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Clinical process and role of diagnostic tools in hypoxic ischemic encephalopathy: a 5-year retrospective review

Hipoksik iskemik ensefalopatide klinik gidiş ve tanı araçlarının rolü: 5 yıllık retrospektif bir inceleme

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Abstract

Purpose: Hypoxic-ischemic encephalopathy (HIE) is a critical clinical process that leads to permanent/temporary brain damage in newborns due to inadequate oxygenation before, during, or after birth. The present study aimed to evaluate the clinical, radiological, and laboratory results of newborns followed up with the diagnosis of HIE in our neonatal intensive care unit for five years. We also aim to reveal the clinical tools' prognostic importance in HIE.

Materials and methods: We retrieved data from the hospital information system for infants who were followed up in Pamukkale University Hospital's neonatal intensive care unit between 2020 and 2025. We drew cord blood at birth and on the 24th day of life for blood gas and biochemistry parameters. We also retrieved the MRI and amplitude EEG results taken within the postnatal 3rd-5th days.

Results: During the five years, 58 newborns were followed up with HIE, and 17 were excluded because there was an insufficient patient record. 23 of the patients were male and 18 were female. Follow-up lactate and albumin levels at the 24th hour were found to be related to the neurodevelopmental process. One of the patients died, and three of the survivors developed hearing loss.

Conclusion: In our current study, we suggested emphasizing the importance of evaluating HIE with multidisciplinary clinical tools.

Keywords: Hypoxic ischemic encephalopathy, clinical diagnostic tools, retrospective analysis.

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Öz

Amaç: Hipoksik-iskemik ensefalopatisi (HIE), doğum öncesi, sırası veya sonrasında yetersiz oksijenizasyon nedeni ile yenidoğanlarda kalıcı ya da geçici beyin dokusu hasarına yol açan klinik bir durumdur. Çalışmamızda beş yıllık süre boyunca hastanemiz yenidoğan yoğun bakım servisinde HİE tanısı ile takip edilen hastaların klinik, radyolojik ve laboratuvar sonuçlarını değerlendirerek, prognozda göz önünde bulundurulması gereken klinik araçları ortaya koymayı amaçladık.

Gereç ve yöntem: Pamukkale Üniversitesi Sağlık Uygulama Araştırma Hastanesi Yenidoğan yoğun bakım servisinde 2020-25 yılları arasında HİE tanısı ile takip edilen hastaların verileri geriye dönük olarak hastane bilgi sisteminden (HBS) alınmıştır. Doğum anında alınan kord kan gazı sonuçları, ilk 24 saatte alınmış rutin biyokimya sonuçları, postnatal 3.-5. gün içinde çekilen MRG ve postnatal ilk saatte kayda başlanan amplitüd entegre EEG HBS den geriye dönük olarak alınmıştır.

Bulgular: Beş yıllık sürede 58 yenidoğanın HİE tanısı ile takip edilirken, 17'sinin dosyasında yeterli veri olmadığından hariç tutulmuştur. Hastaların 23'ü erkek, 18'i kız idi. İzlemde 24 saatte alınan laktat düzeyi ve albümin nörolojik gelişimle ilişkili bulundu. Bebeklerden biri ex olurken, üç hastada işitme kaybı gelişti.

Sonuç: Beş yıllık HİE verisi değerlendirdiğimiz mevcut çalışmamızda HİE'nin multidisipliner klinik araçlar ile değerlendirilmesinin önemini vurgulamaya çalıştık.

Anahtar kelimeler: Hipoksik iskemik ensefalopati, klinik tanı araçları, retrospektif değerlendirme.

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Introduction

During fetal life, brain tissue relies predominantly on glucose that crosses the placenta by facilitated diffusion for energy. Under normal conditions there is little endogenous glucose production, which increases in conditions such as intrauterine growth retardation and placental insufficiency. Before, during, and after birth, the fetus is exposed to physiologic challenges that require metabolic adaptation to maintain brain energy balance [1]. One of the most common of these physiologic challenges is perinatal asphyxia [2].

Perinatal asphyxia is the absence of blood flow or gas exchange to or from the fetus just before, during or after the birth process [3]. Worldwide, asphyxia accounts for 24% of neonatal deaths and causes approximately 800,000 deaths under 5 years of age annually. Approximately 4 million of the 130 million newborns worldwide experience asphyxia each year; an estimated 1 million die, and nearly 1 million develop severe, long-term sequela [2, 4].

