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Research

Cranial Magnetic Resonance Imaging Findings in Neonates with Mild Hypoxic-Ischemic Encephalopathy (Sarnat Stage I): A Retrospective Cohort Study

Hafif Hipoksik-İskemik Ensefalopati (Sarnat Evre I) olan Yenidoğanlarda Kraniyal Manyetik Rezonans Görüntüleme Bulguları: Retrospektif Kohort Çalışması

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ABSTRACT

Objective: Perinatal asphyxia is among the leading causes of morbidity in the newborn period and can give rise to hypoxic-ischemic encephalopathy (HIE). While therapeutic hypothermia is well established for moderate-to-severe HIE, the optimal management of infants with mild HIE—Sarnat stage I—remains controversial. What is becoming increasingly clear, however, is that a mild HIE may not always be a benign condition and that subtle brain injury may be present even with a mild clinical presentation. We aimed to evaluate cranial magnetic resonance imaging (MRI) findings in newborns with perinatal asphyxia classified as Sarnat stage I and to explore whether infants with normal versus abnormal imaging differ in their clinical presentation or laboratory markers.

Methods: We conducted a retrospective cohort study of newborns admitted to our neonatal intensive care unit with perinatal asphyxia who met the criteria for Sarnat stage I HIE. Demographic data, Apgar scores, umbilical cord blood gas values, maternal risk factors, and neuroimaging results were recorded. Cranial MRI scans were classified as normal or abnormal, and the two groups were compared.

Results: Sixty-six neonates were enrolled. MRI was normal in 54 (81.8%) patients and abnormal in 12 (18.2%) patients. Infants in the abnormal group tended to have lower Apgar scores and more pronounced metabolic acidosis, although neither difference reached statistical significance. The most common abnormal findings were hemorrhagic in nature-subdural, intraventricular, and parenchymal hemorrhages each accounted for a third of abnormal scans.

Conclusion: Nearly one-fifth of neonates with mild HIE demonstrated abnormal cranial MRI findings. Closer follow-up may be considered, since mild HIE may be associated with subclinical brain injury.

Keywords: Cranial MRI, hypoxic-ischemic encephalopathy, intracranial hemorrhage, perinatal asphyxia

ÖZ

Amaç: Perinatal asfiksi, yenidoğan döneminde morbiditenin önde gelen nedenlerinden biridir ve hipoksik-iskemik ensefalopatiye (HİE) yol açabilir. Orta ve ağır HİE için terapötik hipotermi iyi tanımlanmış bir tedavi yaklaşımıdır; ancak hafif HİE (Sarnat evre I) olan bebeklerin optimal yönetimi halen tartışmalıdır. Bununla birlikte giderek daha net anlaşılmaktadır ki hafif HİE her zaman benign bir durum değildir ve klinik olarak hafif seyretse bile altta yatan ince (subklinik) beyin hasarı bulunabilir. Bu çalışmada, perinatal asfiksiye bağlı Sarnat evre I HİE tanısı alan yenidoğanlarda kraniyal manyetik rezonans görüntüleme (MRG) bulgularını değerlendirmeyi ve MRG'si normal olanlar ile anormal olanlar arasında klinik ve laboratuvar özellikler açısından fark olup olmadığını araştırmayı amaçladık.

Gereç ve Yöntem: Yenidoğan yoğun bakım ünitemize yatırılan, perinatal asfiksi öyküsü olan ve Sarnat evre I HİE kriterlerini karşılayan bebeklerin dahil edildiği retrospektif bir kohort çalışması yürütüldü. Demografik veriler, Apgar skorları, umbilikal kord kan gazı değerleri, maternal risk faktörleri ve nörogörüntüleme sonuçları kaydedildi. Kraniyal MRG bulguları normal ve anormal olarak sınıflandırıldı ve iki grup karşılaştırıldı.

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ÖZ

Bulgular: Toplam 66 yenidoğan çalışmaya dahil edildi. MRG bulguları 54 (%81,8) hastada normal, 12 (%18,2) hastada anormal olarak saptandı. Anormal MRG grubundaki bebeklerde daha düşük Apgar skorları ve daha belirgin metabolik asidoz eğilimi gözlenmekle birlikte, bu farklar istatistiksel olarak anlamlı değildi. En sık saptanan anormallikler hemorajik nitelikte olup; subdural, intraventriküler ve parankimal kanamalar anormal MRG bulgularının her biri yaklaşık üçte birini oluşturdu.

