

## РЕЗУЛЬТАТИ ДИСЕРТАЦІЙНИХ ТА НАУКОВО – ДОСЛІДНИХ РОБІТ/ RESULTS OF DISSERTATIONS AND RESEARCH WORKS

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ON THE QUESTION OF HEARING  
IMPAIRMENT IN PREMATURE CHILDREN  
WHO HAVE EXPERIENCED OXIDATIVE  
STRESS AT BIRTH

### **Summary**

**Introduction.** Hearing impairment (HI) occupies an important place among perinatal pathology. According to the WHO, the frequency of severe hearing impairment is observed in 1–2 per 1000 newborns and in 15% of newborns who required intensive therapy after birth. Mild and moderate HI occurs in 1–2% of children with perinatal pathology.

**The aim of the work** is to study the predictors of hearing impairment and the factors that determine the severity of deafness in children aged 2–3 months who suffered oxidative stress at birth.

**Material and methods.** 131 cases of observation of newborns of 27–36 weeks of gestation with HI in Communal nonprofit enterprise «City perinatal center» Kharkiv city council were analyzed. Children whose families had cases of HI were excluded from the study. During the observation, the audiological examination was carried out in the newborn period (primary examination) and at 2–3 months of age. To meet the aim of the work, alternative groups were formed: Group I ( $n=51$ ) with unilateral and Group II ( $n=80$ ) with bilateral hearing impairment.

To determine the predictors of the severity of PS in the comparison groups, the factors determining deafness were studied, and their prognostic informativeness was established. The t-Student and  $\varphi$ -Fisher criteria were determined, the Wald-Henkin heterogeneous sequential procedure algorithm was used, predictive coefficients (PC) and informativeness (I) were determined.

By decision of the Bioethics Commission № 3 dated March 21, 2023, the study materials comply with the Tokyo Declaration of the World Medical Association, the International Recommendations of the Helsinki Declaration on Human Rights, the Council of Europe Convention on Human Rights and Biomedicine, the Laws of Ukraine, and the requirements of the Code of Ethics of a Doctor of Ukraine.

The study was carried out within the framework of the scientific research work of the Department of Pediatrics № 3 and Neonatology of KhNMU «Study of peculiarities of the course of oxidant stress diseases in newborns» 2022–2024 (state registration № A22U000025).

**Results.** Factors of obstetric and somatic anamnesis of the mother did not influence the nature of HI in the child. Among the complications of pregnancy and childbirth in the anamnesis of children with bilateral HI, dysfunction of placenta was more often observed 33.8 and 13.7 % ( $p<0.001$ ), threat of abortion 30.0 and 17.6 % ( $<0.05$ ), anemia pregnant women 31.2 and 13.7 % ( $p<0.001$ ), fetal distress 56.2 and 37.3 % ( $p<0.01$ ), cesarean delivery 68.8 and 47.1 % ( $p<0.001$ ), especially regarding fetal distress – 67.3 and 29.2 % ( $p<0.001$ ).

The frequency of bilateral HI in children is inversely proportional to gestational age and birth weight and is associated with a low Apgar score. Sexual dimorphism was revealed: girls predominated in the group with bilateral hearing loss, 56.2 and 35.3 % ( $p<0.001$ ). Children with bilateral HI more often required surfactant therapy 78.8 and 33.3 % ( $p<0.001$ ), as well as longer respiratory support and oxygen therapy.

In the study, bilateral HI was more common in children with diseases whose pathogenesis is closely related to oxidative stress: periventricular leukomalacia 55.0 and 7.8 % ( $<0.001$ ); bronchopulmonary dysplasia (BPD) of the 2nd and 3rd degree: 23.7 and 2.0 % ( $p<0.001$ ) and 23.7 and 0 % ( $p<0.001$ ), respectively; retinopathy of prematurity grade 2–3 42.5 and 17.6 % ( $p<0.001$ ); with an PDA 81.3 and 41.2 % ( $p<0.001$ ), including when surgical closure was necessary, 18.5 and 9.5 % ( $p<0.05$ ). The highest informativeness of hearing impairment in children who have undergone oxidative stress belongs to the following characteristics: gestational age (6.14), total duration of mechanical ventilation (5.54), body weight (5.44), BPD (5.4), duration of mechanical ventilation in mode of normoventilation (4.1), duration of oxygen therapy (3.91), PDA (3.72).

The most significant prognostic factors of bilateral hearing impairment: the presence of BPD 2–3 stages. (-13.8); intraventricular hemorrhage (IVH) 2–3 st. (-12.4); total duration of ventilator  $\geq$  21 days (-10.33); gestation period  $\leq$  29 weeks (-8.6); periventricular leukomalacia (PVL) 2–3 st. (-8.48); duration of oxygen therapy  $\geq$  21 days (-7.38); body weight (-6.94).