Perinatal asphyxia is the most common cause of neonatal encephalopathy. Neonatal hypoxic-ischemic encephalopathy (HIE) is a condition of fetal or neonatal brain damage that develops because of perinatal asphyxia characterized by hypoxia in the fetus or infant during or after delivery [1, 5]. In term newborns, HIE may cause a series of motor and neurodevelopmental disabilities [6]. The basis of these neurologic sequelae is the inadequacy of glucose, which is the basic fuel, and impaired oxygenation. When hypoxia is prolonged, acidosis caused by anaerobic mechanisms disrupts the continuity of metabolism [7]. As a result, HIE may cause neurodevelopmental disorders in addition to motor retardation, which may be permanent [8, 9]

Therapeutic hypothermia, which is the only treatment method with proven efficacy in case of developing HIE, is applied to infants under neonatal intensive care conditions. Its administration in the first 6 hours after birth is significant in terms of preventing the development of sequelae [4, 7, 9, 10]. In the application of therapeutic hypothermia, the targeted body core temperature should be reached in the first half hour and applied for 72 hours [11].

To facilitate the diagnosis of neonatal HIE, umbilical cord blood gas tests, blood glucose, arterial blood gas, magnetic resonance imaging (MRI) and ultrasonography, amplitude-integrated electroencephalograms (EEGs), and similar tools are used. APGAR scoring (skin color, heart rate, reflexes, muscle tone, and respiration) is obtained by assigning points as a measure of the babies' well-being after birth. This scoring should be checked until the 10^{th} minute at the latest, and ≤5 is considered a poor prognosis. APGAR≤5 at 10 minutes of life, pH ≤7.0, and a base excess <-12 indicate the need for resuscitation.

Blood gas parameters (lactate, pH, HCO3, base excess), routine biochemistry tests (glucose, CK, LDH, AST, ALT, urea, creatinine), APGAR scoring, MRI, and amplitude-integrated EEG gain importance in predicting the sequelae that may develop in the follow-up of these patients. Because HIE is one of the most significant causes of neonatal mortality and morbidity. For this purpose, in this study, we aimed to examine the etiologic, clinical, laboratory, and radiologic findings of newborns who were followed up with a diagnosis of HIE between January 2020 and January 2025 in the Neonatal Service of Pamukkale University Health Practice Research Hospital. We aimed to reveal the findings that affect the neurologic sequelae that may develop in the future in newborns diagnosed with HIE.

Materials and methods

Ethics committee approval was approved by Pamukkale University Non-Interventional Clinical Research Ethics Committee on 27.06.2025 with the number E-60116787-020-713037.

The study included patients admitted to the Neonatal Intensive Care Unit of Pamukkale University Medical Faculty Hospital between

2020 and 2025 with a diagnosis of hypoxic ischemic encephalopathy and who received hypothermia treatment. Patients for whom complete demographic data or laboratory data were not available from hospital records were excluded from the study. The diagnosis and treatment criteria for hypoxic ischemic encephalopathy were determined according to the recommendations of the Turkish Neonatology Association's neonatal encephalopathy diagnosis and treatment guideline [12]. Cord blood gas results, pH, HCO3, base excess and lactate results, blood glucose, creatinine, AST, ALT, and CK values taken in the first 24 hours, blood glucose, creatinine, AST, ALT, and CK values taken at the time of birth of infants followed up with a diagnosis of HIE in the Neonatal Service of Pamukkale University Health Practice Research Hospital between January 2020 and January 2025 were obtained retrospectively from the Hospital Information System. The results of the routine MRI performed on the 3rd-5th postnatal day and the results of amplitude-integrated EEG, which started to be recorded in the first postnatal hour, were obtained retrospectively from the hospital information system.

Encephalopathy was evaluated with the Sarnat Score system. According to the Sarnat staging system, neonates are classified as having mild (stage I), moderate (stage II), or severe (stage III) hypoxic-ischemic encephalopathy based on a comprehensive assessment of clinical and neurophysiological parameters, including the level of consciousness, muscle tone, posture, tendon reflexes, primitive reflexes, presence of seizures, and amplitude-integrated electroencephalography (aEEG) findings.

