Turkish Journal of Pediatric Disease

Original Article

Two-year neurodevelopmental outcomes after therapeutic hypothermia in neonatal hypoxic-ischemic encephalopathy: a retrospective cohort study

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ABSTRACT

Objective: Therapeutic hypothermia is the standard neuroprotective treatment for neonates with hypoxic-ischemic encephalopathy (HIE). However, neurodevelopmental outcomes may still vary depending on the severity of encephalopathy. This study aimed to evaluate two-year neurodevelopmental outcomes in infants with HIE treated with therapeutic hypothermia and compare outcomes between Stage 2 and Stage 3 cases classified according to the Sarnat & Sarnat staging system.

Material and Methods: We conducted a retrospective cross-sectional study including 138 infants born at ≥35 weeks of gestation who were diagnosed with HIE and received therapeutic hypothermia in a Level III NICU between January 2016 and December 2017. Neurodevelopment was assessed at 24 months using the Bayley Scales of Infant and Toddler Development-II (BSID-II), focusing on Mental Development Index (MDI) and Psychomotor Development Index (PDI) scores.

Results: Infants in the Stage 3 group required significantly more respiratory support, had a higher frequency of aEEG abnormalities, and more often received anticonvulsant therapy (p=0.020, p<0.001 and p<0.001, respectively). The Stage 3 group had significantly lower mean MDI and PDI scores (84±10 and 71±11, respectively) than the Stage 2 group (89±17 and 94±18; p=0.049 and p=0.001). Neurodevelopmental impairment was more prevalent in Stage 3 patients (36.5% vs. 17.3%, p=0.012).

Conclusion: Despite uniform application of therapeutic hypothermia, neurodevelopmental outcomes at 24 months differ significantly by HIE severity. These findings highlight the importance of timely intervention, individualized follow-up, and the need for additional strategies in managing severe HIE cases.

Keywords: Hypothermia, hypoxic-ischemic encephalopathy, newborn

INTRODUCTION

Neonatal encephalopathy is a clinical condition characterized by altered consciousness or seizures in the early postnatal period, accompanied by respiratory depression and hypotonia, in infants born at or above 35 weeks of gestation (1,2). The combination of early hypoperfusion followed by abrupt reperfusion can lead to significant damage in brain tissue (3). Neonatal encephalopathy can develop due to various causes such as intrauterine growth restriction (IUGR), maternal thyroid diseases, thrombophilia, fetal inflammation, infection, and hypoxic-ischemic encephalopathy (HIE) (4,5). Although the incidence varies depending on the cause, studies have reported an incidence of 1-3 per 1000 live births (6). According to data from the Turkish Neonatal Society Hypoxic Ischemic Encephalopathy Study Group, the incidence was found as 2.6 per 1000 live births (4).

Despite advances in perinatal and neonatal care, reductions in neonatal mortality rates and significant improvements in long-term prognosis, HIE remains a major cause of neonatal death, acute neurological injury in the early period and severe long-term neurodevelopmental impairments (7,8). HIE has been associated with neurodevelopmental disorders, neuromotor retardation, epilepsy, behavioral and speech difficulties, visual

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Received : 08.05.2025
Accepted : 23.06.2025
DOI: 10.12956/TJPD.2025.1151

and hearing loss, academic failure, learning disabilities, growth retardation, and autism, many of which have not yet been fully elucidated in terms of their etiology (9,10).

In addition to these diagnostic criteria, various scoring systems have been developed in recent years for the follow-up of HIE (11-14). The Sarnat & Sarnat classification, which has been widely used since 1976, is a scoring system that helps predict neurological prognosis in HIE (14).

The most effective neuroprotective approach in the treatment of HIE is the application of therapeutic hypothermia within the first 6 hours of life, as soon as possible (15). Therapeutic hypothermia has been shown to reduce the risk of mortality, moderate-to-severe neurodevelopmental disorders in childhood, cerebral palsy (CP), cognitive impairment, and psychomotor retardation (10).