**Conclusions:** The most significant prognostic factors of bilateral hearing impairment: the presence of BPD 2–3

st. (-13.8); IVH 2–3 st. (-12.4); total duration of ventilator  $\geq 21$  days (-10.33); gestation period  $\leq 29$  weeks (-8.6); periventricular leukomalacia 2–3 st. (-8.48); duration of oxygen therapy  $\geq 21$  days (-7.38); body weight (-6.94), etc. Bilateral hearing impairment is predicted in newborns based on the presence of gestational immaturity (gestational term  $\leq 29$  weeks), BPD grade 2–3, IVH grade 2–3, total duration of mechanical ventilation and oxygen therapy  $> 21$  days, PVL grade 2–3. In our study, no reliable relationship was found between the nature of the hearing impairment of a prematurely born child and the somatic and obstetric anamnesis of the mother. Gender characteristics among premature infants with bilateral HI were characterized by the predominance of the female gender, 56.2 and 35.3 % ( $p < 0.001$ ).

**Key words:** Preterm Infants; Hearing Impairment; Oxidative Stress.

## Introduction

Hearing impairment (HI) occupies an important place among perinatal pathology. According to the WHO, the frequency of severe hearing impairment is observed in 1–2 per 1000 newborns and in 15 % of newborns who required intensive therapy after birth. Mild and moderate HI occurs in 1–2% of children with perinatal pathology [1–4].

Oxidative stress is the process of damage and death of cells as a result of oxidation under the action of reactive oxygen species – superoxide and hydrogen peroxide, which are formed in the child's body under the influence of hypoxia [5–8]. Reactive oxygen species play an important role in the pathogenesis of such diseases of prematurely born children as bronchopulmonary dysplasia [9, 10], periventricular leukomalacia [11, 12], retinopathy of prematurity [13, 14], patent ductus arteriosus [15], etc. [16–18].

Despite the significant progress achieved in understanding the mechanisms of development, diagnosis, therapy and prevention of HI, there are a number of scientific and practical problems of this pathology in infants and young children [19, 20]. One of the most important is the organization of specialized step-by-step care for children with hearing impairment [14, 21, 22]. The creation of an effective program of follow-up monitoring of children with deafness is impossible without knowledge of the factors that determine the nature and severity of HI in children and the consequences of the disease [3, 4, 23]. The pediatrician's ability to predict the course and consequences of HI in children with perinatal pathology allows to increase the effectiveness of medical and social monitoring of this contingent of patients [20–27].

**The aim of the work** is to study the predictors of hearing impairment and the factors that determine the nature and severity of deafness in children aged 2–3 months who suffered oxidative stress at birth.

## Material and methods

131 cases of observation of newborns of 27–36 weeks of gestation with HI in Communal nonprofit enterprise «Kharkiv city perinatal center» Kharkiv city council were analyzed. Children whose families had cases of HI were excluded from the study. During the observation, the audiological examination was carried out in the newborn period (primary examination) and at 2–3 months of age. To solve the aim of the work, alternative groups were formed: Group I (n=51) with unilateral and Group II (n=80) with bilateral hearing impairment.

To determine the predictors of the severity of HI in the comparison groups, the factors determining deafness were studied, and their prognostic

informativeness was established. Statistical processing of the obtained data was carried out using the STATISTICA 7 program (StatSoft Inc. USA). The parametric t-Student test and the non-parametric φ-Fisher test were used to determine the reliability of the differences between groups. To determine the prognostic significance of the indicators, the Wald non-uniform sequential procedure algorithm was used, prognostic coefficients (PC) and informativeness (I) [28].

The study was carried out within the framework of the scientific research work of the Department of Pediatrics № 3 and Neonatology of KhNMU «Study of peculiarities of the course of oxidant stress diseases in newborns» 2022–2024 (state registration № A22U000025). By decision of the Bioethics Commission № 3 dated March 21, 2023, the study materials comply with the Tokyo Declaration of the World Medical Association, the International Recommendations of the Helsinki Declaration on Human Rights, the Council of Europe Convention on Human Rights and Biomedicine, the Laws of Ukraine, and the requirements of the Code of Ethics of a Doctor of Ukraine.

## Results and discussion

In the group with unilateral HI, boys predominated 64.7 & 43.8 %, and in the group with bilateral hearing loss – girls 56.2 % & 35.3 % ( $p < 0.001$ ). More severe HI was inversely proportional to gestational age and birth weight: bilateral HI was more prevalent among children 29 weeks gestation and less 85.0 % & 11.8 % ( $p < 0.001$ ) and with a birth weight less than 1200.0 87.5 % & 17.7 % ( $p < 0.001$ ) (Table 1).

Studying the factors of obstetric and somatic anamnesis of the mother, reliable influence on the nature of HI in the child of the mother's age, the number of pregnancies and births in the anamnesis, as well as the presence of chronic somatic pathology was not found. Only in the presence of artificial termination of pregnancy in the history of the mother, bilateral PS prevailed 30.0% versus 13.7% ( $p < 0.05$ ).

A study of pregnancy data showed that some factors demonstrated a reliable relationship with the nature of deafness. Among the complications of pregnancy, bilateral HI in a child was more often observed in the presence of fetoplacental insufficiency 33.8 % & 13.7 % ( $p < 0.001$ ), threat of termination of pregnancy 30.0 % & 17.6 % ( $p < 0.05$ ), anemia of pregnant women 31.2 % & 13.7 % ( $p < 0.001$ ), fetal distress 56.2 % & 37.3 % ( $p < 0.01$ ) (Table 2). Among children born by caesarean section, children with bilateral HI predominated 68.8 % & 47.1 % ( $p < 0.001$ ), and among indications for caesarean section in case of fetal distress, children had bilateral PS significantly more often 67.3 % & 29.2 % ( $p < 0.001$ ).

