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MULTIPARAMETRIC ANALYSIS FOR HYPOXIC-ISCHEMIC ENCEPHALOPATHY IN NEWBORNS: IMPACT OF ENVIRONMENTAL, CLINICAL, AND BIOCHEMICAL FACTORS

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✓ ***Resume***

Introduction: Hypoxic-ischemic encephalopathy (HIE) is a significant cause of neonatal mortality and both short-term and long-term morbidity.
Aim: To evaluate neurological damage in term infants with HIE following perinatal asphyxia and predict outcomes associated with the condition.

Materials and Methods: The study included 120 term infants (gestational age ≥37 weeks, birth weight ≥2500 grams) from birth to 1 year of age. The primary cohort consisted of 90 neonates with HIE, classified by severity using a modified Sarnat scale: mild (11.1%), moderate (51.1%), and severe (37.8%).

Results: The study results revealed that living in rural areas and lower rates of operative deliveries were associated with an increased risk of HIE. Higher severity of HIE correlated with more pronounced central nervous system (CNS) damage, blood gas composition abnormalities, and electrolyte imbalances. Seizures were most commonly observed in moderate HIE, whereas more severe neurological impairments were recorded in cases of severe HIE. Fractional tissue oxygen extraction (FTOE) decreased with increasing HIE severity and proved to be a reliable predictor of adverse outcomes. A logistic regression model incorporating FTOE and clinical parameters effectively predicted unfavorable outcomes.

Conclusion: This study underscores the critical role of environmental, anamnestic, and clinical factors in influencing outcomes in newborns with HIE. Early and comprehensive monitoring is essential for improving prognosis and guiding targeted clinical interventions.

Key words: Hypoxic-ischemic encephalopathy, neonatal mortality.

МНОГОПАРАМЕТРИЧЕСКИЙ АНАЛИЗ ГИПОКСИЧЕСКИ-ИШЕМИЧЕСКОЙ ЭНЦЕФАЛОПАТИИ У НОВОРОЖДЕННЫХ: ВЛИЯНИЕ ЭКОЛОГИЧЕСКИХ, КЛИНИЧЕСКИХ И БИОХИМИЧЕСКИХ ФАКТОРОВ

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✓ ***Резюме***

Гипоксически-ишемическая энцефалопатия (ГИЭ) является значимой причиной неонатальной смертности, а также краткосрочной и долгосрочной заболеваемости. Цель: Оценить степень неврологических повреждений у доношенных новорожденных с ГИЭ вследствие перинатальной асфиксии и спрогнозировать исходы данного состояния. Материалы и методы: В исследование включены 120 доношенных новорожденных (гестационный возраст ≥37 недель, масса тела при рождении ≥2500 г) в возрасте от рождения до 1 года. Основная группа состояла из 90 новорожденных с ГИЭ,

классифицированных по степени тяжести с использованием модифицированной шкалы Сарната: легкая (11,1%), средняя (51,1%) и тяжелая (37,8%).

Результаты: Результаты исследования выявили, что проживание в сельской местности и низкие показатели оперативных родов ассоциировались с повышенным риском ГИЭ, а более высокая степень тяжести ГИЭ коррелировала с более выраженными повреждениями центральной нервной системы, нарушениями газового состава крови и электролитного баланса. Судороги чаще всего наблюдались при умеренной степени ГИЭ, тогда как при тяжелой степени фиксировались более выраженные неврологические нарушения. Фракционная экстракция кислорода тканями (FTOE) снижалась с увеличением тяжести ГИЭ и оказалась надежным предиктором неблагоприятных исходов. Логистическая регрессионная модель, включающая FTOE и клинические параметры, эффективно предсказывала неблагоприятные исходы.

Заключение: Данное исследование подчеркивает значительное влияние экологических, анамнестических и клинических факторов на исходы у новорожденных с ГИЭ. Ранний и комплексный мониторинг имеет решающее значение для улучшения прогноза и разработки целенаправленных клинических вмешательств.

Ключевые слова: Гипоксически-ишемическая энцефалопатия, неонатальная смертност.

