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NEUROSONOGRAPHIC FINDINGS IN TERM NEWBORNS WITH HYPOXIC-ISCHEMIC ENCEPHALOPATHY OF VARYING SEVERITY

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Objective. To describe neurosonographic findings in term newborns with hypoxic-ischemic encephalopathy (HIE) of different severity and compare the frequency of pathological neurosonography (NSG) results across clinical groups. **Material and methods.** This prospective observational study was conducted from January 1, 2024, to June 30, 2025, and included 58 term newborns: 27 with mild, 22 with moderate, and nine with severe HIE. NSG was performed on days 3–5 through the anterior fontanelle in sagittal and coronal planes. Clinical characteristics and ultrasound findings were summarized descriptively. Overall means and standard deviations were reconstructed from group-level aggregate data. Pathological-result frequencies were compared using exact tests; pairwise comparisons were adjusted using the Holm method. Wilson 95% confidence intervals (CIs) were calculated for the main proportions. **Results.** Mean gestational age was 38.84±1.24 weeks and mean birth weight was 3.48±0.71 kg. Participants included 26 boys and 32 girls. Pathological NSG results were recorded in 30/58 newborns (51.7%; 95% CI 39.2–64.1%): 7/27 (25.9%) with mild, 14/22 (63.6%) with moderate, and 9/9 (100%) with severe HIE. The overall group difference was significant (p=0.0001). After Holm adjustment, the mild-versus-moderate (p=0.0210) and mild-versus-severe (p=0.0004) comparisons remained significant; the moderate-versus-severe comparison did not reach the 0.05 threshold (p=0.0677). Moderate periventricular echogenicity was recorded in 6/27 newborns (22.2%) in the mild group. In the moderate group, focal white-matter echogenicity was recorded in 9/22 (40.9%) and cortical sulcal effacement in 10/22 (45.5%). In the severe group, heterogeneous hypoechoic echostructure was recorded in 5/9 (55.6%) and ventricular-system deformation in 3/9 (33.3%). **Conclusion.** Recorded NSG findings differed across clinical groups. The practical contribution is a structured description of early ultrasound findings. Small sample size, incomplete reporting of individual findings, and unavailable long-term outcomes limit conclusions about diagnostic specificity and prognostic value.

Keywords: term newborns, hypoxic-ischemic encephalopathy, neurosonography, perinatal asphyxia, echogenicity, neonatal period

Introduction. Hypoxic-ischemic encephalopathy (HIE) remains a significant cause of neonatal morbidity, mortality, and adverse neurological outcomes in term newborns. It develops following impaired cerebral oxygenation and perfusion around the time of birth and may result in a wide spectrum of neurological manifestations, ranging from transient abnormalities to severe encephalopathy with long-term neurodevelopmental consequences. The clinical course and response to neuroprotective interventions may vary considerably depending on the severity of the hypoxic-ischemic insult, timing of treatment, and the overall clinical context. Concomitant infectious and inflammatory processes may also modify the presentation and course of neonatal encephalopathy and should therefore be considered during clinical assessment [1, 2].

Early recognition and accurate assessment of brain injury are important for determining the severity of HIE, selecting appropriate management strategies, monitoring clinical progression, and counseling parents regarding potential outcomes. Clinical examination and neurological staging remain central components of assessment; however, imaging and neurophysiological investigations provide additional information regarding the extent and characteristics of cerebral involvement [3, 4].

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Because brain injury may evolve during the first days after the hypoxic-ischemic event, early imaging can contribute to the identification of structural abnormalities that may not be apparent from clinical examination alone.

Neurosonography (NSG) is a widely accessible, non-invasive, bedside imaging method that can be repeatedly performed in newborns through the open fontanelle. It allows assessment of cerebral parenchymal echogenicity, the ventricular system, periventricular regions, cortical structures, and other gross structural abnormalities without exposing the infant to ionizing radiation or requiring transportation outside the neonatal intensive care unit. These characteristics make NSG particularly useful in critically ill or clinically unstable newborns [5, 6].