Sonuç: Hafif HİE tanısı alan yenidoğanların yaklaşık beşte birinde kraniyal MRG'de anormal bulgular saptanmıştır. Hafif HİE'nin subklinik beyin hasarı ile ilişkili olabileceği göz önünde bulundurularak bu hastaların daha yakın izlenmesi düşünülebilir.

Anahtar Kelimeler: Beyin MRG, hipoksik-iskemik ensefalopati, intrakraniyal kanama, perinatal asfiksi

INTRODUCTION

Perinatal asphyxia remains one of the emerging problems in the neonatal period-responsible for about a quarter of all neonatal deaths and disproportionately affecting low- and middle-income settings. It is characterized by a failure of gas exchange and a cascade of hypoxemia, hypercapnia, and metabolic acidosis that can ultimately injure multiple organ systems, including the brain. Despite advances in perinatal care over recent decades, asphyxia continues to drive a substantial share of neonatal mortality and long-term neurodevelopmental disability (1-3).

Hypoxic-ischemic encephalopathy (HIE) represents the neurological manifestation of perinatal asphyxia and is graded using the Sarnat staging system (4). For moderate-to-severe disease (Sarnat stage II-III), therapeutic hypothermia is the standard treatment for neonates (5). The management of mild hypoxic-ischemic encephalopathy remains controversial, as emerging data suggest that a subset of these infants may still develop neurodevelopmental impairment (6). Current guidelines do not recommend routine hypothermia for mild HIE due to insufficient evidence regarding long term benefit, although emerging data suggest that a subset of these infants may still be at risk for adverse neurodevelopmental outcomes (7,8).

Neuroimaging, particularly cranial magnetic resonance imaging (MRI), plays a critical role in the evaluation of hypoxic-ischemic brain injury. MRI is considered the most sensitive modality for detecting hypoxic-ischemic brain injury and identifying characteristic injury patterns associated with perinatal asphyxia, including white matter injury, basal ganglia-thalamic involvement, and hemorrhagic lesions (9-12). However, the prognostic value of MRI in infants with mild HIE remains less well defined, and normal early neuroimaging does not necessarily exclude later neurodevelopmental impairment (8).

The aim of this retrospective observational study was to evaluate cranial MRI findings in neonates with perinatal asphyxia classified as Sarnat stage I and to compare clinical and laboratory characteristics between infants with normal and abnormal MRI findings, particularly focusing on the presence of intracranial hemorrhage (ICH) on early MRI.

METHODS

Ethics Committee and Patient Consent

This single-center retrospective study was conducted in accordance with the Declaration of Helsinki. This study was approved by the University of Health Sciences Türkiye, Haseki Training and Research Hospital Non-Interventional Ethics Committee (approval no: 34-2026, date: 25.02.2026). Due to the retrospective design and the use of anonymized data, informed consent procedures were addressed in accordance with institutional policies and ICMJE requirements. The study was performed in accordance with the Declaration of Helsinki.

Study Design and Population

This cohort study was carried out in the Neonatal Intensive Care Unit of University of Health Sciences Türkiye, Haseki Training and Research Hospital. We reviewed the medical records of all newborns admitted between March 2022 and March 2026 who had a diagnosis of perinatal asphyxia.

Infants were eligible if they were born at or after 28 weeks of gestation and showed evidence of perinatal asphyxia, defined as an umbilical cord or first-hour arterial blood gas pH ≤7.10 and/or base excess ≤-12 mmol/L. In addition, they were required to be classified as Sarnat stage I (mild HIE) on clinical examination, to have a normal amplitude-integrated electroencephalography (aEEG) tracing, and to show no indication for therapeutic hypothermia under our unit's protocol.

We excluded infants with moderate or severe HIE (Sarnat stage II-III) requiring therapeutic hypothermia, major congenital anomalies or chromosomal abnormalities, inborn errors of metabolism, incomplete clinical or imaging records, and gestational age below 28 weeks.