**Table 1**

**Characteristics of comparison groups by anthropometric data and gender**

Indicator	Gradation	I group (n=51), abs abs (%)	II group (n=80), abs abs (%)	P
Gender	Male	33 (64,7)	35 (43,8)	<0,001
	Female	18 (35,3)	45 (56,2)	<0,001
Age of gestation, weeks	≤29 тижнів	6 (11,8)	68 (85,0)	<0,001
	30–31	21 (41,1)	8 (10,0)	<0,001
	≥32 тижнів	24 (47,1)	4 (5,0)	<0,001
Body weight, g	<1200 г	9 (17,7)	70 (87,5)	<0,001
	1200,0–1500,0	31 (60,8)	8 (10,0)	<0,001
		12 (23,5)	2 (2,5)	<0,001

**Table 2**

**Characteristics of the comparison groups according to the obstetric history of the mother,  
the course of pregnancy, and the method of delivery**

Indicator	Gradation	I group (n=51), abs (%)	II group (n=80), abs abs (%)	P
Chronic pathology of the mother	Yes	14 (27,5)	25 (31,3)	>0,05
	No	37 (72,5)	55 (68,7)	>0,05
Medical abortion	Yes	7 (13,7)	19 (23,8)	<0,05
	No	44 (86,2)	61 (76,2)	<0,05
Threat of abortion	Yes	9 (17,6)	24 (30,0)	<0,05
	No	42 (82,4)	56 (70,0)	<0,05
Dysfunction of placenta	Yes	7 (13,7)	27 (33,8)	<0,001
	No	44 (86,3)	53 (66,2)	<0,001
Fetal distress	Yes	19 (37,3)	45 (56,2)	<0,01
	No	32 (62,7)	35 (43,8)	<0,01
Anemia in Pregnancy	Yes	7 (13,7)	25 (31,2)	<0,001
	No	44 (86,3)	55 (68,8)	<0,05
Cesarean delivery	Yes	27 (52,9)	25 (31,2)	<0,001
	No	24 (47,1)	55 (68,8)	<0,001
* Indications for cesarean section	Fetal distress	7 (29,2)	37 (67,3)	<0,001
	Placental abruption	4 (16,7)	10 (18,2)	>0,05
	Other indications	13 (54,1)	8 (14,5)	<0,001

\* To calculate statistical differences, the number of groups n1=24 and n2=55 was used, according to the number of children born by caesarean section.

Bilateral HI was more often observed among children who had a low Apgar score: at the 1st minute ≤4 points 78.7 % & 27.5 % (p<0.001) and at the 5th minute ≤5 points 40.0 % & 11.7 % (p<0.001) (Table 3). The degree of respiratory distress syndrome (RDS) in our study was correlated with bilateral HI. Among children without RDS at birth or with RDS 1st unilateral HI prevailed 25.6 % & 6.2 % (p<0.001) and 30.0 % & 4.0 % (p<0.001), respectively. Among children with RDS of the 2nd degree, no significant difference in the nature of HI was found. And among children with RDS of the 3rd century bilateral hearing loss prevailed 78.8 % & 33.3 % (p<0.001). Surfactant therapy was more often required by children with bilateral HI, 78.8 % & 33.3 % (p<0.001), which

indicates their gestational immaturity and the severity of respiratory disorders at birth.

Among children who required high-frequency ventilation, ventilation with MAP>12 cm H2O, FiO<sub>2</sub>≥35%, as well as long-term ventilation with MAP=8–12 cm H2O, FiO<sub>2</sub>=21–30%, children with bilateral HI prevailed: 6.3% & 0% (p<0.001), 35.0% & 7.8% (p<0.001), and 73.8% & 11.8% (p<0.001), respectively. Also, children with bilateral HI required longer respiratory support and oxygen therapy. The total duration of mechanical ventilation ≤5 days and oxygen therapy ≤20 days are associated with unilateral HI 66.7% & 8.8% (p<0.001) and 86.3% vs. 25.0% (p<0.001), respectively. Conversely, among children with a total duration of mechanical ventilation and oxygen therapy

$\geq 21$  days, children with bilateral HI predominated 63.8% & 5.9% ( $p<0.001$ ) and 75.0% & 13.7%, respectively. Among children who required mechanical ventilation for a total duration of 6–20 days, no significant difference in the nature of HI was found.

We paid special attention to CNS pathology, since hearing is anatomically and functionally very closely

related to the nervous system. Bilateral HI was significantly more often observed in the presence of intraventricular hemorrhage (IVH) in the child: 1st 30.0 % & 19.6 % ( $p<0.05$ ); 2–3rd 17.5 % & 0 % ( $<0.001$ ); periventricular ischemia of the 3rd degree. 90.0 % & 51.0 % ( $<0.001$ ), periventricular leukomalacia (PVL) 2–3 degrees 55.0 % & 7.8 % ( $<0.001$ ).

