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РЕЗУЛЬТАТИ ДИСЕРТАЦІЙНИХ ТА НАУКОВО-ДОСЛІДНИХ РОБІТ

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BIOMARKERS OF NEONATAL AND MATERNAL STRESS IN THE NEONATAL INTENSIVE CARE UNIT

***H. Pavlyshyn*[1], *I. Sarapuk*[1], *U. Saturska*[1]**

I. Horbachevsky Ternopil National Medical University,
Ministry of Health of Ukraine
(Ternopil, Ukraine)

Summary.

Treatment of newborns in neonatal intensive care units (NICUs) is associated with exposure to multifactorial stressors, which adversely affect the physical and psychological status of infants as well as the psycho-emotional state of their mothers. In this context, the use of non-invasive assessment of stress biomarkers has gained increasing importance.

Aim. *To evaluate neonatal and maternal stress in the NICU by measuring indicators of sympathoadrenal and serotonergic system function and to analyze stress-inducing factors.*

Materials and Methods. *The study included 117 newborns admitted to the NICU of the regional perinatal center. The infants were divided into three groups according to gestational age at birth: Group 1 – extremely and very preterm infants (EVPI), <32 weeks, n = 35; Group 2 – moderate and late preterm infants (MLPI), ≥32 weeks, n = 61; Group 3 – term newborns, n = 21. The following stress biomarkers were measured: 5-hydroxyindoleacetic acid (5-HIAA), a serotonin metabolite and functional marker of the serotonergic system; and salivary alpha-amylase (sAA), a biomarker of the sympathoadrenal system activity reflecting the sympathetic division of the autonomic nervous system response to stress. Written informed consent was obtained from the parents of all participants. The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Bioethics Committee of I. Ya. Horbachevsky Ternopil National Medical University, Ministry of Health of Ukraine (Protocol No. 73, April 3, 2023). Statistical analysis was conducted using STATISTICA 13.0 software (StatSoft Inc., Tulsa, OK, USA). Medians (Me), upper quartiles (Uq), and lower quartiles (Lq) were calculated. For comparison of numerical variables with non-normal distribution, the Mann-Whitney U test (for two independent groups), the Kruskal–Wallis test (for three independent groups), and the Wilcoxon signed-rank test (for two dependent groups) were applied. Statistical significance was set at p < 0.05. The research project was entitled «Assessment of neonatal and parental stress in the neonatal intensive care unit and methods of its correction», State registration No. 0123U100063, the study period was December 2022 – November 2025.*

Results. *In extremely preterm infants, urinary 5-HIAA levels increased after skin-to-skin contact (SSC) from 2.064 [1.423; 3.402] to 4.366 [2.592; 9.468] mg/L (p = 0.008). In the moderate and late preterm group, levels increased from 2.247 [1.530; 3.217] to 5.001 [2.812; 9.567] mg/L (p < 0.001). In term infants, 5-HIAA levels increased from 2.452 [1.861; 5.587] to 4.293 [3.565; 8.420] mg/L; however, this change was not statistically significant (p = 0.075). Decreased 5-HIAA levels in preterm infants were associated with low Apgar scores (<7 points), need for resuscitation, surfactant administration, mechanical ventilation, intraventricular hemorrhage, necrotizing enterocolitis, patent ductus arteriosus, anemia, and neonatal jaundice requiring phototherapy. In infants <32 weeks' gestation, sAA levels after SSC decreased from 52.74 [38.54; 107.10] to 19.65 [15.15; 26.98] U/mL (p = 0.001). In infants ≥32 weeks, sAA levels decreased from 71.49 [34.98; 106.46] to 23.51 [17.39; 34.36] U/mL (p < 0.001). In term infants, sAA levels decreased from 84.24 [61.25; 101.03] to 31.37 [25.62; 42.78] U/mL (p < 0.005). Maternal sAA levels decreased correspondingly: in mothers of extremely and very preterm infants from 88.85 [51.66; 109.90] to 34.13 [23.59; 57.45] U/mL (p = 0.033); in mothers of moderate and late preterm infants from 68.85 [42.30; 98.64] to 25.03 [17.30; 29.59] U/mL (p < 0.001); and in mothers of term infants from 79.34 [54.21; 92.77] to 38.29 [22.88; 47.50] U/mL (p < 0.005). Breastfeeding in the NICU was associated with additional reduction in maternal stress: maternal sAA levels before SSC were 49.20 [28.19; 75.64] U/mL in breastfeeding mothers compared with 105.90 [80.41; 148.10] U/mL in mothers who formula-fed their infants (p = 0.046).*

Conclusions. *Skin-to-skin contact and rooming-in in the NICU are evidence-based interventions that effectively reduce stress in both mothers and newborns, as indicated by changes in markers of serotonergic and sympathoadrenal system activity, whereas neonatal morbidity is associated with increased stress levels. Breastfeeding of preterm infants in the NICU is associated with a significant reduction in maternal stress.*

Keywords: *Neonatal Stress; Maternal Stress; Skin-to-skin Contact; Neonatal Intensive Care Unit; 5-hydroxyindoleacetic Acid (5-HIAA); Salivary Alpha-amylase (sAA).*

Introduction

Treatment of newborns in neonatal intensive care units (NICUs) constitutes an essential component of modern neonatal care, especially for preterm infants [1, 2]. However, the NICU environment is associated with numerous adverse effects on the physical and psycho-emotional status of infants and on the psychological well-being of their mothers [3, 4]. In recent years, increasing attention has been directed toward the investigation of stress biomarkers, which enable an objective assessment of stress levels and their effects on health [5, 6].