Magnetic resonance imaging (MRI) provides more detailed characterization of hypoxic-ischemic brain injury and remains an important neuroimaging modality in neonatal encephalopathy. Nevertheless, MRI may not always be immediately available and may require transportation, monitoring, and additional organizational resources. In this context, NSG can serve as a practical complementary method for early bedside evaluation and serial assessment, particularly during the first days of life [5, 6].

The diagnostic utility of cranial ultrasound has also been extensively studied in preterm infants, in whom it is routinely used for the detection and follow-up of intracranial and periventricular abnormalities [7, 8]. However, patterns of brain injury and the anatomical vulnerability of the developing brain differ between preterm and term newborns. Therefore, findings derived from preterm populations cannot be directly extrapolated to term infants with HIE, highlighting the need for studies specifically evaluating neurosonographic changes in term newborns according to clinical severity.

The aim of the study was to describe NSG changes in term newborns with HIE of varying severity and to compare the frequency of pathological NSG findings between the clinical groups.

Material and methods. *Design and participants.* The prospective observational study included 58 term newborns and was conducted from January 1, 2024 to June 30, 2025 at the Research Institute of Obstetrics and Gynecology.

The inclusion criteria were: term newborns with perinatal asphyxia admitted to the neonatal intensive care unit; inability to initiate and maintain breathing at birth; moderate asphyxia manifested by slow gasping respiration or an Apgar score of 4–6 at the 1st minute of life, and severe asphyxia manifested by absence of breathing or a score of 0–3 at the 1st minute of life; a history of difficult delivery with weak or absent crying immediately after birth (in cases where newborns were referred to the neonatal intensive care unit and the Apgar score was unavailable). Exclusion criteria were: brain injury caused by metabolic disorders, cerebral dysgenesis, infections, hyperbilirubinemia; newborns with life-threatening congenital malformations; birth-related head trauma due to assisted or forced delivery, or any other condition causing head injury; newborns with vitamin K deficiency, thrombocytopenia, or thrombotic events (e.g., sinovenous thrombosis, etc.).

Informed consent was obtained from the parents after explanation of the procedure. Sex, birth weight, mode of delivery, maternal risk factors, presence of meconium, Apgar scores at the 1st and 5th minutes, neurological signs, duration of hospitalization, and the infant's condition at discharge were recorded.

Clinical assessment and neurosonography. Newborns were divided into groups with mild (n=27), moderate (n=22), and severe (n=9) HIE. The clinical classification of HIE severity and the ultrasound description of injuries should be considered separately; the Sarnat scale is one of the approaches used for clinical assessment [9].

NSG was performed on days 3–5 of life through the anterior fontanelle in sagittal and coronal planes. The Papile classification is applicable to the classification of hemorrhages rather than to the entire spectrum of HIE-related changes; in the present report, individual grades of hemorrhage were not analyzed [10].

Statistical analysis. In the original study, statistical analysis was performed using IBM SPSS Statistics for Windows, version 21.0 (IBM Corp., Armonk, NY). In the present revision, a reanalysis of the aggregated data reported in the manuscript was performed using Python and SciPy. Quantitative variables are presented as mean ± standard deviation (SD), and categorical variables as n (%). Overall means and SDs were reconstructed from the sample sizes, means, and SDs of the three groups, taking into account within-group and between-group variation. The calculations assume that the reported sample sizes apply to all corresponding variables and that "±" in the original table denotes SD. The original individual-level data were unavailable for verification of distributions, missing data, and calculation of medians.

For the main proportions, 95% confidence intervals (CIs) were calculated using the Wilson method. The overall difference in the frequency of pathological NSG findings among the three groups was assessed using the Fisher–Freeman–Halton exact test for a 2×3 table with a two-sided p value based on table probabilities. Pairwise comparisons were performed using the two-sided Fisher exact test with Holm correction for three comparisons. Between-group comparisons of mean Apgar scores and duration of hospitalization were performed using Welch's t-test based on aggregated data; for each outcome, a separate Holm correction for three comparisons was applied. These parametric comparisons are exploratory; the validity of their assumptions cannot be verified using summary data. The threshold for statistical significance after correction was 0.05.

