( $n = 49$ ) with several variants of pathological immaturity of the placenta, which did not correspond to gestational age. The classification identified a variant of embryonic villi that occurs as a result of stopping placental development in the early stages of embryogenesis. Macroscopically – the placenta is enlarged in size due to oedema, lobular structure; microscopically – villi with a loose stroma predominate, Kashchenko-Hofbauer cells and stromal channels, interstitial spaces are expanded; hypovascularized chaotic villi in which, macroscopically – the placenta is hypoplastic, and microscopically – small villi with single narrow capillaries (sclerotic growth zones) predominate; a variant of dissociated development – in the placenta together with mature ones there are groups of embryonic, hypovascularized villi and islets of compensatory capillary hyperplasia.

The placentas of another 53 women ( $n = 53$ ) formed group V. Placental examination showed that organometric, macroscopic, and microscopic features

indicated the absence of infectious manifestations, dystrophic changes, immaturity of the afterbirth components, and other compensatory and adaptive changes, and can be considered physiological. This was confirmed by hyperplasia of resorption villi, syncytiotrophoblast, and chorionic capillaries, which is a variant of the norm for this gestational age.

In the course of the study, this category of children was under observation of the doctors the Prematurity and High-risk Neonate Post-discharge Follow-up Department, in order to systematically assess their health. Clinical indicators such as body weight, height, head circumference, neurological, general cognitive development, and low severity dysfunction, and the post-discharge history including respiratory diseases, skeletal system problems, haematological and metabolic disorders were analysed. Ophthalmological and audiological examinations were performed prospectively to assess vision and hearing.

The patients ( $n = 220$ ) were divided into 3 groups depending on the severity of disabling pathology: group 1 – children with severe disabling consequences ( $n = 54$ ) – 24.5%; group 2 – children with long-term consequences with the possibility to correction ( $n = 31$ ) – 14.1%; and group 3 – somatically healthy children without signs of disabling pathology ( $n = 135$ ) – 61.4%. The Neonate Post-discharge Follow-ups Department followed the children during the first year of life once every 3 months, and from the second to the sixth year of life – in accordance with individual rehabilitation plans. Further analysis concerned the health status of children with severe disability consequences, the results of which are described in this article.

Diagnoses were established based on clinical, laboratory, instrumental (ultrasound, radiological), and bacteriological examinations in accordance with ICD-10. The work was carried out on the basis of the Vinnytsia regional children's clinical hospital of the Vinnytsia Regional Council, m. Vinnytsia, Ukraine.

In the course of the study, the following research methods were used: clinical and anamnestic, instru-

mental: brain ultrasound (US), magnetic resonance imaging (MRI), electroencephalography (EEG), hearing screening by otoacoustic emission and audiometry, determination of visual acuity by binocular ophthalmoscope using special lenses, the method of visual evoked potentials in the newborn period, and anthropometric using special tables in subsequent age periods.

### Compliance with Ethics Requirements

The research was carried out in compliance with the basic principles of bioethics: information consent of parents for the child's participation in this study was obtained, and the principles of the Helsinki Declaration were observed. The study was approved by the Bioethics Committee of Vinnytsia National Medical University named after M. I. Pirogov. The authors did not express any conflict of interest. All expenses lie on the authors.

### Statistical analysis

Statistical processing of the obtained results was carried out using Microsoft Excel 2010 (14.0.6024.1000) SP 1 MSO (14.0.6023.1000). The calculation was carried out using standard statistical calculations, as well as the Fischer method, Pearson's  $\chi^2$  criterion, and  $t$ -test.

### Results

The analysis of clinical parameters of children with severe disability consequences was carried out; these were divided into 5 groups according to the changes detected in their mothers' placentas (Table 1).