The assessment of stress hormones in newborns and their mothers in the NICU is especially relevant given the heightened vulnerability of this population to various stressors [7]. Non-invasive measurement of stress markers in biological fluids such as saliva and urine permits evaluation of stress responses without inflicting additional trauma on the infant [6].

Urinary 5-hydroxyindoleacetic acid (5-HIAA) levels reflect the intensity of serotonin metabolism and the functional status of serotonergic neurotransmission [8]. In newborns, the serotonergic system remains functionally immature, rendering it particularly sensitive to perinatal stressors [9].

Salivary alpha-amylase (sAA) serves as a non-invasive biomarker of sympathoadrenal system activity, reflecting activation of the sympathetic division of the autonomic nervous system in response to stress, and is widely employed in psychophysiological research for the assessment of acute stress responses [10, 11].

Aim. To evaluate neonatal and maternal stress in the NICU by measuring indicators of sympathoadrenal and serotonergic system function and to analyze stress-inducing factors.

Materials and Methods. The study included 117 newborns admitted to the NICU of the Ternopil Regional Clinical Perinatal Center «Mother and Child». The infants were divided into three groups based on gestational age at birth: Group 1 – extremely and very preterm infants (EVPI), <32 weeks, n = 35; Group 2 – moderate and late preterm infants (MLPI), ≥32 weeks, n = 61; Group 3 – term newborns, n = 21.

Quantitative determination of stress biomarkers in biological fluids – including urinary 5-HIAA in newborns and sAA in both newborns and their mothers – was performed using enzyme-linked immunosorbent assay (ELISA) using commercial kits (IBL International GmbH, Hamburg, Germany). Saliva and urine samples were collected from newborns, and saliva samples from their mothers, before and after skin-to-skin contact (SSC) or rooming-in with the mother for at least 60 minutes per day over 7 consecutive days. Written informed consent was obtained from the parents of all participants. The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Bioethics Committee of I. Ya. Horbachevsky Ternopil National Medical University, Ministry of Health of Ukraine (Protocol No. 73, April 3, 2023).

Statistical analysis was conducted using STATISTICA 13.0 software (StatSoft Inc., Tulsa, OK, USA). Medians (Me), upper quartiles (Uq), and lower quartiles (Lq) were calculated. For comparison of numerical variables with non-normal distribution, the Mann-Whitney U test (for two independent groups), the Kruskal–Wallis test (for three independent groups), and the Wilcoxon signed-rank test (for two dependent groups) were applied. Statistical significance was set at $p < 0.05$.

The research project was entitled «Assessment of neonatal and parental stress in the neonatal intensive care unit and methods of its correction» (State registration No. 0123U100063). The study period was December 2022 – November 2025.

Results and discussion

A detailed analysis of antenatal, intrapartum, and postnatal factors was performed, with comparisons across the study groups. Among maternal factors, the most prevalent across all groups were complicated obstetric history (including previous miscarriages, missed abortions, and complications in prior pregnancies), placental dysfunction, anemia, and somatic disorders (Table 1).

Table 1

General characteristics of newborns according to gestational age: maternal factors

Indicator, [n (%)]	EVPIs (< 32 weeks), n = 35	MLPIs (> 32 weeks), n = 61	Term newborns, n = 21	Kruskal–Wallis test, p
Pregnancy 1 ≥ 2	 12 (34.29) 23 (65.71)	 18 (29.51) 43 (70.49)	 10 (47.62) 11 (52.38)	H = 2.26; p = 0.323
Delivery 1 ≥ 2	 15 (42.86) 20 (57.14)	 26 (42.62) 35 (57.38)	 10 (47.62) 11 (52.38)	H = 0.16; p = 0.919
Spontaneous vaginal delivery Cesarean section	12 (34.29) 23 (65.71)	17 (27.87) 44 (72.13)	14 (66.67) 7 (33.33)	H = 10.16; p = 0.006*
Pregnancy type: Singleton Multiple	 28 (80.00) 7 (20.00)	 38 (62.30) 23 (37.70)	 21 (100.00) 0 (0.00)	H = 12.38; p = 0.002*
Complicated obstetric history	20 (57.14)	35 (57.38)	5 (23.81)	H = 7.26; p = 0.027*
In vitro fertilization	5 (14.29)	10 (16.39)	0 (0.0)	H = 3.82; p = 0.148
Preeclampsia, gestational hypertension	7 (20.0)	22 (36.07)	5 (23.81)	H = 3.10; p = 0.212
Placental dysfunction	26 (74.29)	49 (80.33)	16 (76.19)	H = 0.52; p = 0.778
Anemia	12 (34.29)	30 (49.18)	12 (57.14)	H = 3.20; p = 0.202
Polyhydramnios	8 (22.86)	12 (19.67)	5 (23.81)	H = 0.22; p = 0.894
Oligohydramnios	2 (5.71)	6 (9.84)	1 (4.76)	H = 0.83; p = 0.656
Acute respiratory viral infection (ARVI)	5 (14.29)	15 (24.59)	8 (38.1)	H = 4.08; p = 0.130
Somatic pathology	17 (48.57)	30 (49.18)	11 (52.38)	H = 0.08; p = 0.959
Thyroid disease	7 (20.0)	10 (16.39)	4 (19.04)	H = 0.22; p = 0.898
Gestational diabetes	5 (14.29)	1 (1.64)	0 (0.0)	H = 8.62; p = 0.013*
Urinary tract infection (UTI)	0 (0.0)	6 (9.84)	4 (19.04)	H = 6.31; p = 0.043*
Chronic TORCH infection	2 (5.71)	1 (1.64)	0 (0.0)	H = 2.13; p = 0.344
Gynecological infections	0 (0.0)	4 (6.56)	1 (4.76)	H = 2.33; p = 0.312
Bleeding, hematoma	10 (28.57)	19 (31.15)	4 (19.04)	H = 1.12; p = 0.570
Fetal distress	6 (17.14)	13 (21.31)	2 (9.52)	H = 1.48; p = 0.476