**Table 3**

**Characteristics of the comparison groups based on the Apgar score, the severity of RDS, and respiratory therapy**

Indicator	Gradation	I group (n=51), abs (%)	II group (n=80), abs (%)	P
Apgar score 1', points	$\leq 4$	14 (27,5)	63 (78,7)	<0,001
	$\geq 5$	37 (72,5)	17 (21,2)	<0,001
Apgar score 5', points	$\leq 5$	6 (11,7)	32 (40,0)	<0,001
	$\geq 6$	45 (88,2)	48 (60,0)	<0,001
RDS, degree	німає	11 (25,6)	5 (6,2)	<0,001
	1	12 (30,0)	3 (4,0)	<0,001
	2	17 (42,5)	32 (42,7)	<0,05
	3	11 (27,5)	40 (53,3)	<0,001
Surfactant therapy	так	17 (33,3)	63 (78,8)	<0,001
	ні	34 (66,7)	17 (21,2)	<0,001
Invasive ventilation: MAP=8–12 cm H <sub>2</sub> O, FiO <sub>2</sub> 21–30%, days	$\leq 5$	45 (88,2)	21 (26,2)	<0,001
	$\geq 6$	6 (11,8)	59 (73,8)	<0,001
High-frequency ventilation	є	0 (0)	5 (6,3)	<0,001
	німає	51 (100,0)	75 (93,7)	<0,001
Invasive ventilation: MAP>12 cm H <sub>2</sub> O, FiO <sub>2</sub> $\geq 35\%$	є	4 (7,8)	28 (35,0)	<0,001
	німає	47 (92,2)	52 (65,0)	<0,001
Total duration of mechanical ventilation, days	$\leq 5$	34 (66,7)	7 (8,8)	<0,001
	6–20	14 (27,4)	22 (27,4)	0
	$\geq 21$	3 (5,9)	51 (63,8)	<0,001
Oxygen therapy, days	$\leq 20$	44 (86,3)	20 (25,0)	<0,001
	$\geq 21$	7 (13,7)	60 (75,0)	<0,001
The total duration of the treatment, days	$\leq 40$	32 (62,7)	18 (22,5)	<0,001
	41–60	14 (27,4)	20 (25,0)	>0,05
	$\geq 61$	5 (9,8)	47 (58,8)	<0,001

HI is more common in children with diseases whose pathogenesis is closely related to oxidative stress (bronchopulmonary dysplasia (BPD), retinopathy of prematurity (ROP), patent ductus arteriosus (PDA)). In our study, bilateral HI was correlated with ROP grade 2–3rd in 42.5 % & 17.6 % ( $p<0.001$ ); BPD 2–3rd degree: 23.7 % & 2.0 % ( $p<0.001$ ) and 23.7 % & 0 % ( $p<0.001$ ), respectively; with an PDA 81.3 % & 41.2 % ( $p<0.001$ ), including when surgical closure was necessary, 18.5 % & 9.5 % ( $p<0.05$ ).

Table 5 shows indicators associated with HI in newborns, which are listed in order of decreasing overall informativeness (Icom).

The highest informativeness of hearing impairment

in children who have undergone oxidative stress belongs to the following characteristics: gestational age (6.14), total duration of mechanical ventilation (5.54), body weight (5.44), BPD (5.4), duration of mechanical ventilation (4.1), duration of oxygen therapy (3.91), open ductus arteriosus (3.72), etc.

The most significant prognostic factors of bilateral hearing impairment: the presence of BPD 2–3 stages (-13.8); IVH 2–3 st. (-12.4); total duration of ventilator  $\geq 21$  days (-10.33); gestation period  $\leq 29$  weeks. (-8.6); periventricular leukomalacia 2–3 st. (-8.48); duration of oxygen therapy  $\geq 21$  days (-7.38); body weight (-6.94), etc.

### Conclusions:

1. The most significant prognostic factors of bilateral hearing impairment: the presence of BPD 2–3 st. (-13.8); IVH 2–3 st. (-12.4); total duration of ventilator  $\geq$ 21 days (-10.33); gestation period  $\leq$ 29 weeks. (-8.6); periventricular leukomalacia 2–3 st. (-8.48); duration of oxygen therapy  $\geq$ 21 days (-7.38); body weight (-6.94), etc.

2. Bilateral hearing impairment is predicted in newborns based on the presence of gestational immaturity (gestational term  $\leq$ 29 weeks), BPD grade 2–3, IVH grade 2–3, total duration of mechanical ventilation and oxygen therapy  $>$  21 days, PVL grade 2–3. In our study, no reliable relationship was found between the nature of the hearing impairment of a prematurely born child and the somatic and obstetric anamnesis of the mother.