Individual NSG findings are presented descriptively: the absence of information on a particular finding in a group was not equated with a zero frequency. Statistical comparisons of different ultrasound findings between groups were not performed. Duration of mechanical ventilation in mild HIE is not presented because of inconsistency in the original data.

The study was approved by the Ethics Committee of the Research Institute of Obstetrics and Gynecology, protocol No. 2023/7.

Results. *Participant characteristics.* The study included 58 newborns: 27 (46.6%) with mild, 22 (37.9%) with moderate, and 9 (15.5%) with severe HIE. Among the participants, 26 were boys (44.8%) and 32 were girls (55.2%); 22 infants (37.9%) were delivered by cesarean section. The mean gestational age reconstructed from the group data was 38.84±1.24 weeks, birth weight was 3.48±0.71 kg, and Apgar scores at the 1st and 5th minutes were 5.73±1.58 and 7.38±1.08, respectively. Group characteristics are presented in Table 1.

Table 1.

Clinical and demographic characteristics of the newborns

Parameter	Total (n=58)	Mild HIE (n=27)	Moderate HIE (n=22)	Severe HIE (n=9)
Gestational age, weeks	38.84±1.24	38.0±1.14	39.4±0.78	40.0±0.65
Birth weight, kg	3.48±0.71	3.5±0.48	3.5±0.82	3.4±1.02
Apgar score at 1 minute, points	5.73±1.58	7.2±0.64	4.6±1.0	4.1±0.38
Apgar score at 5 minutes, points	7.38±1.08	8.4±0.46	6.6±0.55	6.2±0.24
Length of hospitalization, days	14.19±4.55	9.5±0.5	17.56±1.02	20.0±0.47
Male sex, n (%)	26 (44.8)	12 (44.4)	8 (36.4)	6 (66.7)
Cesarean delivery, n (%)	22 (37.9)	9 (33.3)	7 (31.8)	6 (66.7)
Suspected clinical seizures, n (%)	34 (58.6)	14 (51.9)	13 (59.1)	7 (77.8)
Seizures confirmed by aEEG/EEG, n (%)	21 (36.2)	6 (22.2)	9 (40.9)	6 (66.7)
Vasopressor use, n (%)	19 (32.8)	8 (29.6)	7 (31.8)	4 (44.4)
Mechanical ventilation, n (%)	27 (46.6)	0 (0.0)	18 (81.8)	9 (100.0)
Duration of mechanical ventilation, days	ND	—	5.0±1.76	5.0±0.88

Note. HIE — hypoxic-ischemic encephalopathy; mechanical ventilation refers to invasive mechanical ventilation; aEEG — amplitude-integrated electroencephalography; EEG — electroencephalography; ND — insufficient data; — value not reported. Quantitative data are presented as mean±SD; categorical data as n (%), with the denominator corresponding to the size of each group. Overall means and SDs were reconstructed from aggregated data. Information regarding the denominator for the duration of mechanical ventilation and the extent of EEG monitoring requires confirmation.

Apgar score at 1 minute: mild vs moderate HIE: t=10.56, df=34.3, Holm-adjusted p<0.001; mild vs severe HIE: t=17.55, df=23.7, Holm-adjusted p<0.001; moderate vs severe HIE: t=2.02, df=29.0, Holm-adjusted p=0.053. Comparisons were calculated from group means and SDs.

Apgar score at 5 minutes: mild vs moderate HIE: t=12.25, df=41.0, Holm-adjusted p<0.001; mild vs severe HIE: t=18.44, df=27.1, Holm-adjusted p<0.001; moderate vs severe HIE: t=2.82, df=28.7, Holm-adjusted p=0.009. Comparisons were calculated from group means and SDs.

Length of hospitalization: mild vs moderate HIE: t=33.89, df=29.1, Holm-adjusted p<0.001; mild vs severe HIE: t=57.11, df=14.5, Holm-adjusted p<0.001; moderate vs severe HIE: t=9.10, df=28.4, Holm-adjusted p<0.001. Comparisons were calculated from group means and SDs.