YANGI TUG'ILGAN CHALLARDAGI GIPOXIK-ISKEMIK ENSEFALOPATİYA UCHUN MULTIPARAMETRİK TAHLILI: ATROF-MUHIT, KLINIK VA BIOKIMYOVIY OMILLARNING TA'SIRI

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✓ ***Rezyume***

Kirish: Gipoksik-ishemik ensefalopatiya (GIE) neonatal o‘lim va qisqa hamda uzoq muddatli kasalliklarning muhim sabablaridan biri hisoblanadi.

Maqsad: Perinatal asfiksiya oqibatida GIE rivojlangan to‘liq muddatli chaqaloqlarda asab tizimi zararlanish darajasini baholash va ushbu holatning natijalarini prognoz qilish

Materiallar va usullar: Tadqiqotga 120 ta to‘liq muddatli chaqaloqlar (homiladorlik yoshi ≥37 hafta, tug‘ilgan vaqtdagi vazn ≥2500 gram) tug‘ilganidan 1 yoshgacha bo‘lgan davrda kiritildi. Asosiy guruh perinatal asfiksiya oqibatida GIE rivojlangan 90 ta chaqaloqdan tashkil topdi va ular Sarnatning modifikatsiyalangan shkalasi bo‘yicha quyidagi darajalarga bo‘lindi: yengil (11,1%), o‘rtacha (51,1%) va og‘ir (37,8%).

Natijalar: Tadqiqot natijalari shuni ko‘rsatdiki, qishloq joylarda yashash va operativ tug‘ruqning past darajasi GIE xavfini oshirgan. GIEning yuqori darajadagi og‘irligi markaziy asab tizimining (MAT) yanada chuqurroq shikastlanishi, qon gazlari tarkibidagi buzilishlar va elektrolit muvozanatidagi o‘zgarishlar bilan bog‘liq edi. Tutqanoqlar ko‘pincha o‘rtacha darajadagi GIEda kuzatilgan, og‘ir darajali GIEda esa yanada jiddiy nevrologik buzilishlar qayd etilgan. To‘qimalarning fraksion kislorod ekstraksiyasi (FTOE) GIEning og‘irlik darajasi ortishi bilan kamaygan va salbiy natijalarni prognozlashda ishonchli indikator sifatida aniqlangan. FTOE va klinik parametrlarni o‘z ichiga olgan logistik regressiya modeli noxush natijalarni samarali prognoz qilgan.

Xulosa: Ushbu tadqiqot gipoksik-ishemik ensefalopatiya bilan tug‘ilgan chaqaloqlarning salomatlik natijalariga atrof-muhit, anamnestik va klinik omillarning katta ta’sirini ko‘rsatdi. Erta va kompleks monitoring prognozni yaxshilash hamda maqsadli klinik choralarni belgilashda muhim ahamiyatga ega.

Kalit so'zlar: Gipoksik-ishemik ensefalopatiya, neonatal o'lim.

Relevance

Hypoxic-ischemic encephalopathy (HIE) is an important cause of mortality as well as short-term and long-term morbidity. 25% of neonates with HIE develop severe and irreversible neuropsychological secular, including mental retardation, cerebral palsy, epilepsy and neurosensory deficits. Neonatal HIE most often occurs as a result of perinatal asphyxia. In the perinatal period, umbilical cord entanglement or abnormal amniotic fluid can cause fetal distress, asphyxia and hypoxia [1,2,3,4].

The morbidity of HIE worldwide ranges from 1 to 3 per 1000 live births in developed countries and from 2.3 to 30.6 per 1000 live births in developing countries. Other estimates put the morbidity of HIE at 1.5 per 1000 live births. However, there are significant differences in the reporting of morbidity between population and hospital studies. The range of HIE is assumed to be about 1-8/1000 live births. Hypoxic-ischemic encephalopathy is a multi-system pathologica process requiring intensive therapeutic support for brain monitoring and monitoring of non-central nervous system organ dysfunction [5,6,7].