From each medical record, we extracted demographic information (gestational age, birth weight, sex), perinatal details (mode of delivery, 1- and 5-minute Apgar scores, maternal risk factors including placental abruption, preeclampsia, gestational hypertension, and diabetes), laboratory values (umbilical cord pH, base excess, lactate, bicarbonate, and pCO_2), and neuroimaging results from cranial MRI and aEEG.

Cord Blood Gas Analysis

After the umbilical cord was clamped for the first time at 30-40 seconds of life, the newborn was transferred to the attending pediatrician or nurse. A second clamp was then placed roughly 4-5 cm from the umbilicus, and 1 mL of blood was drawn into Sarstedt Monovette lithium heparin tubes. Samples were analyzed without delay on Siemens Rapidlab 1265 analyzers.

Neuroimaging Evaluation

All MRI examinations were performed within the first 7 days of life using a 1.5-T Philips system. (Intera 1.5 T; Healthcare, Best, The Netherlands). Sagittal T1-weighted images (T_R=450-550 ms; T_E=15-30 ms; slice thickness=5 mm) and axial T2-weighted images (T_R=3,000-3,150 ms; T_E=150 ms; slice thickness=2-5 mm) were acquired.

Because of the study's retrospective design, MRI acquisition was not fully standardized across all patients. In particular, advanced sequences such as diffusion-weighted imaging (DWI)—which is highly sensitive for detecting acute hypoxic-ischemic injury—were not routinely performed on all infants. Similarly, susceptibility-weighted imaging (SWI) was obtained when clinically indicated rather than as part of a uniform imaging protocol.

This variability in imaging sequences may have limited detection of subtle ischemic lesions and should therefore be considered when interpreting the frequency and pattern of MRI abnormalities in this cohort.

The average imaging time was approximately 30 minutes. A neonatologist was present throughout the procedure and administered bolus midazolam sedation if needed.

Neonatal ICH was assessed on SWI and T1-weighted images. ICH was categorized into five subtypes: subdural, subarachnoid, germinal matrix, intraventricular, and parenchymal hemorrhage (11). MRI findings were reported by experienced radiologists. Because of the retrospective design, formal inter-rater reliability testing was not feasible-a limitation we acknowledge.

Amplitude-Integrated Electroencephalography

All enrolled neonates underwent continuous neurological monitoring with aEEG during the first 24 hours of life. Two-channel recordings were routinely obtained for any infant admitted with perinatal asphyxia or neurological concern—including a 5-minute Apgar score below 5, cord pH below 7.10, multiorgan failure, or clinical seizures—both to characterize the background pattern and to help detect subclinical seizure activity. A normal aEEG background was defined as a continuous or discontinuous normal-voltage pattern.

Statistical Analysis

All analyses were performed with IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). Before selecting tests, we assessed the distribution of continuous variables using histogram inspection and the Shapiro-Wilk test. Variables with a normal distribution are reported as mean±standard deviation; those with a non-normal distribution are reported as median and interquartile range (IQR). Categorical data are presented as counts and percentages.

Group comparisons between infants with normal and abnormal MRI were performed using Student's t-test for normally distributed continuous variables and the Mann-Whitney U test for non-normally distributed variables. Categorical variables were compared using either the chi-square test or Fisher's exact test, depending on expected cell counts.

We also performed a multivariable logistic regression analysis to identify independent predictors of abnormal MRI. With only 12 outcome events and seven predictor variables, the event-per-variable ratio was approximately 1.7-well short of the conventional threshold of 10. These results should therefore be taken as exploratory and interpreted with appropriate caution. All tests were two-tailed; a p-value below 0.05 was considered statistically significant.

RESULTS

General Characteristics of the Study Population

Sixty-six neonates with perinatal asphyxia who were classified as Sarnat stage I HIE were included in the analysis. Mean gestational age was 37.1±2.9 weeks (range: 30-41.6 weeks), and mean birth weight was 2844±801 g (range: 1100-4120 g). Most infants were male (63.6%; n=42). Delivery was by cesarean section in 59.1% (n=39) and by vaginal delivery in 40.9% (n=27). The median 1-minute Apgar score was 6 (IQR: 4-7), rising to 7.5 (IQR: 6-8) at five minutes.