All statistical analyses were performed using SPSS 25.0 (IBM SPSS Statistics 25 software (Armonk, NY: IBM Corp.)). Continuous variables were defined by the mean ± standard deviation; median (IQR:25th-75th percentiles), and categorical variables were defined by number and percent. The Shapiro Wilk test was used for determination of normal distribution.

For independent group comparisons, when parametric test assumptions were provided, we used the Independent samples t-test; when parametric test assumptions were not provided the Mann-Whitney U test was used. Cohen's d effect size (0.00-0.19: negligible; 0.20-0.49: small; 0.50-0.79: medium; 0.80-1.29: large; 1.30-1.99: very large; ≥2.00: huge) was used for effect clinical significance interpretation. Logistic regression models were used to examine the risk factors that have a statistical effect on the presence of neurological sequelae. Statistical significance was determined as $p<0.05$.

Results

In our retrospective study, file information of 58 newborns was analyzed in a five-year period. Seventeen HIE patients in whom sufficient data could not be obtained from the file information were excluded from the study.

Descriptive information about the patients is given in Table 1. Of the 41 patients included in the study, 23 (56.1%) were male and 18 (43.9%) were female. The mean gestational week was 38±1.7 (between 34 and 41 weeks), and the mean birth weight was 3211±595 (1840-4555g) grams. The mean age of the mothers was 29±5 (17-40) years.

When birth weights were evaluated according to gestational weeks, 34 (82.9%) babies were classified as appropriate for gestational age (AGA), 4 (9.8%) as large for gestational age (LGA), and 3 (7.3%) as small for gestational age (SGA). According to mode of delivery, 23 (56.1%) were born by caesarean section (C/S) and 18 (43.9%) were born by vaginal delivery (NSVD). Five (12.2%) of the patients had no encephalopathy findings in the encephalopathy evaluation. According to Sarnat staging, 19 (46.3%) patients were in stage 1, 14 (34.1%) were in stage 2, and 3 (7.3%) were in stage 3. Only one of 41 patients died. While no congenital defect was detected in 35 (92.1%) of the newborns, 3 (7.9%) were found to have congenital defects (Table 2).

Table 1. Descriptive statistics of newborns and their mothers'

Variables		n	%
Gender	Male	23	56.1
	Female	18	43.9
Gestation week	Mean ± S.D	38±1.7	
	Med (IQR)	38 (37-39)	
Gestation weight	Mean ± S.D	3211.83±595.84	
	Med (IQR)	3170 (2905-3515)	
Mother age (year)	Mean ± S.D	29.05±5	
	Med (IQR)	29 (25.5-33)	
Gestational age (week)	AGA	34	82.9
	LGA	4	9.8
	SGA	3	7.3
Delivery	C/S	23	56.1
	NSVD	18	43.9
Sarnat score	Encephalopathy (-)	5	12.2
	1	19	46.3
	2	14	34.1
	3	3	7.3
Exitus	-	40	97.6
	+	1	2.4
Abnormality	-	38	92.6
	+	3	7.4

S.D: Standard deviation, Med (IQR): Median (25^{th} – 75^{th} percentiles), SGA: Small gestational age, AGA: Appropriate gestational age
LGA: Large gestational age, C/S: cesarean section NSVD: normal spontaneous vaginal delivery

Table 2. Clinical, radiological and laboratory status of newborns

		n	%
Newborn resuscitation	(-)	22	55.0
	CPR	3	7.5
	PBV	15	37.5
APGAR at 5th min	Mean ± S.D	7.63±1.92	
	Med (IQR)	8 (6-9)	
APGAR at 10th min	Mean ± S.D	8.49±1.57	
	Med (IQR)	9 (8-10)	
Difficult birth	(-)	26	65.0
	(+)	14	35.0
Prenatal risk factor	(-)	20	50.0
	(+)	20	50.0
Respiratory support	(-)	21	51.2
	Intubates	11	26.8
	Nasal	9	22.0
Hypoglycaemia	(-)	38	92.7
	(+)	3	7.3
Inotropic support	(-)	29	70.7
	Monotherapy	7	17.1
	More than >1	5	12.2
aEEG finding	Normal	4	9.8
	Mild abnormality	8	19.5
	Moderate abnormality	23	56.1
	Severe abnormality	6	14.6
MRI abnormality	Normal	22	55.0
	Pathologic	18	45.0
Echocardiography	(-)	12	29.3
	(+)	29	70.7
Echocardiography pathology	(-)	9	31.0
	(+)	20	69.0
Seizure	(-)	32	78.0
	(+)	9	22.0
Hearing loss	(-)	35	92.1
	(+)	3	7.9
Neurological follow-up	(-)	18	43.9
	(+)	23	56.1
Neurological follow-up finding	(-)	16	69.6
	(+)	7	30.4
EEG finding	(-)	13	92.9
	(+)	1	7.1