Important diagnostic and prognostic information for children with HIE is provided by neuromonitoring. The continuous monitoring method includes near-infrared spectroscopy (NIRS) to provide clear and complete information about brain function and oxygen use. Cerebral near-infrared spectroscopy is a non-invasive technology used to evaluate the perfusion of the brain in the patient's bed. Trends in cerebral perfusion using NIRS may provide information on cerebral metabolism as HIE progresses, which may provide insight into the extent of brain damage [8,9,10].

The high frequency of brain development disorders in children who have undergone perinatal asphyxia determines the need to find objective methods for timely diagnosis of changes in oxygenation of brain tissue and targeted application of adequate therapy. In recent years, researchers and clinicians have been particularly interested in using non-invasive, safe and sufficiently informative infrared spectroscopy for this purpose. All this makes it advisable to carry out the work.

Aim of the Study. To assess the extent of neurological damage in term infants with hypoxic-ischemic encephalopathy following perinatal asphyxia and to predict the outcomes of this condition.

Materials and methods

A total of 120 term infants (gestational age ≥37 weeks, birth weight ≥2500 grams) from birth to 1 year of age were included. The main group consisted of 90 neonates with hypoxic-ischemic encephalopathy (HIE) following perinatal asphyxia, categorized into three severity groups based on a modified Sarnat scale: mild (11.1%), moderate (51.1%), and severe (37.8%). The control group comprised 30 healthy neonates without asphyxia or CNS pathology, with Apgar scores of 8–10 at 1 and 5 minutes.

Maternal, perinatal, and family history, including neonatal growth parameters and nutrition, were thoroughly collected. Clinical evaluation covered somatic and neurological status and physiological reflexes. HIE severity was assessed using the modified Sarnat scale (Stoll & Kliegman, 2004). Child development over 12 months was monitored by pediatricians and neurologists, focusing on comorbidities.

NIRS technology (Somanaties İNVOS 5100C Covidien, Medtronic, USA, 2006) was used upon hospital admission to assess cerebral perfusion. The device, with a pediatric sensor placed on the newborn's forehead, measured regional hemoglobin oxygen saturation (rSO_2) and fractional tissue oxygen extraction (FTOE), updated every 5 seconds, which were recorded for 2 hours; fractional tissue oxygen extraction (FTOE-fractional tissue oxygen extraction), calculated by the formula [$FTOE=(SaO_2-rSO_2)/SaO_2$].

Brain structure was evaluated via neurosonography using transcranial techniques with high-frequency transducers (4–8 MHz), including Doppler studies and polypositional scanning. Cerebral blood flow parameters in the anterior and middle cerebral arteries were analyzed to calculate the resistance index (RI). Electroencephalograms were conducted to assess brain function and HIE severity.

Hematological studies assessed hemoglobin levels, hematocrit, and peripheral blood elements. Acid-base state (ABS) analysis included pH, partial pressures of carbon dioxide (pCO_2) and oxygen (pO_2), bicarbonate (HCO_3) levels, and oxygen saturation (sO_2). Blood gas and electrolyte balance were evaluated to determine hematopoiesis and gas exchange disorders in newborns during the neonatal period upon hospital admission.

Result and discussions

A multiparametric analysis of the impact of environmental factors, pathologies and procedures on the health of newborns with HIE was carried out. The study of anamnestic characteristics showed that in the control group 90.0% of families lived in the city, in the main group this percentage was 34.4%, and 65.6% of families in the main group lived in the regions ($p<0.001$). In the main group, first births accounted for 57.8% and in the control group most of the births were repeated 63.3%. 27.8% of children with HIE were born operatively, in the control group 80% ($p<0.001$).

Analysis of the types of feeding showed that only 30% of the children in both groups were completely breastfed. It was also noted that the frequency of operative delivery was significantly lower in children with HIE compared to the control group, indicating that operative intervention in childbirth may be associated with a reduced risk of HIE.

The study of the structure of CNS pathologies depending on the severity of HIE revealed that the 1st degree of HIE was characterized by a high level of combined non-traumatic CNS injuries 16.7% and intraventricular hemorrhages of the 1st degree 13.3%; HIE grade II - brain edema 40.0%, traumatic intracranial hemorrhages 13.3%; HIE grade 3 - traumatic damage to cranial bones, soft tissues 20.0%, brain edema 40.0% and 1 case of traumatic spinal cord injury.