Cord blood gas values reflected the expected degree of metabolic acidosis. Mean umbilical cord pH was 7.02±0.10, base excess -14.1±3.7 mmol/L, lactate 8.7±3.4 mmol/L, bicarbonate 14.0±3.2 mmol/L, and pCO_2 69.9±16.6 mmHg. The full clinical characteristics are presented in Table 1.

A maternal risk factor was identified in 45.5% of pregnancies. Placental abruption was the most common (18.2%), followed by gestational hypertension (7.6%) and preeclampsia (6.1%). In just over half of cases (54.5%), no maternal risk factor was documented.

Comparison Between Neonates with Normal and Abnormal MRI Findings

Cranial MRI was normal in 54 infants (81.8%) and abnormal in the remaining 12 (18.2%). Infants with abnormal MRI findings tended to be slightly younger (36.1±3.5 vs. 37.4±2.7 weeks; p=0.18) and lighter at birth (2630±890 vs. 2890±780 g; p=0.24), though neither difference was statistically significant. Males were somewhat more common in the abnormal MRI group (75.0% vs. 61.1%; p=0.36).

Apgar scores at both time points were lower in the abnormal MRI group. At one minute, the median was 5 (IQR: 3-6) compared with 6 (IQR: 4-7) in those with normal scans. At five minutes, median scores were 7 (IQR: 6-7) and 8 (IQR: 7-8), respectively (p=0.19 for both comparisons).

Biochemical markers also indicated the same trend. Mean cord pH was 6.96±0.11 in the abnormal MRI group versus 7.04±0.09 in those with normal scans (p=0.13). Base excess was more negative (-16.2±4.1 vs. -13.5±3.4 mmol/L; p=0.09), and lactate levels were higher (10.1±3.9 vs. 8.2±3.1 mmol/L; p=0.08). None of these differences achieved statistical significance (all p>0.05). The full comparative dataset is presented in Table 1.

In multivariable logistic regression analysis, none of the variables examined—gestational age, birth weight, sex, 5-minute Apgar score, cord pH, base excess, or lactate—showed a statistically significant association with abnormal MRI; however, given the limited number of events, these findings should be interpreted as exploratory rather than conclusive." Full results are shown in Table 2, and a forest plot of odds ratios and their 95% confidence intervals for each predictor is presented in the Figure 1.

Among the 12 infants with abnormal scans, subdural hemorrhage, intraventricular hemorrhage, and parenchymal hemorrhage each appeared in four cases (33.3% each). Subarachnoid hemorrhage and germinal matrix hemorrhage were not identified in any infant.

DISCUSSION

In this single-center, retrospective cohort of neonates with mild HIE, most infants had normal cranial MRI findings; yet nearly one in five infants showed structural abnormalities despite being classified as Sarnat stage I, lending further support to the view that mild HIE is not a uniformly benign diagnosis.

Recent studies in this area consistently show that infants with mild HIE can present with subtle white matter injury or hemorrhagic lesions on MRI even when their clinical picture

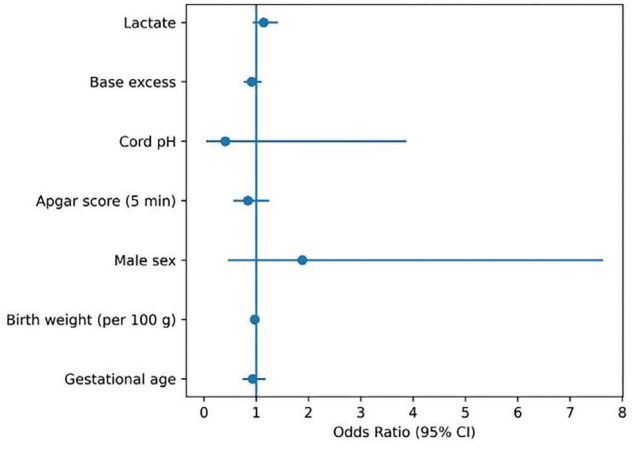

Figure 1. A forest plot showing odds ratios and 95% confidence intervals for each predictor

Table 1. Clinical and biochemical characteristics of the study population by MRI findings