Note 1. H – Kruskal–Wallis test, p – significance for the Kruskal-Wallis test.
*Note 2. * – statistically significant results.*

In the extremely and very preterm infants (EVPI) and moderate and late preterm infants (MLPI) groups, the most frequent neonatal factors included Apgar score < 7 at 1 minute, need for resuscitation after birth, surfactant administration, respiratory distress syndrome (RDS), necrotizing enterocolitis (NEC), intraventricular hemorrhage (IVH grades II-IV), anemia requiring blood transfusion, and continuous positive airway pressure (CPAP) therapy. Pathological neurological symptoms, neonatal sepsis, and jaundice were also commonly observed across all newborn groups (Table 2).

The effectiveness of skin-to-skin contact (SSC) as the primary stress-reducing intervention in the NICU for preterm infants, and rooming-in with the mother for term infants, was evaluated by measuring levels of 5-HIAA and sAA.

Table 2

General characteristics of newborns according to gestational age: neonatal factors

Indicator, [n (%)]	EVPIs (< 32 weeks), n = 35	MLPIs (> 32 weeks), n = 61	Term newborns, n = 21	Kruskal–Wallis test, p
Sex male female	 25 (71.43) 10 (25.57)	 35 (57.38) 26 (42.62)	 10 (47.62) 11 (52.38)	H = 3.39; p = 0.184
Apgar score at 1 minute < 7	26 (74.29)	15 (24.59)	6 (28.57)	H = 24.08; p = 0.000*
Apgar score at 5 minutes < 7	11 (31.43)	4 (6.56)	5 (23.81)	H = 10.43; p = 0.005*
Resuscitation after birth	24 (68.57)	11 (18.03)	4 (19.05)	H = 27.67; p = 0.000*
Respiratory distress syndrome (RDS)	35 (100.0)	37 (60.66)	0 (0.0)	H = 55.02; p = 0.000*
Surfactant administration	22 (62.86)	3 (4.92)	1 (4.76)	H = 47.30; p = 0.000*
Bronchopulmonary dysplasia (BPD)	16 (45.71)	1 (1.64)	0 (0.0)	H = 40.06; p = 0.000*
Early-onset sepsis	6 (17.14)	4 (6.56)	3 (14.29)	H = 2.76; p = 0.252
Late-onset sepsis	15 (42.86)	24 (39.34)	9 (42.86)	H = 0.15; p = 0.929
Necrotizing enterocolitis (NEC)	13 (37.14)	18 (29.51)	1 (4.76)	H = 7.16; p = 0.028*
Neurological symptoms (seizures, depression, coma)	35 (100.0)	53 (86.89)	20 (95.23)	H = 5.65; p = 0.059
Intraventricular hemorrhage (IVH, grades II-IV)	15 (42.86)	9 (14.75)	5 (23.81)	H = 9.35; p = 0.009*
Neonatal jaundice	19 (54.29)	51 (83.61)	10 (47.62)	H = 13.82; p = 0.001*
Patent ductus arteriosus (PDA)	12 (34.29)	9 (14.75)	1 (4.76)	H = 8.79; p = 0.012*
Retinopathy of prematurity	16 (45.71)	8 (13.11)	0 (0.0)	H = 20.92; p = 0.000*
Anemia	18 (51.43)	20 (32.79)	2 (9.09)	H = 10.27; p = 0.006*
CPAP therapy	34 (97.14)	44 (72.13)	7 (33.33)	H = 26.68; p = 0.000*
Mechanical ventilation (MV)	17 (48.57)	7 (11.48)	8 (38.1)	H = 16.74; p = 0.000*

Note 1. H – Kruskal-Wallis test, p – significance for the Kruskal-Wallis test.
*Note 2. * – statistically significant results.*

Analysis of urinary 5-HIAA, a serotonin metabolite, in newborns enabled assessment of the impact of skin-to-skin contact on serotonergic system activity as a component of the stress response across different gestational ages. In newborns <32 weeks' gestation, urinary 5-HIAA levels before SSC were 2.064 [1.423; 3.402] mg/L and increased to 4.366 [2.592; 9.468] mg/L after SSC (p = 0.008), indicating enhanced serotonin metabolism and reduced stress load. A comparable effect was observed in infants ≥ 32 weeks' gestation, with 5-HIAA levels rising from 2.247 [1.530; 3.217] mg/L to 5.001 [2.812; 9.567] mg/L after SSC (p < 0.001). These findings demonstrate the high responsiveness of the neonatal serotonergic system to the calming influence of maternal contact during NICU treatment. In term newborns, a tendency toward increased metabolite levels was observed after rooming-in with the mother (from 2.452 [1.861; 5.587] mg/L to 4.293 [3.565; 8.420] mg/L); however, the change did not reach statistical significance (p = 0.075). This lack of significance may be attributable to the presence of more mature compensatory mechanisms of stress regulation in term infants (Fig. 1).

An association was identified between baseline urinary 5-HIAA levels and selected neonatal factors. In particular, urinary 5-HIAA levels were associated with the Apgar score at 1 minute. Newborns with an Apgar score <7 had lower 5-HIAA levels than those with an Apgar score >7 (1.830 [1.418; 2.701] mg/L vs 3.027 [1.710; 4.432] mg/L, p = 0.048, in EPVIs, and 1.651 [1.220; 2.499] mg/L vs 2.572 [1.736; 4.694] mg/L, p = 0.042, in MLPIs). No such association was observed in term newborns. Lower 5-HIAA levels were also noted in association with an Apgar score <7 at 5 minutes; however, these differences did not achieve statistical significance, likely due to the small number of infants with Apgar scores <7 at 5 minutes (Table 3).