Although 22 (55.0%) of the patients did not need resuscitation at delivery, 15 (37.5%) patients received positive pressure ventilation (PBV), and 3 (7.5%) patients received PBV and cardiac compression. The APGAR scores of the patients were 7.63±1.92 at the fifth minute and 8.49±1.57 at the 10th minute.

Fourteen patients (35%) had a history of difficult delivery. Prenatal factors that may pose a risk for HIE were present in 50% of the neonates. During follow-up, 20 (50.8%) patients needed respiratory support; 11 (26.8%) of the patients who needed respiratory support were intubated, and 9 (22%) were followed up with nasal respiratory support. Hypoglycaemia was detected in 3 (7.3%) patients during follow-up. 12 (29.3%) patients needed inotropes, and 5 (12.2%) patients received two or more inotropes.

Amplitud-integrated electroencephalography (aEEG) findings were normal in 4 patients (9.8%). Mild impairment was found in 8 (19.5%), moderate impairment in 23 (56.1%), and severe impairment in 6 (14.6%) patients. While 22 (55%) patients had normal MR imaging, 18 (45%) had pathologic findings. Echocardiographic (ECHO) evaluation was performed in 29 (70.7%) patients, and pathologic ECHO findings were detected in 20 patients. Myocardial dysfunction was present in 4 of these 20 patients, pulmonary hypertension was present in 2 patients, and structural defects were detected in 14 patients.

The results of blood gas tests (lactate, pH, HCO3, base excess), routine biochemistry tests (glucose, albumin, CK, LDH, AST, ALT, creatinine), hemogram (white blood cell, haemoglobin, haematocrit, platelet count), coagulation tests (aptt, pt, inr) obtained at birth and at the 24th hour of life, which were routinely evaluated during follow-up, are given in detailed Table 3.

Among laboratory values, pH and lactate at birth or in the first hour of life, pH and lactate at 24 hours of life, and albumin were analysed in terms of the presence/absence of seizures, neurologic sequelae, prenatal risk factors, and pathologic MR findings (Table 4).

Table 3. Laboratory findings of newborns

	Mean ± S.D	Med (IQR)
pH	6.99±0.15	7.02 (6.9-7.1)
pH at 24th hour	7.31±0.12	7.34 (7.28-7.39)
Lactate (mmol/L)	9.04±3.94	8.5 (6.35-11.6)
Lactate at 24th hour (mmol/L)	3.45±1.82	2.8 (2.09-4.65)
Base excess (mmol/L)	-16±4.88	-15.5 (-18--13.3)
Base excess 24th hour (mmol/L)	-6.17±4.05	-5.5 (-7.8--3.7)
Creatinine (mg/dl)	0.86±0.22	0.83 (0.71-1.02)
ALT (U/L)	37.68±105.29	12 (8-27)
AST (U/L)	101.41±105.39	63 (50-90)
CK (U/L)	1725.63±1556.86	1217 (767.25-2278.75)
LDH (U/L)	1119.59±1219.8	775 (592.5-1029)
Albumin (g/L)	3.52±0.35	3.5 (3.3-3.8)
WBC (K/uL)	19288.29±7308.39	17910 (14490-23350)
Hemoglobin (g/dl)	16.04±2.33	16 (14.3-17.5)
Haematocrit (%)	47.86±7.11	48.2 (43.05-52.55)
Platelet (K/uL)	235731.71±64202.81	231000 (211000-275000)
PT (sn)	17.66±5.53	16.2 (14.9-17.75)
aPTT (sn)	45.87±16.89	41.4 (33.85-50.45)
INR	1.5±0.51	1.39 (1.22-1.5)