Variable	All patients (n=66)	Normal MRI (n=54)	Abnormal MRI (n=12)	p-value
Gestational age (weeks), mean±SD	37.1±2.9	37.4±2.7	36.1±3.5	0.18
Birth weight (g), mean±SD	2844±801	2890±780	2630±890	0.24
Male sex, n (%)	42 (63.6)	33 (61.1)	9 (75.0)	0.36
Cesarean delivery, n (%)	39 (59.1)	31 (57.4)	8 (66.7)	0.55
Apgar score at 1 min, median (IQR)	6 (4-7)	6 (4-7)	5 (3-6)	0.21
Apgar score at 5 min, median (IQR)	7.5 (6-8)	8 (7-8)	7 (6-7)	0.19
Umbilical cord pH, mean±SD	7.02±0.10	7.04±0.09	6.96±0.11	0.13
Base excess (mmol/L), mean±SD	-14.1±3.7	-13.5±3.4	-16.2±4.1	0.09
Lactate (mmol/L), mean±SD	8.7±3.4	8.2±3.1	10.1±3.9	0.08
HCO_3 (mmol/L), mean±SD	14.0±3.2	14.3±3.1	13.2±3.4	0.27
pCO_2 (mmHg), mean±SD	69.9±16.6	68.8±15.9	74.6±18.8	0.29

Continuous variables are presented as mean±SD or median (interquartile range) depending on data distribution. Categorical variables are presented as number (percentage). Comparisons between the normal MRI and abnormal MRI groups were performed using Student's t-test or Mann-Whitney U test for continuous variables and chi-square or Fisher's exact test for categorical variables
SD: Standard deviation, MRI: Magnetic resonance imaging

Table 2. Multivariable logistic regression analysis of factors associated with abnormal MRI findings

Variable	OR	95% CI	p-value
Gestational age (per week)	0.93	0.74-1.18	0.55
Birth weight (per 100 g)	0.97	0.89-1.06	0.49
Male sex	1.88	0.46-7.63	0.38
Apgar score (5 min)	0.84	0.56-1.25	0.38
Cord pH	0.41	0.04-3.87	0.43
Base excess (per mmol/L)	0.91	0.76-1.10	0.33
Lactate (per mmol/L)	1.14	0.93-1.41	0.21

Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using multivariable logistic regression analysis. Variables included in the model were selected based on clinical relevance and univariate associations

appears reassuring (6,7). Wu et al. (8) noted that while MRI carries strong prognostic weight in moderate-to-severe disease, its predictive accuracy is appreciably lower when encephalopathy is mild.

The findings of our study—lower Apgar scores, more pronounced metabolic acidosis, and higher lactate in infants with abnormal MRI—appear to be in line with prior reportssuggesting that biochemical markers may capture the severity of cerebral injury more accurately than clinical staging alone however, these observations should be interpreted cautiously given the limited sample size and lack of statistical significance (7,10). Glass et al. (7) and Chalak et al. (6) have both drawn attention to the limited ability of the Sarnat system to identify the highest-risk infants within the mild HIE group (13). Importantly, the biochemical trends we observed are biologically coherent: lower cord pH and more negative base excess in the abnormal MRI group fit well with what we know about the pathophysiology of hypoxic-ischemic brain injury and mirror findings from earlier series that relied primarily on biochemical severity rather than on clinical scoring to gauge cerebral injury risk.

Neuroprotective pharmacotherapy remains an open and active area of research. Magnesium sulfate has been proposed as a means of limiting excitotoxic neuronal damage through N-methyl-D-aspartate receptor blockade, while allopurinol may help curb oxidative stress during reperfusion (13-15). Both agents have shown encouraging signals in experimental and early clinical work (15,16), though our study was not designed to evaluate treatment effects.