**Table 5**

### Prognostic significance of indicators associated with HI in newborns

Indicator	Gradation	I group (n=51), abs (%)	II group (n=80), abs (%)	PC	I	I <sub>com</sub>
Age of gestation, weeks	$\leq$ 29	6 (11,8)	68 (85,0)	-8,6	3,14	6,14
	30–31	21 (41,1)	8 (10,0)	6,14	0,95	
	$\geq$ 32	24 (47,1)	4 (5,0)	9,74	2,05	
Total duration of mechanical ventilation, days	$\leq$ 5	34 (66,7)	7 (8,8)	8,8	2,55	5,54
	6–20	14 (27,4)	22 (27,4)	0	0	
	$\geq$ 21	3 (5,9)	51 (63,8)	-10,33	2,99	
Body weight, g	<1200.0	9 (17,7)	70 (87,5)	-6,94	2,42	5,44
	1200.0–1500.0	31 (60,8)	8 (10,0)	7,84	2,0	
	>1500.0	12 (23,5)	2 (2,5)	9,73	1,02	
Invasive ventilation: MAP 8–12 cm H <sub>2</sub> O, FiO <sub>2</sub> 21–30%, days	$\leq$ 5	45 (88,2)	21 (26,2)	5,27	1,63	4,1
	$\geq$ 6	6 (11,8)	59 (73,8)	-7,96	2,47	
Oxygen therapy, days	$\leq$ 20	44 (86,3)	20 (25,0)	5,38	1,65	3,91
	$\geq$ 21	7 (13,7)	60 (75,0)	-7,38	2,26	
Patent ductus arteriosus (PDA)	No	28 (54,9)	3 (3,7)	11,71	3,0	3,72
	Yes	21 (41,2)	65 (81,3)	-2,95	0,59	
	surgery clousing of PDA	2 (9,5)	12 (18,5)	-2,89	0,13	
Bronchopulmonary dysplasia, degree	No	47 (92,3)	36 (45,0)	3,12	0,74	3,46
	1	3 (5,9)	6 (7,6)	-1,1	0,01	
	2	1 (2,0)	19 (23,7)	-10,7	1,16	
	3	0 (0)	19 (23,7)	-13,8	1,56	
Apgar score 1', points	$\leq$ 4	14 (27,5)	63 (78,7)	-4,57	1,7	3,07
	$\geq$ 5	37 (72,5)	17 (21,2)	5,34	1,37	
The total duration of the treatment, days	$\leq$ 40	32 (62,7)	18 (22,5)	4,45	0,89	2,81
	41–60	14 (27,4)	20 (25,0)	0,4	0,004	
	$\geq$ 61	5 (9,8)	47 (58,8)	-7,78	1,91	
Periventricular leukomalation, degree	No	35 (68,6)	21 (26,2)	-1,17	0,12	2,14
	1	12 (23,6)	15 (18,8)	0,99	0,02	
	2–3	4 (7,8)	44 (55,0)	-8,48	2,0	
RDS, degree	No	11 (25,6)	5 (6,2)	6,16	0,6	2,1
	1	12 (30,0)	3 (4,0)	8,75	1,14	
	2	17 (42,5)	32 (42,7)	0	0	
	3	11 (27,5)	40 (53,3)	-2,87	0,37	
Surfactant therapy	Yes	17 (33,3)	63 (78,8)	-3,74	0,85	1,98
	No	34 (66,7)	17 (21,2)	4,98	1,13	
Retinopathy of prematurity, degree	No	17 (33,3)	3 (3,7)	9,54	1,41	1,89
	1	25 (49,0)	43 (53,8)	-0,41	0,01	
	2–3	9 (17,7)	34 (42,5)	-3,8	0,47	

Indications for cesarean section	Fetal distress	7 (29,2)	37 (67,3)	-3,63	0,69	1,83
	Placental abruption	4 (16,7)	10 (18,2)	-0,37	0,002	
	Other indications	13(54,1)	8 (14,5)	5,72	1,13	
Periventricular ischemia, degree	1–2	25 (49,0)	8 (10,0)	6,9	1,35	1,83
	3	26 (51,0)	72 (90,0)	-2,47	0,48	
INTRAVENTRICULAR HEMORRHAGES, DEGREE	No	41 (80,4)	42 (52,5)	1,85	0,26	1,38
	1	10 (19,6)	24 (30,0)	-1,85	0,1	
	2–3	0 (0)	14 (17,5)	-12,4	1,02	
Invasive ventilation: MAP >12 cm H2O, FiO2 21–30%	Yes	4 (7,8)	28 (35,0)	-6,52	0,89	1,1
	No	47 (92,2)	52 (65,0)	1,52	0,21	
Apgar score 5', points	≤5	6 (11,7)	32 (40,0)	-5,34	0,76	1,0
	≥6	45 (88,2)	48 (60,0)	1,67	0,24	
Dysfunction of placenta	YES	7 (13,7)	27 (33,8)	-3,95	0,39	0,51
	No	44 (86,3)	53 (66,2)	1,15	0,12	
Cesarean birth	Yes	27 (52,9)	25 (31,2)	2,29	0,25	0,43
	No	24 (47,1)	55 (68,8)	-1,65	0,18	
Anemia in Pregnancy	Yes	7 (13,7)	25 (31,2)	-3,57	0,31	0,4
	No	44 (86,3)	55 (68,8)	0,98	0,09	
Gender	Male	33 (64,7)	35 (43,8)	1,69	0,18	0,39
	Female	18 (35,3)	45 (56,2)	-2	0,21	
Fetal distress	Yes	19 (37,3)	45 (56,2)	-1,8	0,17	0,32
	No	32 (62,7)	35 (43,8)	1,56	0,15	
High-frequency ventilation	Yes	0 (0)	5 (6,3)	-8,0	0,21	0,22
	No	51 (100,0)	75 (93,7)	0,28	0,01	
Threat of abortion	Yes	9 (17,6)	24 (30,0)	-2,32	0,14	0,18
	No	42 (82,4)	56 (70,0)	0,71	0,04	

3. Gender characteristics among premature children with bilateral hearing impairment were characterized by the predominance of the female gender, 56.2% versus 35.3% ( $p<0.001$ ).