We analyzed neurological symptoms in newborns with HIE based on its severity. Seizures were most frequent in the 2nd-degree HIE group (97.1%, $p<0.001$). Most patients with 2nd-degree HIE (97.1%) were in severe condition, while 69.6% of those with 3rd-degree HIE were in a preagonal state ($p<0.001$).

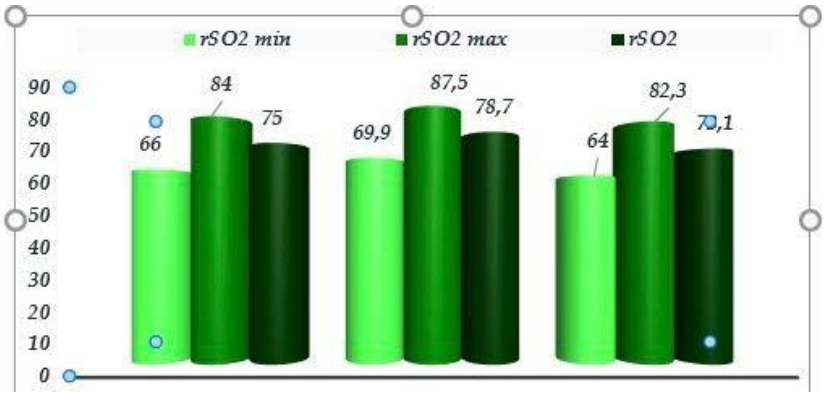
The average depth of the right lateral ventricles was 3.70 mm in 1st-degree HIE, 4.69 mm in 2nd-degree HIE, and 3.42 mm in 3rd-degree HIE ($p<0.05$). The anterior horn dimensions of the right lateral ventricles were significantly larger, measuring 3.70 mm, 4.79 mm, and 3.29 mm, respectively, across the three degrees of HIE ($p<0.05$). Periventricular echogenicity was significantly increased in 40.0% of 1st-degree cases, 8.8% of 2nd-degree cases, and 30.4% of 3rd-degree cases ($p<0.05$). Ultrasound of internal organs showed increased echogenicity of the kidneys and liver, along with hepatomegaly ($p<0.001$).

We analyzed the gas composition and acid-base parameters of venous blood in newborns with HIE following perinatal asphyxia. The PCO2 level in the HIE group was significantly lower than in the control group (33.8±1.0 mmHg vs. 41.8±0.4 mmHg, $p<0.001$). Similarly, the pO2 level in the HIE group was markedly reduced and outside the normal range (56.6±2.7 mmHg) compared to the control group (100.7±0.9 mmHg).

Blood oxygen saturation (sO2) in the HIE group was 86.7±1.2%, significantly lower than 97.9±0.2% in the control group. Electrolyte levels (Na+, K+, Cl-) were within reference ranges for both groups, but calcium levels were significantly lower in the HIE group (0.77±0.02 mg/dl) compared to the control group (1.22±0.01 mg/dl, $p<0.001$). The mean glucose level in the HIE group was also significantly lower (2.44±0.24 mmol/L) than in the control group (5.76±0.13 mmol/L, $p<0.001$). The metabolic component of blood pH (HCO3), indicative of buffer system and metabolic function, was reduced in the HIE group (19.8±0.2 mmol/L, $p<0.001$).