Neurosonographic findings. Pathological NSG findings were recorded in 30/58 infants (51.7%; 95% CI 39.2–64.1%). In the mild group, pathological findings were observed in 7/27 infants (25.9%; 95% CI 13.2–44.7%), in the moderate group in 14/22 (63.6%; 95% CI 43.0–80.3%), and in the severe group in 9/9 (100%; 95% CI 70.1–100%). The overall difference among the groups was statistically significant (Fisher–Freeman–Halton exact test, p=0.0001).

Table 2.

Neurosonographic findings in the clinical groups

Finding	Mild HIE (n=27)	Moderate HIE (n=22)	Severe HIE (n=9)
Any pathological NSG finding	7 (25.9)	14 (63.6)	9 (100)
Moderate periventricular hyperechogenicity	6 (22.2)	ND	ND
Mild parenchymal edema	1 (3.7)	ND	ND
Marked focal white-matter hyperechogenicity	ND	9 (40.9)	ND
Narrowing of the ventricular cavities	ND	7 (31.8)	ND
Poor definition of the vascular pattern and sulcal effacement	ND	10 (45.5)	ND
Subependymal cysts or transient ischemic foci	ND	8 (36.4)	ND
Heterogeneous hyperechoic echostructure	ND	ND	4 (44.4)
Heterogeneous hypoechoic echostructure	ND	ND	5 (55.6)
Deformation of the ventricular system	ND	ND	3 (33.3)

Note. HIE — hypoxic-ischemic encephalopathy; NSG — neurosonography; ND — data on this finding were not reported for the corresponding group. ND does not indicate absence of the finding. In the mild HIE group, hyperechogenicity was observed in 6 infants, while edema was observed in one different infant. In the other groups, multiple findings could occur in the same infant; therefore, the sum of the frequencies of individual findings does not correspond to the number of infants with any pathological NSG finding.

Table 3.

Pairwise comparisons of the frequency of pathological NSG findings

Comparison	p, Fisher's exact test	Holm-adjusted p
Mild vs moderate HIE	0.0105	0.0210
Mild vs severe HIE	0.0001	0.0004
Moderate vs severe HIE	0.0677	0.0677

Note. All tests were two-sided; the Holm correction was applied to three pairwise comparisons of the frequency of the same outcome — any pathological NSG finding.

After Holm adjustment, the differences between mild and moderate HIE, as well as between mild and severe HIE, remained statistically significant. In the mild group, moderate periventricular hyperechogenicity was observed in 6 infants (22.2%). In the moderate group, the most frequently reported findings were poor definition of the vascular pattern and sulcal effacement (10 infants; 45.5%). In the severe group, a heterogeneous hypoechoic echostructure was observed in 5 infants (55.6%), a heterogeneous hyperechoic echostructure in 4 (44.4%), and deformation of the ventricular system in 3 (33.3%). Intergroup comparisons of individual findings were not performed because of incomplete reporting.

Discussion. In this study, the proportion of pathological NSG findings was higher in the severe HIE group than in the mild HIE group. After accounting for the three pairwise comparisons, statistically significant differences remained between the mild and moderate groups and between the mild and severe groups; the difference between the moderate and severe groups did not reach statistical significance. Lack of statistical significance does not prove equivalence between the groups; the small sample size and wide CIs limit the precision of the estimates.

Ultrasound findings included changes in echogenicity, signs of edema, and deformation of the ventricular system. These observations are consistent with the diversity of neurosonographic findings described in the literature [11, 12]. However, the structure of the original reporting does not allow the prevalence of each finding to be determined across all three groups. Therefore, the observed findings cannot be considered proven to be specific to a particular severity of HIE.

Comprehensive assessment of newborns with encephalopathy requires integration of the clinical condition, neurophysiological data, and imaging findings [13–16]. NSG may be used for accessible early structural assessment, but sensitivity, specificity, and prognostic accuracy of the method were not determined in the present study. Quantitative assessment of echogenicity represents a promising direction for further research [17].

Differences between clinical groups are not equivalent to the evolution of injury within an individual infant. In the absence of repeated examinations, MRI correlation, and long-term follow-up, the present results do not confirm irreversibility of the changes, necrosis, hemodynamic decompensation, or an association between individual NSG findings and subsequent neurological outcomes. The practical value of the study lies in the description of early findings and in supporting the need for standardized recording of the same findings across all groups.