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#### Reference:

- Hirvonen M, Ojala R, Korhonen P, Haataja P, Eriksson K, Gissler M, et al. Visual and Hearing Impairments After Preterm Birth. Pediatrics [Internet]. 2018[cited 2023 May 15];142(2):e20173888. Available from: [https://publications.aap.org/pediatrics/article-pdf/142/2/e20173888/1064603/peds\\_20173888.pdf](https://publications.aap.org/pediatrics/article-pdf/142/2/e20173888/1064603/peds_20173888.pdf) doi: 10.1542/peds.2017-3888
- Bielecki I, Horbulewicz A, Wolan T. Risk factors associated with hearing loss in infants: an analysis of 5282 referred neonates. Int J Pediatr Otorhinolaryngol. 2011;75(7):925-30. doi: 10.1016/j.ijporl.2011.04.007
- Han JH, Shin JE, Lee SM, Eun HS, Park MS, Park KI. Hearing Impairments in Preterm Infants: Factors Associated with Discrepancies between Screening and Confirmatory Test Results. Neonatal Med. 2020;27(3):126-32. doi: 10.5385/nm.2020.27.3.126
- Stadio AD, Molini E, Gambacorta V, Giommetti G, Volpe AD, Ralli M, et al. Sensorineural Hearing Loss in Newborns Hospitalized in Neonatal Intensive Care Unit: An Observational Study. Int Tinnitus J. 2019;23(1):31-6. doi: 10.5935/0946-5448.20190006
- Kishimoto-Urata M, Urata S, Fujimoto C, Yamasoba T. Role of Oxidative Stress and Antioxidants in Acquired Inner Ear Disorders. Antioxidants [Internet]. 2022[cited 2023 May 15];11(8):1469. Available from: <https://www.mdpi.com/2076-3921/11/8/1469> doi: 10.3390/antiox11081469
- Falsaperla R, Lombardo F, Filosco F, Romano C, Saporito MAN, Puglisi F, et al. Oxidative Stress in Preterm Infants: Overview of Current Evidence and Future Prospects. Pharmaceuticals (Basel) [Internet]. 2020[cited 2023 May 15];13(7):145. Available from: <https://www.mdpi.com/1424-8247/13/7/145> doi: 10.3390/ph13070145
- Gonzalez-Gonzalez S. The role of mitochondrial oxidative stress in hearing loss. Neurol Disord Therap. 2017;1(4):1-5. doi: 10.15761/NDT.1000117
- Lembo C, Buonocore G, Perrone S. Oxidative Stress in Preterm Newborns. Antioxidants [Internet]. 2021[cited 2023 May 15];10(11):1672. Available from: <https://www.mdpi.com/2076-3921/10/11/1672> doi: 10.3390/antiox10111672
- Kimble A, Robbins ME, Perez M. Pathogenesis of Bronchopulmonary Dysplasia: Role of Oxidative