Among EVPIs requiring resuscitation, the median urinary 5-HIAA level was 1.812 [1.414; 2.407] mg/L, compared with 2.994 [1.813; 3.709] mg/L in those who did not require resuscitation (p = 0.046). In MLPIs, those requiring resuscitation had median 5-HIAA levels of 1.400 [1.064; 1.783] mg/L, compared with 2.619 [1.869; 4.694] mg/L in those who did not (p = 0.003).

In infants < 32 weeks' gestation, median 5-HIAA levels were significantly lower in presence of certain postnatal factors, including surfactant administration and intraventricular hemorrhage (IVH grades, II-IV). Infants who received surfactant had median 5-HIAA levels of 1.607 [1.414; 2.407] mg/L, compared with 2.994 [1.813; 3.709] mg/L in those who did not require surfactant therapy (p = 0.044). Newborns with IVH exhibited lower urinary 5-HIAA levels than those without IVH (1.423 [1.174; 2.407] mg/L vs 2.392 [1.813; 3.644] mg/L, p = 0.041).

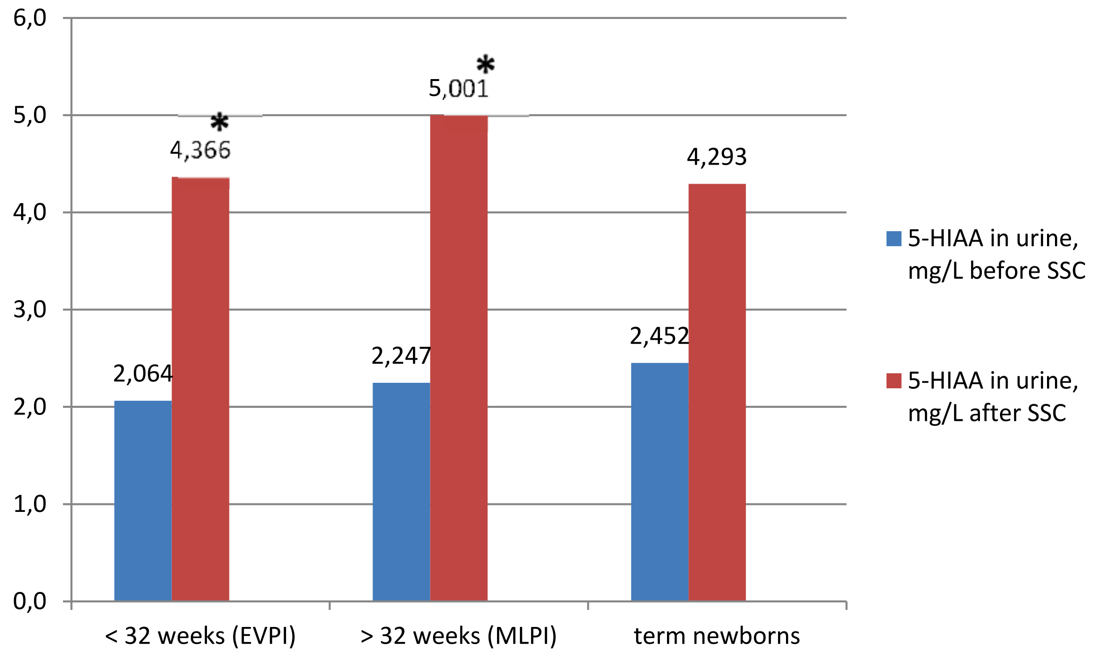

Fig. 1. Effect of skin-to-skin contact (SSC) on urinary 5-HIAA levels in newborns of different gestational ages.

*Note. * – p < 0.05.*

Table 3

Association of urinary 5-HIAA levels before SSC in children of different gestational ages with specific neonatal history factors