S.D: Standard deviation, Med (IQR): Median (25th – 75th percentiles), PT: Prothrombin time, aPTT: Active prothrombin thromboplastin time

Table 4. Evaluation of seizure, neurodevelopmental follow-up, prenatal factor MRI pathology according to pH, lactate, albumin levels

	ph	Ph at 24th hour	Lactate	Lactate at 24th hour	Albumin
Seizure					
(-)	7.02 (6.9-7.1)	7.34 (7.28-7.39)	8.64±3.11	2.75 (1.8-4.2)	3.57±0.29
(+)	7.05 (6.8-7.11)	7.34 (7.27-7.38)	10.47±6.08	2.9 (2.65-5.35)	3.33±0.49
p	0.631 (z=-0.511)	0.958 (z=-0.071)	0.406 (t=-0.871)	0.226 (z=-1.223)	0.07 (t=1.860)
Cohen's d effect size	-0.08	-0.011	-0.468	-0.191	0.702
Neurodevelopmental follow-up finding					
(-)	6.9 (6.9-7.1)	7.35±0.06	8.13±3.35	2.85±1.04	3.64±0.24
(+)	6.9 (6.8-7.15)	7.3±0.09	11.79±5.13	5.05±2.3	3.13±0.47
p	0.222 (z=-1.270)	0.157 (t=1.481)	0.05* (t=-2.046)	0.01* (t=-2.917)	0.002* (t=3.476)
Cohen's d effect size	-0.265	0.731	-0.927	-1.44	1.575
Prenatal risk factor					
(-)	7.05 (7.14-0.18)	7.32 (7.38-0.12)	7.1 (8.13-3.49)	2.8 (4.05-1.79)	3.5±0.33
(+)	6.96 (7.09-0.12)	7.34 (7.39-0.12)	9.95 (13.25-3.53)	2.75 (4.83-1.85)	3.53±0.37
p	0.414 (z=-0.838)	0.276 (z=-1.103)	0.0001* (z=-3.355)	0.56 (z=-0.59)	0.79 (t=-0.268)
Cohen's d effect size	-0.132	-0.174	-0.53	-0.093	-0.085
MRI pathology					
(-)	7.02 (6.9-7.11)	7.34 (7.29-7.39)	8.94±3.58	2.8 (2.05-3.98)	3.56±0.27
(+)	7.06 (6.88-7.12)	7.34 (7.25-7.39)	9.27±4.51	2.75 (2-5.28)	3.44±0.43
p	0.946 (z=-0.083)	0.791 (z=-0.286)	0.794 (t=-0.263)	0.606 (z=-0.523)	0.289 (t=1.076)
Cohen's d effect size	-0.013	-0.048	-0.083	-0.087	0.342

*$p<0.05$ statistically significant; Mean±SD (standard deviation) summary statistics were used for variables showing a normal distribution and tested using the independent samples t-test; median (IQR: 25th – 75th percentiles) summary statistics were used for variables not showing a normal distribution and tested using the Mann-Whitney U test; For cohen's d effect size 0.00 – 0.19: negligible; 0.20 – 0.49: small; 0.50 – 0.79: medium; 0.80 – 1.29: large; 1.30 – 1.99: very large; ≥ 2.00: huge

When evaluated in terms of the presence of seizure, no statistically significant result was obtained in any of the analysed factors ($p>0.05$). However, it was observed that albumin values were higher in patients without seizures than in patients with clinical seizures (Cohen's d=0.702). In the evaluation according to abnormal neurologic findings, it was observed that lactate and 24-hour lactate values were statistically significantly higher in patients with abnormal findings ($p=0.05$ and $p=0.01$, respectively) and albumin values were statistically significantly higher in patients without abnormal findings ($p=0.002$). There was no statistically significant difference in twenty-four-hour pH values according to the findings; however, clinically low values were found in patients with abnormal neurologic findings (Cohen's d=0.731). There was no statistically significant difference in pH values in relation to neurologic findings ($p>0.05$). When the presence of prenatal risk factors was evaluated, a statistically significant difference was observed only in lactate levels ($p=0.0001$). It was found that lactate levels were significantly higher in patients with prenatal risk factors. When the presence of pathology on MRI was evaluated, no statistically significant difference was found in any examination ($p>0.05$).