Analysis of the health of children with severe disabling consequences during the newborn period showed that children of groups III and IV had the lowest birth weight ( $959.7 \pm 40.3$  g;  $p = 0.02$ ) and ( $980.8 \pm 50.5$  g;  $p = 0.04$ ), which is significantly lower than in children of group 5 ( $1310.0 \pm 95.6$  g), which demonstrates increased risks for the children of groups 3 and 4 in the future. The analysis of the general con-

**Table 1.** Clinical characteristics of prematurely born children with severe (disabling) consequences at the neonatal stage

Indicators		Group I ( $n = 6$ )	Group II ( $n = 10$ )	Group III ( $n = 17$ )	Group IV ( $n = 18$ )	Group V ( $n = 3$ )
Weight [g]	$M \pm m$	$1132.5 \pm 65.6$	$1301.3 \pm 55.6$	$959.7 \pm 40.3^*$	$980.8 \pm 50.5^*$	$1310 \pm 95.6$
Gestation term [weeks]	$M \pm m$	$29 \pm 0.8$	$29.6 \pm 0.48$	$27.6 \pm 0.5$	$27.8 \pm 0.68$	$30.7 \pm 2.16$
Assessment according to Apgar score at 1 min [points]	< 4	2 (33.33%)	1 (11.11%)	9 (52.94%)*	10 (55.55%)*	0 (0%)
	4–6	4 (66.66%)	9 (88.88%)	8 (47.06%)*	8 (44.44%)*	3 (100%)
Mechanical ventilation [days]	$M \pm m$	$10 \pm 4.87$	$8 \pm 4.19$	$23.9 \pm 6.69^*$	$19.1 \pm 3.21^*$	$1.7 \pm 2.04$
Duration of inpatient treatment [days]	$M \pm m$	$59.67 \pm 9.09$	$60.7 \pm 9.74$	$83.47 \pm 9.67^*$	$76.17 \pm 6.79^*$	$42.33 \pm 5.71$

Note: \*the probability of differences relative to the comparison group is  $p < 0.05$  (see value in the text).

dition at birth did not reveal significant differences between newborns of groups III and IV, but it was more severe, which is demonstrated by the Apgar score, because it was newborns of group III who were 9 times more likely to need resuscitation in the delivery room (9 (52.94%) vs. 0 (0%)) in children of the comparison group ( $p < 0.09$ ), and children of group IV were 10 times more likely to require urgent measures (10 (55.55%) vs. 0 (0%)) than children of the comparison group ( $p = 0.07$ ). The duration of respiratory support in children of group III ( $23.9 \pm 6.69$  days;  $p = 0.03$ ) and group IV ( $19.1 \pm 3.21$  days;  $p = 0.01$ ), respectively, was found to be significantly higher than in group V, i.e. the need for mechanical ventilation in newborns of groups III and IV was 10 times higher than in newborns of the comparison group. The study of data describing the duration of children's hospital stay did not reveal a significant difference between newborns of groups III ( $83.47 \pm 9.67$  days;  $p = 0.02$ ) and IV groups ( $76.17 \pm 6.79$  days;  $p = 0.01$ ) but showed that the duration of inpatient care of children in these groups was 1.5–2 times longer than in the comparison group. There were no significant differences in gender and gestational age.

All children involved in the study had a disease combination in the neonatal period that caused a severe condition. The condition of the placenta significantly affected the course of the neonatal period. Thus, newborns with signs of inflammatory and immaturity changes were 10 times more likely to suffer generalized intrauterine infections and neonatal sepsis; they also significantly more frequently had intraventricular haemorrhages, periventricular leukomalacia, and bronchopulmonary dysplasia. The course of the neonatal period in groups of children with signs of premature aging of placenta and blood flow disorders was characterized by a low frequency of infections, but periventricular leukomalacia was diagnosed 5 times more often.

All children included in the study received medical care in the neonatal period, in accordance with guidelines and standards; namely: patients were treated with respiratory support with appropriate parameters, and if necessary, therapy with exogenous surfactant and caffeine citrate was carried out. It is also worth noting the availability of adequate parenteral and enteral nutrition in accordance with the individual parameters of each child.

The analysis of the use of exogenous surfactant preparations showed that children of group III – 15 (88.23%) and group IV – 14 (77.77%) had a significantly greater need than representatives of the comparison group – 0 (0%) ( $p = 0.01$ ). The need for surfactant therapy among children of group I (2 (33.33%) patients;  $p = 0.25$ ) and group II (4 (40%) children) showed no significant differences with children from group V (0 (0%);  $p = 0.18$ ).