Limitations. The sample included 58 newborns, of whom only 9 had severe HIE; this limits the precision of the estimates and the generalizability of the findings. Individual ultrasound findings were not reported for all clinical groups. Information on standardization of the clinical classification, investigator blinding, EEG coverage, missing data, and treatments used requires clarification. The manuscript does not present MRI correlation or long-term neurological outcomes. Overall means, SDs, and statistical comparisons in this revision were reconstructed from rounded aggregate data; medians, interquartile ranges, distributions, and potential confounding factors could not be assessed. Parametric comparisons of Apgar scores, which are based on a discrete scale, require cautious interpretation and verification using individual-level data. The analysis is exploratory and does not establish the diagnostic or prognostic accuracy of NSG.

Conclusion. Different NSG findings were described in term newborns with HIE of varying

severity. The frequency of any pathological NSG finding was 25.9% in mild HIE, 63.6% in moderate HIE, and 100% in severe HIE; after Holm adjustment, statistically significant differences remained between the mild and moderate groups and between the mild and severe groups. The findings systematize early ultrasound changes but do not confirm the specificity of individual findings or their prognostic value. Further evaluation requires standardized recording of findings, complete data across all groups, and correlation with subsequent clinical outcomes.

Conflict of interest. The authors declare no conflict of interest.

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XÜLASƏ

MÜXTƏLİF AĞIRLIQ DƏRƏCƏLİ HİPOKSİK-İŞEMİK ENSEFALOPATİYASI OLAN VAXTINDA DOĞULMUŞ YENİDOĞULMUŞLARDA NEYROSONOQRAFİYA NƏTİCƏLƏRİ

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Məqsəd. Müxtəlif ağırlıq dərəcəli hipoksik-işemik ensefalopatiyası (HİE) olan vaxtında doğulmuş yenidoğulmuşlarda neyrosonoqrafik dəyişiklikləri təsvir etmək və klinik qruplar arasında patoloji neyrosonoqrafiya (NSQ) nəticələrinin tezliyini müqayisə etmək. **Material və metodlar.** Prospektiv müşahidə tədqiqatı 1 yanvar 2024-cü ildən 30 iyun 2025-ci ilədək aparılmış və 58 vaxtında doğulmuş yenidoğulmuşu əhatə etmişdir: 27 yüngül, 22 orta və 9 ağır dərəcəli HİE. NSQ həyatın 3–5-ci günlərində ön əmgək vasitəsilə sagittal və koronal müstəvilərdə aparılmışdır. Klinik xüsusiyyətlər və ultrasəs əlamətləri təsviri şəkildə təqdim edilmişdir. Ümumi orta göstəricilər və standart kənarlaşmalar qrupların aqreqat məlumatlarından yenidən hesablanmışdır. Patoloji nəticələrin tezliyi dəqiq testlərlə müqayisə edilmiş, cüt müqayisələrə Holm düzəlişi tətbiq olunmuşdur. Əsas paylar üçün Wilson üsulu ilə 95% etibar intervalları (Eİ) hesablanmışdır. **Nəticələr.** Orta gestasiya yaşı 38,84±1,24 həftə, doğum çəkisi 3,48±0,71 kq olmuşdur. İştirakçılardan 26-sı oğlan, 32-si qız idi. Patoloji NSQ nəticələri 30/58 uşaqda qeydə alınmışdır (51,7%; 95% Eİ 39,2–64,1%): yüngül HİE-də 7/27 (25,9%), orta HİE-də 14/22 (63,6%), ağır HİE-də 9/9 (100%). Qruplar arasında ümumi fərq statistik əhəmiyyətli olmuşdur (p=0,0001). Holm düzəlişindən sonra yüngül və orta (p=0,0210), həmçinin yüngül və ağır HİE qrupları arasındakı fərqlər (p=0,0004) statistik əhəmiyyətli qalmışdır; orta və ağır qruplar arasındakı fərq statistik əhəmiyyətli olmamışdır (p=0,0677). Yüngül qrupda periventrikulyar exogenliyin mülayim artması 6/27 uşaqda (22,2%) qeydə alınmışdır. Orta qrupda ağ maddənin lokal exogenlik artımı 9/22 (40,9%), kortikal şırımların hamarlaşması 10/22 (45,5%) uşaqda müşahidə edilmişdir. Ağır qrupda qeyri-bircins hipoexogen struktur 5/9 (55,6%), mədəcik sisteminin deformasiyası 3/9 (33,3%) uşaqda aşkarlanmışdır. **Yekun.** Təsvir edilən NSQ tapıntıları klinik qruplar arasında fərqlənmişdir. Tədqiqatın praktik əhəmiyyəti erkən ultrasəs dəyişikliklərinin sistemləşdirilməsidir. Seçmənin kiçik həcmi, ayrı-ayrı əlamətlər üzrə məlumatların natamamlığı və uzunmüddətli nəticələrin təqdim edilməməsi NSQ-nin diaqnostik spesifikliyi və proqnostik dəyəri barədə nəticələri məhdudlaşdırır.