The aim of this study was to examine neonatal HIE patients who completed their neurodevelopmental assessment at the postnatal 24th month in our clinic. Additionally, the study aimed to compare the clinical features of Stage 2 and Stage 3 patients, as classified by the Sarnat & Sarnat system, who received therapeutic hypothermia.

MATERIALS and METHODS

This study included toddlers who were followed in a level III neonatal intensive care unit (NICU) between January 2016 and December 2017, born at a gestational age of ≥35 weeks, diagnosed with HIE, and treated with therapeutic hypothermia, and who presented to the outpatient clinic for their second-year follow-up. Data related to the neonatal period were retrieved from patient records and files. Infants with major congenital or chromosomal anomalies were excluded from the study.

Procedures performed in the delivery room followed current neonatal resuscitation guidelines. A history of cardiopulmonary resuscitation (CPR) was recorded. Umbilical cord blood gas samples were analyzed using standardized and calibrated devices, and pH, BE, and HCO3 values were documented.

The diagnosis of hypoxic-ischemic encephalopathy was made according to the diagnostic criteria outlined in the Turkish Neonatology Association (TND) Neonatal Encephalopathy Diagnosis and Treatment Guidelines (4):

The presence of the following findings/acute events:

APGAR score <5 at the 5th and 10th minutes

Fetal umbilical cord blood gas pH<7.00 or BE<-12 mmol/L

Brain injury consistent with HIE detected on magnetic resonance imaging (MRI) or magnetic resonance spectroscopy (MRS)

Presence of multiple organ failure or dysfunction

The presence of an acute peripartum-intrapartum event:

Conditions such as uterine rupture, placental abruption, cord prolapse, maternal hypotension, amniotic fluid embolism, maternal hypoxemia, maternal cardiovascular collapse, vasa previa, or fetomaternal hemorrhage during delivery.

Typical imaging findings such as deep gray matter lesions or cortical injury (watershed areas)

Exclusion of the following conditions: abnormal fetal growth, maternal infections, fetomaternal hemorrhage, neonatal sepsis, or chronic placental lesions

Patients were classified into two groups based on the Sarnat & Sarnat classification as Stage 2 and Stage 3 encephalopathy (14).

During the study period, the Arctic Sun® (Medivance, Inc., Louisville, CO) hypothermia device was used for whole-body cooling. Therapeutic hypothermia treatment was applied according to protocols lasting 72 hours, followed by slow rewarming, in line with current guidelines (15).

Data on the number of days the patients remained intubated were obtained from physician observations and nurse records. The duration and need for oxygen support were documented. aEEG was performed on all neonates receiving therapeutic hypothermia, and aEEG traces were categorized as normal or abnormal based on voltage and pattern classification. Neonates receiving anticonvulsant therapy were also recorded.

The Bayley Scales of Infant and Toddler Development (BSID), developed by Nancy Bayley in 1969, is designed to assess the neurodevelopment of children aged 1-42 months. While BSID-II evaluates cognitive, motor, and behavioral domains, BSID-III consists of subscales that assess cognitive, language, motor, social-emotional development, and adaptive behaviors (16, 17). This scale not only provides detailed information about the developing skills of the child from birth but also offers a comprehensive evaluation of children by integrating parental questionnaires (16).

At the second-year follow-up, neurodevelopmental assessments were conducted using the BSID-II by a Developmental Pediatrician and Child Development Specialists. Mental Development Index (MDI) and Psychomotor Development Index (PDI) scores were evaluated (17). Standardized scores were calculated with a mean score of 100 and a standard deviation (SD) of 15. Scores below -2 SD were considered abnormal. Scores between -2 SD and -3 SD (50-69 points) were categorized as moderate delay, while scores below -3 SD (<50 points) were categorized as severe delay. Neurodevelopmental impairment (NDI) was defined as a score below 70 on at least one of the indices (17).