Neonatal history factors	Yes (+)/ no (–)	Baseline urinary 5-HIAA, mg/L Me [Lq; Uq]		
		EVPIs (< 32 weeks), n = 35	MLPIs (> 32 weeks), n = 61	Term newborns, n = 21
Apgar score at 1 minute < 7	+	1.830 [1.418; 2.701]	1.651 [1.220; 2.499]	2.428 [1.861; 5.587]
	-	3.027 [1.710; 4.432]	2.572 [1.736; 4.694]	3.114 [1.805; 5.994]
	p	p = 0.048*	p = 0.042*	p = 0.095
Apgar score at 5 minutes < 7	+	1.563 [1.414; 3.268]	2.499 [1.291; 6.085]	2.428 [1.861; 5.587]
	-	2.374 [1.607; 3.644]	2.243 [1.530; 3.217]	3.114 [1.805; 5.994]
	p	p = 0.310	p = 0.094	p = 0.948
Resuscitation after birth	+	1.812 [1.414; 2.407]	1.400 [1.064; 1.783]	2.452 [1.158; 8.213]
	-	2.994 [1.813; 3.709]	2.619 [1.869; 4.694]	3.102 [2.075; 5.230]
	p	p = 0.046*	p = 0.003*	p = 0.135
Surfactant administration	+	1.607 [1.414; 2.407]	1.405 [1.405; 1.405]	8.213 [8.213; 8.213]
	-	2.994 [1.813; 3.709]	2.373 [1.541; 3.589]	2.440 [1.861; 4.873]
	p	p = 0.044*	p = 0.995	p = 1.000
Intraventricular hemorrhage (grades II-IV)	+	1.423 [1.174; 2.407]	1.551 [0.826; 2.247]	2.452 [1.550; 5.715]
	-	2.392 [1.813; 3.644]	2.510 [1.530; 3.960]	3.209 [2.396; 4.788]
	p	p = 0.041*	p = 0.169	p = 0.074
NEC	+	2.110 [1.688; 2.839]	1.530 [1.291; 2.239]	-
	-	2.064 [1.399; 3.590]	2.634 [1.765; 5.193]	-
	p	p = 0.783	p = 0.042*	
Neonatal jaundice requiring phototherapy	+	1.830 [1.422; 3.644]	2.212 [1.519; 3.078]	1.861 [1.223; 5.715]
	-	2.344 [1.607; 2.994]	3.044 [2.247; 7.140]	3.221 [2.396; 5.230]
	p	p = 0.838	p = 0.048*	p = 0.098
PDA	+	1.812 [1.423; 2.407]	1.291 [0.845; 1.508]	1.223 [1.223; 1.223]
	-	2.374 [1.422; 3.709]	2.510 [1.765; 4.327]	3.114 [2.288; 5.587]
	p	p = 0.371	p = 0.033*	p = 1.000
Anemia requiring blood transfusion	+	1.830 [1.422; 3.268]	1.508 [1.220; 2.572]	1.158 [1.158; 1.158]
	-	2.345 [1.607; 3.644]	2.608 [1.952; 5.193]	3.114 [2.288; 5.587]
	p	p = 0.501	p = 0.028*	p = 1.000
Mechanical ventilation	+	1.812 [1.414; 2.374]	1.177 [1.133; 1.220]	2.440 [2.364; 3.775]
	-	2.410 [1.607; 3.709]	2.499 [1.551; 3.960]	3.990 [1.861; 5.715]
	p	p = 0.118	p = 0.049*	p = 0.068

Note 1. p – significance for the Mann-Whitney U test.
*Note 2. * – statistically significant results.*

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In MLPIs, postnatal complications h were similarly associated with lower median urinary 5-HIAA levels compared with those without complications. Specifically, infants with necrotizing enterocolitis (NEC) had median 5-HIAA levels of 1.530 [1.291; 2.239] mg/L vs 2.634 [1.765; 5.193] mg/L in those without NEC ($p = 0.042$); infants with neonatal jaundice requiring phototherapy had levels of 2.212 [1.519; 3.078] mg/L vs 3.044 [2.247; 7.140] mg/L in those without jaundice ($p = 0.048$); infants with patent ductus arteriosus (PDA) had levels of 1.291 [0.845; 1.508] mg/L vs 2.510 [1.765; 4.327] mg/L in those without PDA ($p = 0.033$); and infants with neonatal anemia had levels of 1.508 [1.220; 2.572] mg/L vs 2.608 [1.952; 5.193] mg/L in those without anemia ($p = 0.028$). The median 5-HIAA level in MLPIs requiring mechanical ventilation was significantly lower than in those who did not require ventilation (1.177 [1.133; 1.220] mg/L vs 2.499 [1.551; 3.960] mg/L, $p = 0.049$).

Salivary alpha-amylase (sAA) levels were measured to evaluate sympathoadrenal system activity and the effectiveness of skin-to-skin contact as a stress-reducing intervention in the NICU. In infants born at <32 weeks' gestation, baseline sAA levels were 52.74 [38.54; 107.10] U/mL and decreased significantly to 19.65 [15.15; 26.98] U/mL following SSC ($p = 0.001$), indicating a substantial reduction in sympathetic activation and improved stress response regulation. In infants ≥32 weeks' gestation, sAA levels decreased from 71.49 [34.98; 106.46] U/mL to 23.51 [17.39; 34.36] U/mL ($p < 0.001$), confirming the marked effectiveness of SSC in reducing stress in preterm infants. In term infants, baseline sAA levels were higher than in preterm infants (84.24 [61.25; 101.03] U/mL) but decreased significantly to 31.37 [25.62; 42.78] U/mL following rooming-in with the mother ($p < 0.005$). These findings demonstrate the consistent anti-stress effect of skin-to-skin contact and rooming-in with the mother, irrespective of gestational age at birth (Fig. 2).