- Stress from ‘Omics’ Studies. *Antioxidants* [Internet]. 2022[cited 2023 May 15];11(12):2380. Available from: <https://www.mdpi.com/2076-3921/11/12/2380> 10.3390/antiox11122380
10. Gray PH, Sarkar S, Young J, Rogers YM. Conductive hearing loss in preterm infants with bronchopulmonary dysplasia. *J Paediatr Child Health*. 2001;37:278-82. doi: 10.1046/j.1440-1754.2001.00690.x
11. Zhang C, Zhao X, Cheng M, Wang K, Zhang X. The Effect of Intraventricular Hemorrhage on Brain Development in Premature Infants: A Synthetic MRI Study. *Front Neurol* [Internet]. 2021[cited 2023 May 15];12:721312. Available from: <https://www.frontiersin.org/articles/10.3389/fneur.2021.721312/full> doi: 10.3389/fneur.2021.721312
12. Egesa WI, Odoch S, Odong RJ, Nakalema G, Asiiimwe D, Ekuk E, et al. Germinal Matrix-Intraventricular Hemorrhage: A Tale of Preterm Infants. *Int J Pediatr* [Internet]. 2021[cited 2023 May 15];6622598. Available from: <https://downloads.hindawi.com/journals/ijpedi/2021/6622598.pdf> doi: 10.1155/2021/6622598
13. Kuzienkova GA, Klymenko TM. Urinary Melatonin Metabolite in Premature Infants with Extremely and Very Low Birth Weight. *Ukr. ž. med. biol. sportu*. 2022;5(39):107-13 doi: 10.26693/jmbs07.05.107
14. Rantakari K, Rinta-Koski OP, Metsäranta M, Hollmén J, Särkkä S, Rahkonen P, et al. Early oxygen levels contribute to brain injury in extremely preterm infants. *Pediatr Res*. 2021;90(1):131-9. doi: 10.1038/s41390-021-01460-3
15. Klymenko T, Sorokolat Y, Karapetyan O, Kononovich M, Kuzenkova A. The role of sexual dimorphism and the state of the arterial duct in the formation of oxidative stress disease in preterm infants. *Georgian Med News*. 2022;322:109-15.
16. Клименко ТМ, Кузенкова АА. Нові дефініції ведення новонароджених із хворобами окислювального стресу. *Неонатологія, хірургія та перинатальна медицина*. 2020;10(3):72-80. doi: 10.24061/2413-4260.X.3.37.2020.10
17. Prasad KN, Bondy SC. Increased oxidative stress, inflammation, and glutamate: Potential preventive and therapeutic targets for hearing disorders. *Mech Ageing Dev* [Internet]. 2020[cited 2023 May 15];185:111191. Available from: <https://www.sciencedirect.com/science/article/abs/pii/S0047637419301964?via%3Dihub> doi: 10.1016/j.mad.2019.111191
18. Klymenko TM, Kononovych MI. Clinical significance of correlation between persistent pulmonary hypertension and 8-hydroxy-2-desoxyguanosine level in premature newborns. *J Neonatal Perinatal Med*. 2023;16(1):81-5. doi: 10.3233/NPM-221005
19. Vohr BR. Language and hearing outcomes of preterm infants. *Semin Perinatol*. 2016;40(8):510-9. doi: 10.1053/j.semperi.2016.09.003.
20. Gentili N, Holwell A. Mental health in children with severe hearing impairment. *Advances in Psychiatric Treatment*. 2011;17(1):54-62. doi: 10.1192/apt.bp.109.006718
21. Frezza S, Catenazzi P, Gallus R, Gallini F, Fioretti M, Anzivino R, et al. Hearing loss in very preterm infants: should we wait or treat? *Acta Otorhinolaryngol Ital*. 2019;39(4):257-62. doi: 10.14639/0392-100X-2116
22. Wroblewska-Seniuk K, Greczka G, Dabrowski P, Szyfter-Harris J, Mazela J. Hearing impairment in premature newborns—Analysis based on the national hearing screening database in Poland. *PLoS One* [Internet]. 2017[cited 2023 May 15];12(9):e0184359. Available from: <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0184359> doi: 10.1371/journal.pone.0184359
23. Salvago P, Immordino A, Plescia F, Mucia M, Albera A, Martines F. Risk Factors for Sensorineural Hearing Loss and Auditory Maturation in Children Admitted to Neonatal Intensive Care Units: Who Recovered? *Children (Basel)* [Internet]. 2022[cited 2023 May 15];9(9):1375. Available from: <https://www.mdpi.com/2227-9067/9/9/1375> doi: 10.3390/children9091375
24. Aldè M, Berardino FD, Ambrosetti U, Barozzi S, Piatti G, Consonni D, et al. Hearing outcomes in preterm infants with confirmed hearing loss. *Int J Ped Otorhinolaryngol* [Internet]. 2022[cited 2023 May 15];161:111262. Available from: <https://www.sciencedirect.com/science/article/abs/pii/S0165587622002233?via%3Dihub> doi: 10.1016/j.ijporl.2022.111262
25. Nakanishi H, Suenaga H, Uchiyama A, Kono Y, Kusuda S; Neonatal Research Network, Japan. Trends in the neurodevelopmental outcomes among preterm infants from 2003-2012: a retrospective cohort study in Japan. *J Perinatol*. 2018;38(7):917-28. doi: 10.1038/s41372-018-0061-7
26. Kayton A, Timoney P, Vargo L, Perez JA. A Review of Oxygen Physiology and Appropriate Management of Oxygen Levels in Premature Neonates. *Adv Neonatal Care*. 2018;18(2):98-104. doi: ANC.0000000000000434
27. Glass HC, Costarino AT, Stayer SA, Brett CM, Cladis F, Davis PJ. Outcomes for extremely premature infants. *Anesth Analg*. 2015;120(6):1337-51. doi: 10.1213/ANE.0000000000000705
28. Wald A. Sequential tests of statistical hypotheses. *Ann Math Statist*. 1945;16(2):117-86. doi: <https://doi.org/10.1214/aoms/1177731118>

**ДО ПИТАННЯ ПРО ПОРУШЕННЯ СЛУХУ У ПЕРЕДЧАСНО НАРОДЖЕНИХ ДІТЕЙ,  
ЩО ПЕРЕНЕСЛИ ОКСИДАТИВНИЙ СТРЕС ПРИ НАРОДЖЕННІ**

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### **Резюме**

**Вступ.** Важливе місце серед перинатальної патології займає порушення слуху (ПС). За даними ВООЗ частота тяжких порушень слуху спостерігається у 1 – 2 дітей на 1000 новонароджених та у 15 % новонароджених, які вимагали проведення інтенсивної терапії після народження, а ПС легкого та середнього ступеня зустрічаються у 1 – 2 % дітей з перинатальною патологією.

**Мета роботи** – вивчити предиктори порушення слуху та фактори, що визначають характер та тяжкість приглухуваності у дітей віком 2–3-х місяців, які перенесли оксидативний стрес при народженні.

**Матеріал та методи дослідження.** Робота виконана в межах НДР кафедри педіатрії №3 та неонатології ХНМУ «Вивчення особливостей перебігу хвороб оксидантного стресу у новонароджених» 2022–2024 рр. (держреєстрація № A22U000025).