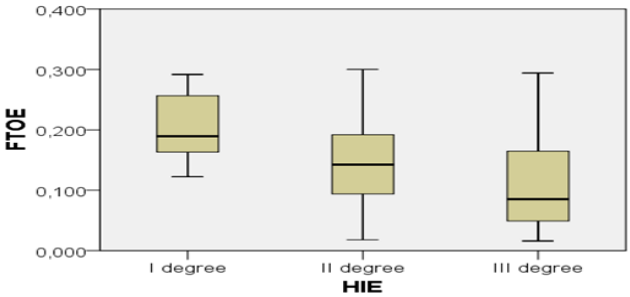
Correlation analysis revealed significant positive relationships between ABS parameters and blood electrolytes. pH showed significant positive correlations with hematocrit ($\rho=0.194$), HCO3 ($\rho=0.395$), Ca+ ($\rho=0.295$), Cl ($\rho=0.311$), and Glc ($\rho=0.464$) ($p<0.05$). pCO2 had positive correlations with hematocrit ($\rho=0.268$), sO2 ($\rho=0.319$), Ca++ ($\rho=0.489$), HCO3 ($\rho=0.594$), and Glc ($\rho=0.191$) ($p<0.05$). sO2 was significantly correlated with HCT ($\rho=0.357$), Glc ($\rho=0.277$), HCO3 ($\rho=0.220$), and Ca+ ($\rho=0.303$) ($p<0.05$). pO2 showed highly significant correlations with Ca++ ($\rho=0.454$), HCT ($\rho=0.289$), Glc ($\rho=0.508$), HCO3 ($\rho=0.292$), and sO2 ($\rho=0.318$) ($p<0.05$).

Regional cerebral oxygen saturation (rSO2) was studied in preterm neonates with HIE following perinatal asphyxia. Analysis showed no significant difference in cerebral saturation values, but fractional tissue oxygen extraction (FTOE) significantly decreased as HIE severity increased ($P<0.001$). FTOE values were higher in the 1st degree HIE group compared to the 2nd and 3rd degree groups ($P<0.05$). Neonates with fatal outcomes had lower FTOE values (0.054+0.008) compared to those with favorable outcomes (0.143) ($p<0.001$). ROC-analysis showed FTOE as the most informative parameter (AUC 0.207; $P<0.001$) with high sensitivity (87.8%) and moderate specificity (56.7%). FTOE may be a useful diagnostic tool for HIE.

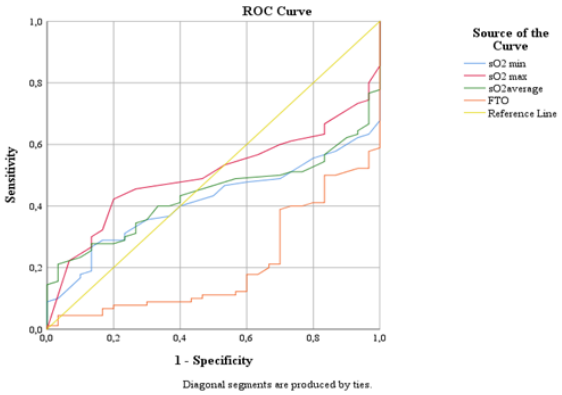


I degree II degree III degree

Picture 1. Regional cerebral oximetry depending on the severity of HIE.



Picture 2. FTOE value in neonates with HIE depending on severity.



Area Under the Curve					
	Area	SE	p	95% CI	
				Lower Bound	Upper Bound
sO_2 min	0,415	0,050	0,164	0,316	0,514
sO_2 max	0,503	0,052	0,964	0,400	0,605
sO_2average	0,437	0,050	0,304	0,338	0,536
FTOE	0,207	0,043	0,000	0,122	0,292

Picture 3. ROC curve of cerebral oximetry indices

Sn	Sp	ODV	pPV	nPV	LR+	LR-
87.8±3.5	56.7±9.0	80.0± 3.7%	85.9±3.6	60.7±9.2	2.03 posr	0.22 otl

Mortality is a key statistical indicator for analyzing healthcare activities, but forecasting it is a complex task. We developed a prognostic model for patients with hypoxic-ischemic encephalopathy

(HIE). Data analysis revealed 77 patients with favorable outcomes and 13 deaths. The logistic regression method was used to build the model, which was evaluated using a four-field contingency table, ROC analysis, and AUC. Variables selected for the model included nutrition, liver size, blood saturation (sO2), resistance index (IR), and fractional tissue oxygen extraction (FTOE).

The formula for predicting the probability of an unfavorable outcome is:

$Pp=40,836+1,008\times F-0,207\times RL-0,272\times sO_2-6,074\times İR-80,334\times FTOE$

Thus, multivariate logistic regression analysis was conducted to identify key predictors of an unfavorable prognosis. The Enter, Backward, and Forward methods in logistic regression were used to select the optimal set of variables for modeling, based on criteria such as accuracy, interpretability, and model simplicity.