When we evaluated the clinical, radiologic, and laboratory findings that may contribute to the risk of developing neurologic sequelae in our study, we found that elevated albumin level had a significant risk-reducing effect on the risk of developing neurologic sequelae (*p*=0.025; O.R.=0.010 (95% CI:0-0. 563)), elevated 24-hour lactate level significantly increased the risk of developing neurological sequelae (*p*=0.038; O.R=2.283 (95% CI:1.045-4.988)), and the presence of any pathologic finding on MR imaging significantly increased the risk of developing neurological sequelae (*p*=0.033; O.R=13.2 (95% CI:1.239-140.679)). The other variables analyzed did not have a statistically significant effect on the risk of neurologic sequelae (Table 5).

Table 5. Possible risk factors for developing sequelae

	Wald	*p*	O.R.	%95 C.I. Lower - Upper
Gender (Female; ref: Male)	0.099	0.753	1.333	0.223-7.98
Gestational week	1.646	0.199	0.676	0.371-1.23
Gestational weight	0.812	0.368	0.999	0.998-1.001
Mother age	0.058	0.809	1.020	0.866-1.203
SGA LGA AGA (lga+sga; ref: aga)	0.067	0.796	0.722	0.062-8.464
Delivery (nsvd; ref:c/s)	0.884	0.347	0.400	0.059-2.702
Sarnat score	0.024	0.877	1.095	0.345-3.481
Resuscitation at birth (+; ref:-)	0.002	0.968	0.964	0.16-5.795
Apgar score in 5th minutes	0.565	0.452	0.815	0.478-1.389
Apgar score in 10th minutes	1.994	0.158	0.605	0.301-1.216
Difficult birth (+; ref:-)	0.016	0.898	0.880	0.125-6.192
Prenatal factor (+; ref:-)	0.002	0.968	0.964	0.16-5.795
Respiratory support (+; ref:-)	0.059	0.809	0.800	0.131-4.874
Hypoglycaemia (+; ref:-)	1.817	0.178	6.000	0.443-81.196
Inotrope (single; ref: -)	0.093	0.760	1.375	0.178-10.65
Inotrope (multiple; ref: -)	0.437	0.508	2.750	0.137-55.166
aEEG	0.046	0.83	1.114	0.416-2.989
MRI (+; ref:-)	4.568	0.033*	13.200	1.239-140.679
Seizure (+; ref:-)	0.717	0.397	2.250	0.345-14.694
pH	0.933	0.334	0.065	0-16.557
pH at 24th hour	1.977	0.160	0.000	0-66.338
Lactate (mmol/L)	3.229	0.072	1.254	0.98-1.606
Lactate at 24th hour (mmol/L)	4.285	0.038*	2.283	1.045-4.988
Base excess (mmol/L)	2.631	0.105	0.856	0.709-1.033
Base excess at 24th hour (mmol/L)	2.507	0.113	0.695	0.443-1.09
CK (U/L)	0.051	0.822	1.000	0.998-1.001
LDH (U/L)	0.984	0.321	1.000	1-1.001
Albumin (g/L)	5.016	0.025*	0.010	0-0.563
PT (sn)	1.030	0.310	1.134	0.89-1.444
aPTT (sn)	0.949	0.330	1.034	0.967-1.104
INR	1.131	0.288	4.759	0.269- 84.325

*p<0.05 statistically significant effect, ref: reference category, O.R: Odds Ratio
95% C. I: %95 Confidence Interval, Wald: Logistic regression coefficient

Discussion

Despite advances in diagnosis and treatment, hypoxic ischemic encephalopathy is still a significant problem in neonatal intensive care units [13]. In our retrospective study evaluating data from the past five years, the incidence of hypoxic-ischemic encephalopathy (HIE) among term neonates who were hospitalized for follow-up care was found to be 2.1%. The HIE study group of the Turkish Neonatology Association reported that the rate of HIE patients treated as inpatients in neonatal intensive care units of 16 university hospitals was 2.6 per thousand [13].

In our study, it was observed that the rate of HIE in male babies was higher compared to female babies. Similarly, while the HIE study group of the Turkish Neonatology Association reported this rate as 75%, it was found to be 63.6% in the study by Kemer et al. [12, 14].