Statistical Analysis

The demographic characteristics, encephalopathy staging, and BSID-II scores of the infants were recorded. Statistical analyses

were performed using the IBM Statistical Package for the Social Sciences, version 22.0 (SPSS Inc., Armonk, NY, IBM Corp., USA). The demographic characteristics of the infants were expressed as frequency and percentage. The normality of the variables was assessed using visual and analytical methods. Descriptive analyses were presented as mean and standart deviation for normally distributed variables. Independent group comparisons for normally distributed variables were performed using the independent samples t-test. Categorical variables were compared using the Fisher's exact test. A $p<0.050$ was considered statistically significant for all tests.

RESULTS

A total of 138 toddlers who had previously received therapeutic hypothermia treatment and presented for their second-year follow-up were included in the study. According to the Sarnat & Sarnat classification, 75 patients were categorized as Stage 2 encephalopathy and 63 patients as Stage 3 encephalopathy. The demographic and clinical characteristics of the patients are summarized in Table I. The mean birth weight of the patients was 3410±447 g in the Stage 2 group and 3321±592 g in the Stage 3 group. Gestational age was 39.1±1.3 weeks for the Stage 2 group and 38.7±1.5 weeks for the Stage 3 group. There were no statistically significant differences between the two groups in terms of birth weight or gestational age (p= 0.317 and p=0.081, respectively). Additionally, no significant differences were found between the groups regarding gender (p=0.397).

In the Stage 3 group, one out of three infants underwent cardiopulmonary resuscitation (CPR), while one out of seven infants in the Stage 2 group required CPR (p=0.002). According to umbilical cord blood gas results, no differences were observed between the two groups in terms of pH and HCO3 levels, but BE was found to be higher in the Stage 3 group (p=0.001).

Infants in the Stage 3 encephalopathy group required more respiratory support, including oxygen and mechanical ventilation, compared to the Stage 2 group (p=0.020 and p=0.001, respectively). Abnormalities in aEEG were more frequently observed in the Stage 3 group, and a higher proportion of these infants required anticonvulsant therapy (p<0.001 and p<0.001, respectively).

The mean Mental Development Index (MDI) score for infants with Stage 2 encephalopathy was 89±17, while the mean Psychomotor Development Index (PDI) score was 94±18 (Table II). For infants with Stage 3 encephalopathy, the mean MDI score was 84±10, and the mean PDI score was 71±11 (p=0.049 and p=0.001, respectively). Neurodevelopmental impairment (NDI) was identified in one out of three infants in the Stage 3 group, compared to one out of six infants in the Stage 2 group (p=0.012).

Table I: Demographic and clinical characteristics of the patients.

	Stage 2	Stage 3	p
Number of patients	75	63	-
Gestational week*	39.1±1.3	38.7±1.5	0.081
Birth weight, gram*	3410±447	3321±592	0.317
C/S†	37 (49)	31 (49)	1.000
Male gender†	36 (48)	35 (55)	0.397
CPR†	10 (13)	23 (36)	0.002
pH*	6.88±0.07	6.86±0.06	0.075
HCO3*	8.85±1.7	8.86±1.5	0.989
BE*	-17.8±1.3	-19.4±1.5	0.001
Days of mechanical ventilation*	2.5±2.3	7.8±9	0.001
Total respiratory support days (O_2 days) **	4.9±2.3	8.8±10	0.020
Disorder in aEEG †	25 (33.3)	40 (63.4)	<0.001
Anticonvulsant history†	30 (40.0)	51 (80.9)	<0.001

:** *mean±SD (independent samples t-test),* **†:** *n(%) (Fisher's exact test),* ***C/S: *Cesarean section,* ***CPR:*** *Cardiopulmonary Resuscitation,* ***HCO3:*** *bicarbonate,* ***BE:*** *Base Excess,* ***aEEG:*** *amplitude-integrated electroencephalography*

Table II: Neurodevelopmental outcomes of the patients.