Analysis of the use of caffeine citrate did not reveal significant differences, but there was a tendency that its use among children in group IV was 1.3 times higher than in the comparison group ( $p = 0.1$ ).

According to the duration of partial parenteral nutrition, there was no significant difference between patients of group I ( $24 \pm 7$  days) and group II ( $26 \pm 5$  days, correspondingly); however, the children in these groups required parenteral nutrition longer than children in the comparison group ( $22 \pm 6$  days). The children of group III ( $50 \pm 6$  days;  $p = 0.03$ ) and group IV ( $48 \pm 5$  days;  $p = 0.05$ ) required partial parenteral nutrition on average twice as long as did newborns of group V ( $22 \pm 6$  days).

The analysis of enteral nutrition at the neonatal stage showed that the duration of nutrition by orogastric tube (OGT) of children of group I ( $24 \pm 7$  days) and group II ( $26 \pm 5$  days) did not differ significantly, but it was on average 6 days longer than in the comparison group ( $24 \pm 4.1$  days). In terms of enteral nutrition duration, significant differences were found: representatives of groups III and IV ( $55 \pm 6.5$  days;  $p = 0.03$ ) and ( $54 \pm 6.6$  days;  $p = 0.01$ ), respectively, needed food through a probe for twice as long compared to children of group V ( $24 \pm 4.1$  days).

The research showed a significantly higher duration of respiratory support in children of group III ( $25 \pm 3.6$  days;  $p = 0.04$ ) and group IV ( $31 \pm 4.8$  days;  $p = 0.01$ ) versus  $14 \pm 0$  days in newborns of the comparison group. There were no significant differences in the need for additional ventilation of newborns in group I ( $24 \pm 6.8$  days), group II ( $14 \pm 2.5$  days), and group V; however, the duration of respiratory support in children in group I was 10 days longer (Table 2).

## Discussion

Our study, carried out for the first time in Ukraine, showed an association between the placenta condition and the consequences of preterm birth, both proximal (RDS, Bpd, PVL, IVH, ICP, ROP, NEC) and long-term (cerebral palsy, cognitive impairment, sensorineural disorders), which provided useful data about the health condition of premature babies. A WHO report declared that pre-term birth has become a growing global health problem, the number of premature babies born worldwide reaching almost 15 million annually and continuing to grow, and the number of premature babies in Ukraine remaining high [6, 8]. The placental condition provides important information for elucidating factors that contributed to preterm birth, but placental features have not been reliably understood, and the relationship between placental changes and neonatal outcomes remains poorly studied [9–11]. Measures aimed at preventing premature birth and improving the life and health prognosis of premature babies in subsequent age periods are important; in particular, the implementation

**Table 2.** Characteristics of modern care technologies for children with severe (disabling) consequences, who were born prematurely at the stage of the neonatal period

Indicators		Group I (n = 6)	Group II (n = 10)	Group III (n = 17)	Group IV (n = 18)	Group V (n = 3)
Surfactant therapy		2 (33.33%)	4 (40%)	15 (88.23%)*	14 (77.77%)*	0 (0%)
Caffeine citrate		2 (33.33%)	4 (40%)	10 (58.82%)	14 (77.77%)	1 (33.33%)
Duration of parenteral nutrition [days]	M ± m	24 ±7	26 ±5	50 ±6*	48 ±5*	22 ±6
Duration of enteral nutrition through the orogastric tube [days]	M ± m	30 ±11	31 ±5.3	55 ±6.5*	54 ±6.6*	24 ±4.1
Duration of respiratory support [days]	M ± m	24 ±6.8	14 ±2.5	25 ±3.6*	31 ±4.8*	14 ±0

Note: \*the probability of differences relative to the comparison group is  $p < 0.05$  (see value in the text).

of modern methods of intensive care, respiratory support, and resuscitation care for newborns, including the use of modern breathing equipment, the use of non-invasive diagnostic measures, and modern drug therapy can save the lives of the youngest patients [12–14]. However, morbidity rates among preterm children remain high due to the occurrence of pathologies associated with morpho-functional immaturity [15, 16]. The mortality among premature newborns in Ukraine is dominated by sepsis (which accounts for almost 40%), intraventricular haemorrhages (IVH), infections specific to the perinatal period, congenital malformations, respiratory distress syndrome (RDS), and necrotic enterocolitis (NEC). Data from the conducted studies indicate that the morbidity and mortality rates of this category of infants is up to 20 times higher than that among children born with normal weight [17, 18]. Although numerous tools have been developed over the past 3 decades to predict long-term adverse outcomes in preterm infants, and new methods have been developed for determining the extent of disorders, no study has provided a comprehensive overview of these tools as well as their strong and weak points [23].