Maternal and perinatal history plays a critical role in the diagnosis of hypoxic-ischemic encephalopathy (HIE).

Maternal and delivery history is of great importance in terms of the diagnosis of HIE [13]. In a cross-sectional retrospective descriptive study conducted by Özel et al. [15], the median maternal age of babies diagnosed with HIE was 29 (18-41) years, while Kemer et al. [14] reported that the mean maternal age was 28.5±3.8 years. Similarly, maternal age was 29 (17-40) years in our study.

In an analysis of seven-year data from 194 member countries by the World Health Organization, it was revealed that cesarean section rates up to 19.1 and 19.4 per 100 live births were inversely proportional to maternal and neonatal mortality rates, respectively [16]. In our study, unlike this data, the cesarean section rate was higher (56.1%). However, considering the birth rates in our hospital, we believe that the higher rate of cesarean section (C/S) deliveries compared to vaginal births may account for the differences observed between studies regarding neonatal mortality.

The staging developed by Sarnat is widely used to indicate the grade of HIE. According to Sarnat staging, mortality rates and prognosis can be interpreted. In our study, 19 (46.3%) patients were in stage 1, 14 (34.1%) were in stage 2, and 3 (7.3%) were in stage 3 according to Sarnat staging. It was reported that the mortality rate was highest in infants in stage 3 [17]. Satar et al. [18] found mortality to be 15% in stage 2, 78.6% in stage 3, and 24.4% in total. In a multicenter study of the Turkish Neonatology Society, all patients in Stage 1 were discharged, while mortality rates were 16.7% in Stage 2, 51.7% in Stage 3, and 22.6% in total [12]. In our study, all patients with Sarnat stages 1 and 2 were discharged, and one of the 3 patients with stage 3 was lost. The total mortality rate was 2.4%, which is low compared to the literature, and we believe that this result is related to the low number of patients with Sarnat stage 3.

In our study, 45% of patients with HIE required resuscitation at birth; 37.5% of these babies received positive pressure ventilation (PBV), and 7.5% received cardiac compression in addition to PBV. The mean APGAR score at the fifth minute was 7.63±1.92 and at the tenth minute, it was 8.49±1.57. According to the HIE management guideline published by the Turkish Neonatology Society in 2018, low APGAR scores at birth and the need for resuscitation are frequently associated with moderate and severe encephalopathy in Sarnat staging and are considered among the indications for hypothermia treatment [19]. In this context, a mean APGAR score of 7.63 at the fifth minute indicates the presence of mild-to-moderate clinical involvement in most of the cases. Similarly, Karadeniz Bilgin et al. [13] reported that the majority of HIE cases required resuscitation at birth, APGAR scores were low, and this was associated with neurologic sequelae.

In our study, 35% of the cases had a history of difficult delivery, and 50% had prenatal factors (preeclampsia, intrauterine growth retardation, meconium aspiration, etc.) that may pose a risk for HIE. These rates reflect the multifactorial causes of HIE. Especially a history of difficult delivery may lead to transient decreases in cerebral perfusion and predispose to hypoxic-ischemic damage. Similarly, Karadeniz Bilgin et al. (2011) [13] reported difficult delivery in 33% of cases and prenatal risk factors in 49%.

In our study, the need for respiratory support was found to be 50.8%, and 26.8% of these required intubations. This finding indicates that neonatal resuscitation is not limited to the moment of birth, and in many cases, respiratory support is needed in the postnatal period. Lee et

al. (2021) [2] found that the need for intubation in cases of HIE was associated with clinical severity.

Hypoglycaemia has a significant place in the pathophysiology of HIE [1]. In our study, hypoglycaemia was found in 7.3%. Boardman and Hawdon (2015) [1] emphasized that impairment in brain glucose metabolism aggravates the damage by affecting cellular energy metabolism more deeply with oxygen deficiency in brain tissue. In our study, the rate of inotrope utilization was 29.3%, and among these patients, 12.2% received two or more agents. This supports that systemic hypoperfusion and cardiovascular instability are common problems in HIE. Boerger et al. (2024) [11] reported that the need for circulatory support increased markedly in cases of severe HIE, and inotrope utilization was inevitable, especially in hypotensive patients with high lactate levels.