Açar sözlər: vaxtında doğulmuş yenidoğulmuşlar, hipoksik-işemik ensefalopatiya, neyrosonoqrafiya, perinatal asfiksiya, exogenlik, neonatal dövr

РЕЗЮМЕ

РЕЗУЛЬТАТЫ НЕЙРОСОНОГРАФИИ У ДОНОШЕННЫХ НОВОРОЖДЕННЫХ С ГИПОКСИЧЕСКИ-ИШЕМИЧЕСКОЙ ЭНЦЕФАЛОПАТИЕЙ РАЗЛИЧНОЙ ТЯЖЕСТИ

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Цель. Описать нейросонографические изменения у доношенных новорожденных с гипоксически-ишемической энцефалопатией (ГИЭ) различной тяжести и сопоставить частоту патологических

результатов нейросонографии (НСГ) между клиническими группами. **Материал и методы.** Проспективное наблюдательное исследование проводилось с 1 января 2024 года по 30 июня 2025 года и включало 58 доношенных новорожденных: 27 с легкой, 22 с умеренной и 9 с тяжелой ГИЭ. НСГ выполняли на 3–5-й день жизни через передний родничок в сагиттальной и корональной плоскостях. Клинические характеристики и ультразвуковые признаки представлены описательно. Общие средние и стандартные отклонения пересчитаны по групповым агрегированным данным. Частоты патологических результатов сравнивали точными тестами; попарные сравнения корректировали методом Холма. Для основных долей рассчитаны 95% доверительные интервалы (ДИ) методом Уилсона. **Результаты.** Средний гестационный возраст составил 38,84±1,24 недели, масса при рождении — 3,48±0,71 кг. Среди участников были 26 мальчиков и 32 девочки. Патологические результаты НСГ отмечены у 30/58 детей (51,7%; 95% ДИ 39,2–64,1%): при легкой ГИЭ — у 7/27 (25,9%), умеренной — у 14/22 (63,6%), тяжелой — у 9/9 (100%). Общая межгрупповая разница была статистически значимой (p=0,0001). После поправки Холма значимыми оставались различия между легкой и умеренной ГИЭ (p=0,0210), а также между легкой и тяжелой ГИЭ (p=0,0004); различие между умеренной и тяжелой ГИЭ не достигало порога 0,05 (p=0,0677). В легкой группе умеренное повышение перивентрикулярной эхогенности отмечено у 6/27 детей (22,2%). В умеренной группе локальное повышение эхогенности белого вещества выявлено у 9/22 (40,9%), сглаженность корковых бороздок — у 10/22 (45,5%). В тяжелой группе неоднородная гипоэхогенная эхоструктура отмечена у 5/9 (55,6%), деформация желудочковой системы — у 3/9 (33,3%). **Заключение.** Описанные НСГ-находки различались между клиническими группами. Практическое значение исследования состоит в систематизации ранних ультразвуковых изменений. Небольшой объем выборки, неполные сведения по отдельным признакам и отсутствие представленных долгосрочных исходов ограничивают выводы о диагностической специфичности и прогностической ценности НСГ.

Ключевые слова: доношенные новорожденные, гипоксически-ишемическая энцефалопатия, нейросонография, перинатальная асфиксия, эхогенность, неонатальный период

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