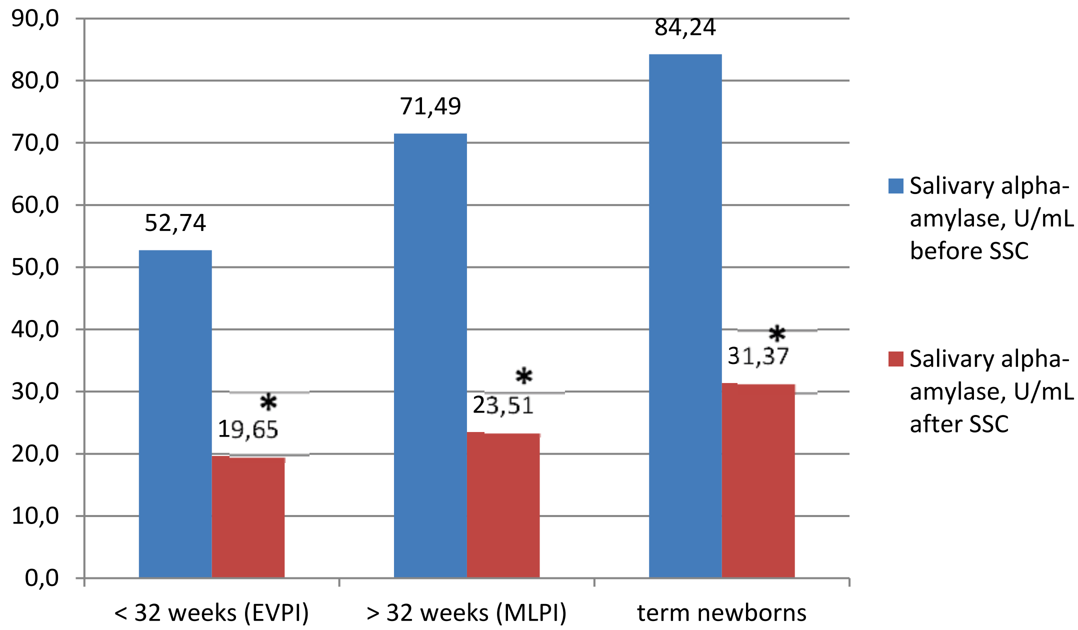

Fig. 2. Effect of skin-to-skin contact (SSC) on stress levels as assessed by salivary alpha-amylase in newborns.

*Note. * – p < 0.05.*

Baseline sAA levels in mothers of EVPIs were 88.85 [51.66; 109.90] U/mL and decreased significantly to 34.13 [23.59; 57.45] U/mL following skin-to-skin contact ($p = 0.033$). In mothers of MLPIs, sAA levels declined from 68.85 [42.30; 98.64] U/mL to 25.03 [17.30; 29.59] U/mL after SSC ($p < 0.001$). In mothers of term infants, baseline sAA levels of 79.34 [54.21; 92.77] U/ mL decreased to 38.29 [22.88; 47.50] U/mL following rooming-in with the infant ($p < 0.005$). These results indicate that SSC and rooming-in significantly reduce maternal sAA levels across all groups, reflecting effective stress relief and decreased sympathetic activation (Fig. 3).

Breastfeeding was associated with lower sAA levels in mothers of EVPIs compared with non-breastfeeding mothers (49.20 [28.19; 75.64] U/mL) vs 105.90 [80.41; 148.10] U/mL, $p = 0.046$). A similar trend, although not statistically significant, was seen in mothers of moderately preterm and term infants. A similar trend, although not statistically significant, was observed in mothers of MLPIs and in mothers of term infants.

The present study demonstrated that skin-to-skin contact and rooming-in with the mother induce significant changes in stress biomarker levels in newborns across different gestational ages, consistent with previous reports [12, 13]. In particular, urinary levels of the serotonin metabolite 5-HIAA increased significantly after SSC in EVPIs and MLPIs ($p = 0.008$ and $p < 0.001$, respectively), whereas a similar though non-significant trend was observed in term newborns following rooming-in with their mothers ($p = 0.075$). These findings indicate heightened sensitivity of the serotonergic system in preterm infants to the beneficial effects of maternal physical contact, in agreement with studies demonstrating active modulation of the hypothalamic-pituitary-adrenal axis during the early neonatal period under maternal influence [13].

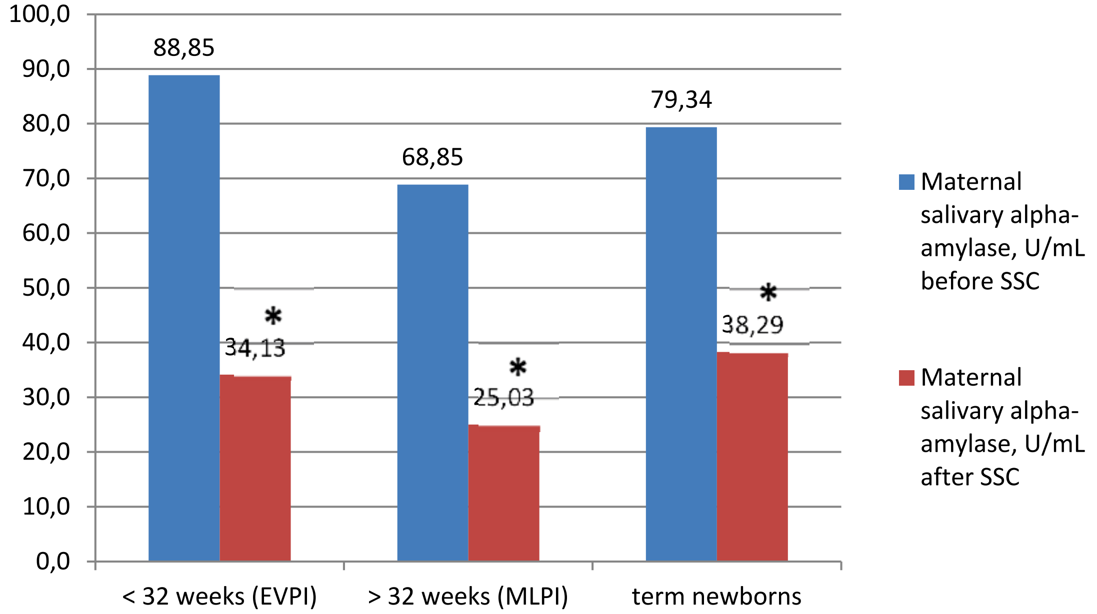

Fig. 3. Effect of skin-to-skin contact (SSC) on maternal stress levels as assessed by salivary alpha-amylase.
*Note. * – p < 0.05.*

The observed reduction in laboratory stress markers following skin-to-skin contact and rooming-in with the mother is aligns with existing literature supporting the effectiveness of this intervention in preterm infants. Previous investigations have reported decreases in cortisol levels – a classical stress marker – along with increases in stress-protective hormones such as oxytocin and melatonin after SSC, collectively indicating an overall anti-stress effect of this intervention in the NICU [14].