	Stage 2	Stage 3	p
MDI*	89±17	84±10	0.049
PDI*	94±18	71±11	0.001
NDI †	13 (17.3)	23 (36.5)	0.012

:** *mean±SD (independent samples t-test),* **†:** *n(%) (Fisher's exact test),* ***MDI: *Mental Development Index,* ***PDI:*** *Psychomotor Development Index,* ***NDI:*** *Neurodevelopmental Impairment*

DISCUSSION

In our study, we observed that the neurodevelopmental scores of patients classified as Stage 3 according to the Sarnat & Sarnat classification and treated with hypothermia were lower than those in Stage 2. These patients required more respiratory support in intensive care units, had more abnormalities detected in aEEG results, and received anticonvulsant therapy more frequently. Given that the first two years of life are critical for establishing the foundations of life and completing a significant portion of brain development, it is essential that these patients are followed by specialized teams. As a center that has been implementing therapeutic hypothermia for HIE for many years, we aimed to share these data, which involve a substantial number of patients. Reviewing the situation in our country and evaluating the outcomes of patients classified as Stage 2 and 3 and treated with therapeutic hypothermia not only provides valuable insights for clinicians but also allows for the evaluation of the long-term effectiveness of applied treatments. Moreover, despite the identical therapeutic hypothermia protocol being

used for these two groups, we demonstrated that there can be differences in their neonatal intensive care follow-up and outcomes in the first two years of life.

Hypoxic-ischemic encephalopathy (HIE) is a significant clinical syndrome that can affect long-term neurodevelopmental outcomes (18). Various studies have reported that early initiation of therapeutic hypothermia treatment after the diagnosis of HIE reduces mortality and improves neurodevelopmental outcomes (18, 19). These findings underscore the critical importance of developing effective strategies to prevent HIE and ensuring the timely initiation of therapeutic hypothermia to improve patient outcomes.

Similar to our findings, a retrospective study conducted in Türkiye by Çelik et al. (20) also emphasized that, despite receiving therapeutic hypothermia, nearly half of the surviving infants with HIE showed neurodevelopmental impairments at follow-up. In their cohort of 47 patients, the median MDI and PDI scores were significantly lower in infants with severe HIE compared to those with moderate HIE, and only 44.6% of the cohort had normal BSID-II scores (20).

In a study conducted in England evaluating the two-year neurological outcomes of 107 children followed with a diagnosis of neonatal HIE, significant deterioration in the BSID-III scores was observed in the group with minor neurological signs compared to the group with normal neurological examinations (21). Although the BSID-III scale was used in that study, the results are consistent with our findings.

In another study evaluating the neurodevelopmental outcomes of 29 HIE cases, 11 patients were found to have brain injury on neonatal MR imaging. At the second-year follow-up, 6 patients had normal outcomes, while 5 had neurodevelopmental issues (22). Although our study does not include neuroimaging data, we found that the neurodevelopmental outcomes of patients with Stage 3 encephalopathy were worse than those of the other group.

Our study utilized the BSID-II. A study comparing the BSID-II and BSID-III found that, in infants diagnosed with neonatal encephalopathy at 18 months, BSID-III scores were higher than BSID-II scores. According to this study, BSID-III scores reduced the proportion of infants classified as severely impaired (23). Similar findings have been reported in other studies (24,25). These findings raise the question of whether BSID-II underestimates scores or BSID-III overestimates neurodevelopmental scores. Both possibilities remain plausible, and further studies will provide more clarity on this matter.

In neonatal hypoxic-ischemic encephalopathy, the therapeutic hypothermia protocol applied in Stage 2 and Stage 3 cases is identical. However, the findings during neonatal intensive care and neurodevelopmental outcomes differ between these groups, necessitating different approaches during follow-up. Further studies are needed to propose strategies for managing these patients effectively.