Проаналізовано 131 випадок спостереження новонароджених 27–36 тижнів гестації з порушенням слуху у КНП «МПЦ» м. Харкова. З дослідження виключено дітей, в сім'ях яких були випадки порушення слуху будь-якого генезу. Для вирішення мети роботи були сформовані альтернативні групи: I група (n=51) з однобічним та II група (n=80) – двобічним порушенням слуху.

Для визначення предикторів тяжкості ПС у групах порівняння вивчалися фактори, що детермінують приглухуваність, встановлена їх прогностична інформативність. Визначалися критерії t-Стьюдента та ф-Фішера, використаний алгоритм неоднорідної послідовної процедури Вальда-Генкіна, визначені прогностичні коефіцієнти (ПК) та інформативність (І).

Рішенням комісії з біоетики №3 від 21.03.2023 року матеріали дослідження відповідають Токійській декларації Всесвітньої медичної асоціації, Міжнародним рекомендаціям Гельсинської декларації щодо прав людини, Конвенції Ради Європи щодо прав людини і біомедицини, Законам України, вимогам Етичного кодексу лікаря України.

**Результати дослідження.** Фактори акушерського та соматичного анамнезу матері не впливали на характер ПС у дитини. Серед ускладнень вагітності та пологів в анамнезі дітей з двобічним ПС частіше спостерігалися фетоплацентарна недостатність 33,8% проти 13,7 % ( $p<0,001$ ), загроза переривання вагітності 30,0 % проти 17,6 % ( $p<0,05$ ), анемія вагітних 31,2 % проти 13,7 % ( $p<0,001$ ), дистрес плода 56,2 % проти 37,3 % ( $p<0,01$ ), народження шляхом кесаревого розтину 68,8 % проти 47,1 % ( $p<0,001$ ), особливо з приводу дистресу плода – 67,3 % проти 29,2 % ( $p<0,001$ ).

Частота двобічного ПС у дітей обернуто пропорційно терміну гестації та масі тіла при народженні та асоціється з низькою оцінкою за шкалою Апгар. Виявлений статевий диморфізм: у групі з двобічним ураженням слуху переважали дівчинки 56,2 % проти 35,3 % ( $p<0,001$ ). Діти з двобічним ПС частіше вимагали сурфактантної терапії 78,8 % проти 33,3 % ( $p<0,001$ ), а також більш тривалої респіраторної підтримки та оксигенотерапії.

У проведенню дослідження двобічне ПС частіше зустрічалося у дітей із захворюваннями, патогенез яких тісно пов’язаний з оксидативним стресом: перивентрикулярною лейкомаліацією (ПВЛ) 55,0 % проти 7,8 % ( $p<0,001$ ); бронхолегеневою дисплазією (БЛД) 2 та 3 ступеню: 23,7 % проти 2,0 % ( $p<0,001$ ) та 23,7 % проти 0 % ( $p<0,001$ ) відповідно; ретинопатією недоношених 2–3 ступеню 42,5 % проти 17,6 % ( $p<0,001$ ); відкритою артеріальною протокою 81,3 % проти 41,2 % ( $p<0,001$ ), у тому числі при необхідності її хірургічного закриття 18,5 % проти 9,5 % ( $p<0,05$ ).

Найвища інформативність порушення слуху у дітей, що перенесли оксидативний стрес належить наступним ознакам: терміну гестації (6,14), загальній тривалості ШВЛ (5,54), масі тіла (5,44), БЛД (5,4), тривалості ШВЛ в режимі нормо-вентиляції (4,1), тривалості оксигенотерапії (3,91), відкритій артеріальній протоці (3,72).

Найбільш значущі прогностичні коефіцієнти двобічного порушення слуху: наявність БЛД 2–3 ст. (-13,8); ВШК 2–3 ст. (-12,4); загальна тривалість ШВЛ ≥21 доби (-10,33); термін гестації ≤29 тиж. (-8,6); ПВЛ 2–3 ст. (-8,48); тривалість оксигенотерапії ≥21 днія (-7,38); маса тіла (-6,94).

**Висновки.** Найбільш значущі прогностичні коефіцієнти двобічного порушення слуху: наявність БЛД 2–3 ст. (-13,8); ВШК 2–3 ст. (-12,4); загальна тривалість ШВЛ ≥21 доби (-10,33); термін гестації ≤29 тиж. (-8,6); перивентрикулярна лейкомаліація 2–3 ст. (-8,48); тривалість оксигенотерапії ≥21 днія (-7,38); маса тіла (-6,94) тощо. Двобічне порушення слуху прогнозується у гестаційно незрілих новонароджених (термін гестації ≤ 29 тижнів), з БЛД 2–3 ступеня, ВШК 2–3 ст., загальній тривалості ШВЛ та оксигенотерапії > 21 доби, ПВЛ 2–3 ступеня. У нашому дослідженні достовірного зв’язку між характером порушення слуху передчасно народженої дитини та соматичним та акушерським анамнезом матері не виявлено. Гендерні особливості серед передчасно народжених дітей із двобічним порушенням слуху характеризувалися перевагою жіночої статі 56,2 % проти 35,3 % ( $p<0,001$ ).

**Ключові слова:** передчасно народжена дитина; порушення слуху; оксидативний стрес.

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