The results of a pathomorphological study of the placentas of 220 children were analysed, and the results enabled us to distinguish 5 groups of mothers according to the classification of changes in the placenta [24, 25]. In the course of the study, this category of children was under the supervision of doctors of the catamnesis observation room, in order to systematically assess their health status. The health condition of patients under study was analysed, namely: clinical indicators such as body weight, height, head circumference; neurological and intellectual development; the presence of somatic pathology, including diseases of the respiratory system, musculoskeletal system, and haematological problems. Ophthalmological and audiological examinations were performed dynamically to assess vision and hearing.

Patients were divided into 3 groups depending on the severity of the disabling pathology. Neonate Post-discharge Follow-up Department followed the children during the first year of life once every 3 months, and from the second to the sixth year of life in accordance with individual rehabilitation plans.

All children included in the study received medical care in the neonatal period in accordance with guidelines and standards, namely: patients were treated with oxygen therapy with appropriate parameters; if necessary, therapy with exogenous surfactant and caffeine citrate was carried out. It is also worth noting the availability of adequate parenteral and enteral nutrition in accordance with the individual parameters of each child.

The analysis of clinical parameters of children with severe disability consequences was carried out; these were divided into 5 groups according to the changes found in their placentas. Analysis of the health status of children with severe disabling consequences during the newborn period showed that children of group III and group IV had the lowest body weight at birth, which was significantly lower than in children of group V, who needed resuscitation 9 times more often and additional ventilation 10 times more often than children of the comparison group, which testifies to increased risks for children of these groups in subsequent age periods. Representatives of the groups with inflammation and pathological immaturity in the placenta doubtlessly needed oxygen therapy more often – on average, 14 days longer – the duration of their enteral nutrition was a month longer, and the need for parenteral nutrition was 2 times higher than the same indicator of the comparison group. Premature aging of the placenta and impaired placental blood flow, according to the results of the study, had a less catastrophic impact on the health of newborns, as shown by the absence of significant differences in body weight and gestational age of newborns and the comparison group. At the same time, children of

groups I and 2 were provided with resuscitation care in the delivery room 2.5 times more often, their need for respiratory support was 4 times greater, and the duration of inpatient treatment exceeded the indicator of the comparison group by almost 2.5 weeks.

With the development of society, economic development, and improvement of medicine, as well as changes in family planning policies, pre-term birth and its management are extremely important in Ukraine. More and more extremely premature babies will be born and will need adequate care, comprehensive dynamic monitoring, an interdisciplinary approach, and rehabilitation plan. To facilitate this, a clear, unified assessment scale for detecting long-term adverse effects of pre-term birth and recommendations for infants and families should be developed and adapted as soon as possible, to form an individual rehabilitation and habilitation program. Prospects for further research are to study health conditions of children at the Neonate Post-discharge Follow-up Department, in particular their physical development, neurological, general cognitive development, speech, behaviour, and the frequency of disabling pathology.

## Conclusions

The research showed that inflammation and pathological immaturity of the placenta had a negative impact on the health status of children in groups III and IV, causing their birth 3 weeks earlier, in contrast to children in comparison group V. Premature aging of the placenta and impaired placental blood flow, as the study shows, had a less catastrophic effect on the health of newborns, which was proven by the absence of significant differences in body weight and gestational age indicators of newborns and the comparison group. The condition of the placenta significantly affected the course of the neonatal period. Thus, newborns with signs of blood flow disorders, inflammatory changes, and immaturity had a significantly greater need for surfactant therapy than representatives of comparison group V. Improving the indicators of early diagnosis of long-term consequences of premature birth at the stage of follow-up and making an individual rehabilitation program are necessary for each patient included in the study.

## Conflict of interest

The authors declare no conflict of interest.

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