Our abnormality rate of 18.2% is notably lower than the rates reported by other groups. Li et al. (17) found brain injury on early MRI in 61% of 142 mild HIE infants, with watershed injury (23%), deep gray nuclei involvement (20%), and punctate white matter lesions (18%) being the most frequent patterns. Glass et al. (7) similarly identified MRI abnormalities in around 54% of neonates with mild neonatal encephalopathy. Several factors likely explain the difference in our cohort: stricter application of Sarnat stage I criteria, variation in MRI scoring systems used across studies, and the limited routine use of DWI—the sequence most sensitive for acute ischemic injury in the neonatal brain—in our protocol. The use of a 1.5-T rather than a 3-T scanner may also have reduced our ability to detect subtle parenchymal changes. Going forward, incorporating DWI and a standardized scoring tool such as the Weeke score—which has been shown to detect abnormalities most frequently in mild HIE populations (18) would strengthen future investigations from our center.

Mild HIE is not a homogeneous condition. Wu et al. (8) have shown that MRI's prognostic accuracy drops considerably in the mild range, and Chalak et al. (6) demonstrated that neuroimaging abnormalities can occur in Sarnat stage I infants who appear neurologically intact on early examination—particularly when Apgar scores are low or biochemical evidence of hypoxia-ischemia is present (10). These observations are entirely consistent with what we found in our cohort.

Taken together, lower cord pH, more negative base excess, and elevated lactate—all of which we also observed as trends in our cohort—have been proposed as markers of heightened cerebral injury risk even when clinical staging points to mild disease (7,13). Wu et al. (8) pointed out that neuroimaging may capture injury severity that clinical scores simply miss, especially in early or attenuated presentations. The absence of statistical significance in our study should, therefore, be interpreted cautiously, as the study may have been underpowered to detect clinically meaningful associations; the absence more likely reflects the constraints of a small sample and the inherent variability of mild HIE populations.

The predominance of hemorrhagic findings in our cohort—subdural, intraventricular, and parenchymal hemorrhages—may be interpreted cautiously. Brouwer et al. (11)

described the full spectrum of ICH in term newborns and highlighted the roles of vascular fragility and reperfusion injury following hypoxia-ischemia. Hemorrhagic lesions can therefore coexist with and complicate the hypoxic-ischemic process, and recognizing them is directly relevant to neurodevelopmental surveillance. Their presence should prompt careful, long-term follow-up regardless of the infant's initial clinical grading.

Study Limitations

Several limitations of this study merit acknowledgment. The retrospective single-center design limits the generalizability of our findings. The relatively small overall sample and particularly the low number of infants with abnormal MRI (n=12) meant that the study was underpowered to detect statistically significant associations; the event-per-variable ratio in the logistic regression was roughly 1.7, far below the conventional threshold of 10, so those results should be viewed as hypothesis-generating rather than confirmatory. Formal inter-rater reliability testing for MRI interpretation was not performed. DWI was not routinely acquired in all patients, which likely led to some underestimation of ischemic injury. Because long-term neurodevelopmental follow-up data were unavailable, we cannot comment on outcomes. Taken together, these constraints mean that the lack of statistical significance is better understood as reflecting methodological limitations than as evidence that the observed clinical trends are unimportant—a question that prospective studies will need to address more rigorously.

CONCLUSION

Although the majority of neonates with mild HIE had normal cranial MRI findings, a clinically meaningful subset—nearly one in five—showed structural brain abnormalities. A reassuring clinical picture does not rule out underlying cerebral injury. Hemorrhagic lesions, in particular, may reflect vascular fragility or reperfusion injury occurring alongside the hypoxic-ischemic process. Our findings support a thorough multimodal assessment—clinical, biochemical, and neuroimaging—in every neonate with Sarnat stage I HIE. Prospective studies using standardized MRI protocols, validated scoring systems, and long-term neurodevelopmental follow-up are needed to improve risk stratification and guide management in this understudied population.

ETHICS

Ethics Committee Approval: This study was approved by the University of Health Sciences Türkiye, Haseki Training and Research Hospital Non-Interventional Ethics Committee (approval no: 34-2026, date: 25.02.2026).

Informed Consent: Retrospective study.

FOOTNOTES

Authorship Contributions

Surgical and Medical Practices: B.C., Concept: B.C., D.K., Design: B.C., H.G.Y., H.Ç., Data Collection or Processing: B.C., H.G.Y., D.K., H.Ç., D.B., N.G., Analysis or Interpretation: B.C., N.G., Literature Search: B.C., H.G.Y., D.K., D.B., Writing: B.C., H.G.Y., D.K., H.Ç., D.B., N.G.

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