The association between 5-HIAA levels in newborns and low Apgar scores (<7), the need for resuscitation, mechanical ventilation, and various neonatal pathologies observed in the present study confirms impaired serotonergic system activity infants treated in NICU. At the same time, it clearly shows the effectiveness of SSC and active parental involvement in reducing infant stress levels and improving neonatal care outcomes [15].

Analysis of salivary alpha-amylase in newborns treated in NICU and their mothers further confirmed that SSC in preterm infants and rooming-in in term newborns result in a significant reduction in sympathoadrenal system activity and associated stress markers. These observations are consistent with recent studies demonstrating that SSC reduces cortisol levels in infants while simultaneously enhancing maternal emotional well-being and alleviating anxiety following preterm birth [16]. Moreover, the reduction in stress markers observed in mothers who breastfed their infants in the NICU supports the established beneficial psychophysiological effects of breastfeeding [17, 18].

The present study provides additional insight into the mechanisms by which SSC and rooming-in exert positive effect on the serotonergic and sympathoadrenal systems of both newborns and their mothers. These results align with international evidence underscoring the benefits of SSC, including reductions in various stress markers and the importance of its early initiation in the NICU to optimize neonatal outcomes and support maternal psycho-emotional well-being [13, 19].

Conclusions. Skin-to-skin contact and rooming-in in the NICU are evidence-based interventions that effectively reduce stress in both mothers and newborns, as demonstrated by changes in serotonergic and sympathoadrenal system biomarkers, whereas neonatal morbidity is associated with elevated stress levels. Breastfeeding of preterm infants in the neonatal intensive care unit is associated with a significant reduction in maternal stress.

Future research directions. Future studies should aim to expand the cohort of newborns to permit more detailed analysis of stress markers across different gestational age groups, thereby facilitating development and implementation of targeted stress-correction strategies.

Author Contribution:

Conceptualization: Halyna Pavlyshyn, Iryna Sarapuk, Uliana Saturska.

Supervision: Halyna Pavlyshyn.

Methodology: Halyna Pavlyshyn, Iryna Sarapuk, Uliana Saturska.

Formal analysis and investigation: Halyna Pavlyshyn, Iryna Sarapuk, Uliana Saturska.

Writing-original draft preparation: Uliana Saturska.

Writing, review and editing: Halyna Pavlyshyn; Iryna Sarapuk.

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БІОМАРКЕРИ НЕОНАТАЛЬНОГО ТА МАТЕРИНСЬКОГО СТРЕСУ У ВІДДІЛЕННІ ІНТЕНСИВНОЇ ТЕРАПІЇ НОВОНАРОДЖЕНИХ

Г. А. Павлишин, І. М. Сарапук, У. В. Сатурська

Тернопільський національний медичний університет імені І. Я. Горбачевського МОЗ України (м. Тернопіль, Україна)

Резюме.

Лікування новонароджених у відділеннях інтенсивної терапії (ВІТН) супроводжується багатофакторним стресовим навантаженням, яке несприятливо позначається як на фізичному, психологічному стані немовлят, так і на психоемоційному стані їхніх матерів. У зв'язку з цим набуває актуальності застосування неінвазивних методів дослідження біомаркерів стресу.

Мета дослідження – оцінити неонатальний та материнський стрес у ВІТН шляхом визначення показників функціонального стану симпатоадреналової та серотонінергічної систем, проаналізувати фактори, що його індукують.

Матеріали та методи. У дослідження було включено 117 новонароджених, що знаходились на лікуванні у ВІТН обласного перинатального центру. Дітей було поділено на 3 групи залежно від їх гестаційного віку при народженні: перша група – (< 32 тижнів) – глибоко недоношені (ГНН) – 35 дітей, друга група – (≥ 32 тижнів) – помірно та пізні недоношені (ПНН) – 61 дитина, третя група – доношені новонароджені – 21 дитина. Вивчали такі біомаркери стресу, як 5-гідроксиіндолооцтова кислота (5-HIAA) – метаболіт серотоніну, функціональний маркер серотонінергічної системи та слинна альфа-амілаза (sAA) – біомаркер симпато-адреналової системи, що відображає реакцію симпатичного відділу вегетативної нервової системи на стрес. Інформовану згоду на участь у дослідженні отримано від батьків усіх дітей. Роботу виконано з дотриманням принципів Гельсінської декларації. Дослідження схвалено комісією з біоетики Тернопільського національного медичного університету ім. І. Я. Горбачевського Міністерства охорони здоров'я України (протокол № 73 від 03 квітня 2023 року). Статистичну обробку даних проведено за допомогою програми «STATISTICA 13.0. WINDOWS» з розрахунком медіани (Me), верхнього (Uq) та нижнього (Lq) квартилю. Для порівняння числових характеристик з неправильним розподілом величин використовували U-тест Манна-Уітні (для двох незалежних груп), тест Краскела-Уолліса (для трьох незалежних груп) й критерій Вілкоксона (W) – для двох залежних груп. Дані вважали достовірними при p<0,05. Наукове дослідження виконано у межах науково-дослідної роботи «Оцінка неонатального та батьківського стресу у відділенні інтенсивної терапії новонароджених, способи їх корекції», № державної реєстрації 0123U100063, терміни виконання: 12.2022 р. – 11.2025 р.