Pathologic findings were found in 20 (69%) of 29 patients who underwent echocardiographic examination. This rate indicates that HIE is not only limited to the central nervous system but also progresses with multi-organ involvement, including the cardiovascular system. Lee et al. (2021) [2] reported that findings of myocardial dysfunction, pulmonary hypertension, and low cardiac output were frequently observed in cases with severe HIE. Galderisi et al. (2023) [7] also emphasized that systemic hypoperfusion and metabolic imbalances may cause deterioration in cardiac performance.

In our study, aEEG findings were normal in only 9.8% of the patients, while moderate and severe impairment were found in 56.1% and 14.6%, respectively. According to the Turkish Neonatology Society guidelines, aEEG is recommended as a significant tool both in the diagnosis of HIE and in the decision to start hypothermia treatment. In addition, it has been reported that aEEG recordings obtained especially in the first 6 hours are correlated with Sarnat stage and are effective in predicting neurodevelopmental outcomes [19].

When MRI findings were analysed, pathologic imaging was found in 45% of patients. Chen et al. (2021) [20] reported that abnormalities detected on brain magnetic resonance imaging were significantly associated with various neurodevelopmental sequelae, including hearing loss. In addition, Boerger et al. (2024) [11] demonstrated that severe MRI findings are an independent risk factor for the development of neurologic sequelae.

Boerger et al. [11] reported that 16 of 45 newborns followed up with a diagnosis of moderate and severe HIE between 2013 and 2019 had seizures between 18 and 24 months. In a study by Shah et al. [21] associating electronic seizures with MRI findings, the rate of seizures in patients receiving therapeutic hypothermia was reported as 68%. In our study, seizure activity was observed in 9 (22%) patients. We believe that the low rate of seizure activity in our study compared to the literature data is related to the low number of Sarnat score 3 patients.

In a meta-analysis published by Edwards et al. [22] in which neurodevelopment of patients with moderate HIE was examined at 18 months, the deafness rate was reported as 4.7% (12/255) in patients receiving hypothermia. In our study, the rate of hearing loss was 7.9% (3/41). We attributed our high rate of deafness to the fact that the patients with moderate and severe encephalopathy were more common in our study group.

In our study, 23 (56.1%) of 41 HIE patients participated in neurologic follow-up at least once, and sequelae (speech retardation, increased tonus, cerebral palsy) were found in 7 (30.4%) of these patients. Long-term EEG was performed in 14 of these 23 patients, and epileptic activity was detected in only one infant (7.1%). In a meta-analysis published by Jacobs et al. [23] in which 1505 patients with moderate and severe encephalopathy were examined, the rate of neurodevelopmental disorders was found to be 26% in patients receiving hypothermia. We believe that the high rate of neurologic sequelae in our study is related to the high number of patients who did not come to follow-up and the fact that these babies could not be evaluated.

In the diagnosis and follow-up of HIE, in addition to clinical and radiological monitoring, laboratory findings play a significant role both in assessing prognosis and evaluating the effectiveness of treatments to be administered. In our study, when we evaluated the relationship between laboratory results and disease prognosis in terms of neurologic findings, we

found that lactate, 24 h lactate, and albumin demonstrated significance. When Michniewicz et al. [24] divided 57 newborns with HIE into two groups as moderate and severe with Sarnat and evaluated the laboratory results, the laboratory results did not show a significant difference between the two groups in terms of damage that may occur in the later period. In the study of Galderisi et al. [7], in which they examined the glucose/lactate ratio in infants with HIE, they demonstrated that the lactate level decreased faster in the group with good neurodevelopmental results. They demonstrated that lactate level decreased by 41% on the second day and 76% on the third day in the group with good neurodevelopmental outcomes and by 24% on the second day and 54% on the third day in the group with poor neurodevelopmental outcomes. In the study by Lee et al. [2], when MR findings and albumin level were evaluated in babies with HIE, it was found that albumin level was lower in the group with severe MR findings.

Our study had some limitations; approximately half of our patients did not have neurologic follow-up findings, and we believe that the low rate of hospital admission during the pandemic and subsequent processes was effective. Since our study was retrospective, we could only make an evaluation with the data in the hospital information system.

In conclusion, we believe that our study, which we conducted with file evaluation, is valuable in terms of providing information about the points to be considered in the follow-up of infants with HIE and will provide guidance for prospective studies to be planned in the future.

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