Conclusion

This study highlights the significant impact of environmental, anamnestic, and clinical factors on the health outcomes of newborns with HIE. Key findings include:

- Rural residency and lower rates of operative delivery were associated with higher HIE risk. Severity of HIE correlates with specific CNS injuries, with higher degrees linked to more severe brain damage. Significant abnormalities in blood gas composition and electrolyte levels were found in HIE cases.

- Seizures were most frequent in 2nd-degree HIE, with more severe conditions seen in 3rd-degree HIE. FTOE decreased with HIE severity and was a strong predictor of outcomes. A logistic regression model, including FTOE and other parameters, effectively predicts unfavorable outcomes in HIE cases.

These findings emphasize the need for early and comprehensive monitoring to improve prognosis and guide clinical interventions for HIE.

LIST OF REFERENCES:

1. Mammadbayli, A.K. "Gender characteristics of age related mortality risk from diseases of the nervous system" //Kazan Medical jurnal 2014;95(5):703-705.
2. Arnautovic T. Neonatal Hypoxic-Ischemic Encephalopathy and Hypothermia Treatment /T.Arnautovic, S.Sinha, AR.Laptook //Obstet Gynecol. 2024 Jan;143(1):67-81.
3. She H-Q. Current analysis of hypoxic-ischemic encephalopathy research issues and future treatment modalities /H-Q She, YF Sun, L.Chen [et al.] //Front. Neurosci, 2023 Jun; 9(17):1136500.
4. Frajewicki A. Perinatal Hypoxic-Ischemic Damage: Review of the Current Treatment Possibilities /A.Frajewicki, Z.Laštůvka, V.Borbélyová [et al.] //Physiological research, 2020 Dec;31/69(3):379-401.
5. McIntyre S. et al. Neonatal encephalopathy: focus on epidemiology and underexplored aspects of etiology /S. McIntyre, KB. Nelson, SB. Mulkey [et al.] //Semin Fetal Neonatal Med., 2021 Aug;26(4):101265. 10.1016 /j.siny.2021.101265.
6. Inder TE, Volpe JJ. Hypoxic-ischemic injury in the term infant: clinical-neurological features, diagnosis, imaging, prognosis, therapy //Volpe's neurology of the newborn (Sixthe Edition), 2018; 510–63p.
7. Али-zade S.F. Characteristics and features of the health condition of preterm children with hypoxic-ischemic encephalopathy/ S.F.Али-zade, S.A.Huseynova, H.F.Aliyeva [et al.] //Topical issues of modern gynecology and perinatology - Baku: 2022;3:29-37.
8. Safarova A.Q. Electroencephalographic and magnetic resonance tomographic predictors of the effectiveness of treatment of neonatal seizures //Baku: Azerbaijan Medical Journal, 2020;3:63-69.
9. Polise O, Newberry, D.The Use of Cerebral Near-Infrared Spectroscopy in Neonatal Hypoxic-Ischemic Encephalopathy: A Systematic Review of the Literature. Adv Neonatal Care, 2023. Dec; 1/23(6):547-554. doi:10.1097/ANC.0000000000001114.
10. Chock VY. Optimal neuromonitoring techniques in neonates with hypoxic ischemic encephalopathy / VY Chock, A.Rao, KP. Van Meurs [et al.] //Fronties in Pediatrics, 2023 Mar; 8(11):1138062. doi:10.3389/fped.2023.1138062.
11. Sultanova N. S. Obesity role in development of psycho-emotional violations at children with different types of feeding //IX international Conference Sharing the Results of Research Towards Closer Global Convergence of Scientists».–Montreal. 2016; 66-68p.
12. Mamatkulov B., Avezova G. S., Adылov Sh. K. Vrojdennые poroki razvitiya u detey i osnovnые puti ix profilaktiki //Sovremennaya meditsina: novые podxodы i aktualnые issledovaniya. 2017; 75-78 str.

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