Результати дослідження та їх аналіз. У ГНН рівень 5-HIAA у сечі зростав після контакту «шкіра до шкіри» (КШШ) з 2,064 [1,423; 3,402] до 4,366 [2,592, 9,468] мг/л (p=0,008), у групі ПНН – з 2,247 [1,530; 3,217] до 5,001 [2,812; 9,567] мг/л (p<0,001), у доношених з 2,452 [1,861; 5,587] до 4,293 [3,565; 8,420] мг/л, проте дані не були статистично достовірними (p=0,075). Зниження рівня 5-HIAA асоціювалося з такими неонатальними станами у передчасно народжених немовлят, як низька оцінка за шкалою Апгар (< 7 балів), потреба в реанімації, введенні сурфактанту; штучною вентиляцією легень, внутрішньошлуночковими крововиливами, некротизуючим ентероколітом, відкритою артеріальною протокою, анемією, неонатальною жовтяницею, що потребувала корекції фототерапією. У групі дітей < 32 тижнів слинна альфа-амілаза після КШШ знижувалася з 52,74 [38,54; 107,10] до 19,65 [15,15; 26,98] од/мл (p=0,001), у дітей ≥ 32 тижнів – з 71,49 [34,98; 106,46] до 23,51 [17,39; 34,36] од/мл (p<0,001), у доношених – з 84,24 [61,25; 101;03] до 31,37 [25,62; 42,78] од/мл (p<0,005); у матерів новонароджених відповідно – у групі ГНН рівень sAA знижувався з 88,85 [51,66; 109,90] до 34,13 [23,59; 57,45] од/мл (p=0,033), у ПНН – з 68,85 [42,30; 98,64] до 25,03 [17,30; 29,59] од/мл (p<0,001), а у матерів доношених дітей – з 79,34 [54,21; 92,77] до 38,29 [22,88; 47,50] од/мл (p<0,005). Грудне вигодовування у ВІТН додатково знижувало рівень материнського стресу, при цьому sAA до КШШ у матерів становив 49,20 [28,19; 75,64] од/мл, порівняно з тими, що годували дитину сумішшю 105,90 [80,41; 148,10] од/мл (p=0,046).

Висновок. Контакт «шкіра до шкіри» та спільне перебування матері й дитини у ВІТН є доказовими методами, які ефективно знижують рівень стресу як у матерів, так і в новонароджених, що відображається за допомогою маркерів активності серотонінергічної та симпатоадреналової систем. Також виявлено зв'язок неонатальної захворюваності з підвищеним рівнем стресу. Грудне вигодовування передчасно народжених немовлят у ВІТН асоціюється зі значним зниженням материнського стресу.

Ключові слова: неонатальний стрес; материнський стрес, контакт «шкіра до шкіри» (КШШ), відділення інтенсивної терапії новонароджених (ВІТН), 5-гідроксиіндолооцтова кислота (5-HIAA), слинна альфа-амілаза (sAA).

Contact Information:

Halyna Pavlyshyn – Doctor of Medical Sciences, Professor, Head of the Department of Pediatrics No. 2, I. Ya. Horbachevsky Ternopil National Medical University, Ministry of Health of Ukraine (Ternopil, Ukraine)
e-mail: pavlishin@tdmu.edu.ua
ORCID ID: https://orcid.org/0000-0003-4106-2235
Scopus Author ID: https://www.scopus.com/authid/detail.uri?authorId=57192925001
ResearcherID: http://www.researcherid.com/rid/H-2220-2018

Sarapuk Iryna – Doctor of Medical Sciences, Professor, Department of Pediatrics No. 2, I. Ya. Horbachevsky Ternopil National Medical University, Ministry of Health of Ukraine (Ternopil, Ukraine)
e-mail: prostoirusya@ukr.net
ORCID ID: https://orcid.org/0000-0003-4206-0995
Scopus Author ID: https://www.scopus.com/authid/detail.uri?authorId=57199328723
ResearcherID: http://www.researcherid.com/rid/KCJ-8321-2024

Saturska Uliana – PhD student, Department of Pediatrics No. 2, I. Ya. Horbachevsky Ternopil National Medical University, Ministry of Health of Ukraine (Ternopil, Ukraine)
e-mail: saturska_uv@tdmu.edu.ua
ORCID ID: https://orcid.org/0009-0008-7227-367X
Scopus Author ID: https://www.scopus.com/authid/detail.uri?authorId=57842553700

Контактна інформація:

Павлишин Галина Андріївна – д. мед. н, професор, завідувач кафедри педіатрії № 2 Тернопільського національного медичного університету імені І. Я. Горбачевського МОЗ України (м. Тернопіль, Україна)
e-mail: pavlishin@tdmu.edu.ua
ORCID ID: https://orcid.org/0000-0003-4106-2235
Scopus Author ID: https://www.scopus.com/authid/detail.uri?authorId=57192925001
ResearcherID: http://www.researcherid.com/rid/H-2220-2018

Сарапук Ірина Мирославівна – д. мед. н, професор кафедри педіатрії № 2 Тернопільського національного медичного університету імені І. Я. Горбачевського МОЗ України (м. Тернопіль, Україна)
e-mail: prostoirusya@ukr.net
ORCID ID: https://orcid.org/0000-0003-4206-0995
Scopus Author ID: https://www.scopus.com/authid/detail.uri?authorId=57199328723
ResearcherID: http://www.researcherid.com/rid/KCJ-8321-2024

Сатурська Уляна Володимирівна – аспірант кафедри педіатрії № 2 Тернопільського національного медичного університету імені І. Я. Горбачевського МОЗ України (м. Тернопіль, Україна)
e-mail: saturska_uv@tdmu.edu.ua
ORCID ID: https://orcid.org/0009-0008-7227-367X
Scopus Author ID: https://www.scopus.com/authid/detail.uri?authorId=57842553700

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