Although the BSID-II is no longer the most current version, it was the standard neurodevelopmental assessment tool used in our institution during the study period. Several comparative studies have indicated that BSID-III often yields higher scores than BSID-II, potentially underestimating developmental delays. As such, the use of BSID-II in this study may present a more conservative estimate of neurodevelopmental impairment. Despite these differences, our results remain relevant and provide a valuable historical benchmark for comparing outcomes across different time periods and assessment tools. Future studies employing BSID-III or BSID-IV may benefit from these findings by evaluating trends in developmental trajectories following therapeutic hypothermia.

Limitations

One significant limitation of our study is the use of the BSID-II system for neurodevelopmental evaluation. However, during the study period, BSID-II was still in use, and all high-risk infants were regularly followed up by an experienced developmental pediatrics unit, where detailed testing and examinations were performed.

The lack of data on cerebral palsy history, hearing, and vision status represents another limitation of our study. Additionally, routine imaging was not performed in the early period, and we were unable to access imaging results, which is a notable drawback. Although nearly all patients underwent cranial ultrasonography, it was not useful for either diagnosis or follow-up in HIE cases, so no additional data analysis was performed. Since cranial MRI was not available in the hospital where the patients were included in the study, and some patients were transferred to other hospitals for cranial MRI, imaging data were incomplete and not analyzed.

A more comprehensive cohort plan could have identified which patients were lost to follow-up, failed to attend follow-ups, or discontinued follow-up care. However, we were able to include only the infants who attended the two-year follow-up, which likely represents those with the best clinical course. Therefore, our results should be interpreted in light of this limitation. Including long-term outcomes of Stage I patients and those who did not receive hypothermia would have strengthened the study. Future studies incorporating these groups, especially those investigating borderline cases or patients with uncertain indications for hypothermia, are needed.

Ethics committee approval

This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by Ankara Bilkent City Hospital (12.03.2020, reference number: E1-19-165).

Contribution of the authors

Küçükoğlu Keser M: Planning methodology to reach the conclusions, Organizing, supervising the course of progress and tak-

ing the responsibility of the research/study, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. ***Kadıoğlu Şimşek G:*** Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the conclusions, Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. ***Beşer E:*** Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the conclusions, Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in necessary literature review for the study, Reviewing the article before submission scientifically besides spelling and grammar. ***Okman E:*** Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the conclusions, Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in necessary literature review for the study, Reviewing the article before submission scientifically besides spelling and grammar. ***Kanmaz Kutman HG:*** Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the conclusions, Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar.

Source of funding

The authors declare the study received no funding.

Conflict of interest

The authors declare that there is no conflict of interest.

Acknowledgment:

We would like to express our sincere respects and gratitude to our esteemed Prof. Dr. Zeynep ÜSTÜNYURT, who carried out the neurodevelopmental follow-up of all our risky infants during the period we worked together.

REFERENCES

1. Russ JB, Simmons R, Glass HC. Neonatal encephalopathy: beyond hypoxic-ischemic encephalopathy. Neoreviews. 2021;22(3):e148-e62. https://doi.org/10.1542/neo.22-3-e148
2. Martinello K, Hart AR, Yap S, Mitra S, Robertson NJ. Management and investigation of neonatal encephalopathy: 2017 update. Arch Dis Child Fetal Neonatal Ed. 2017;102(4):F346-F58. https://doi.org/10.1136/archdischild-2015-309639
3. Tierradentro-García LO, Saade-Lemus S, Freeman C, Kirschen M, Huang H, Vossough A, et al. Cerebral blood flow of the neonatal brain after hypoxic-ischemic injury. A J perinatol. 2023;40(05):475-88. https://doi.org/10.1055/s-0041-1731278
4. Akisu M, Kumral A, Canpolat FE. Turkish Neonatal Society Guideline on neonatal encephalopathy. Turk Pediatri Ars. 2018;53(Suppl 1):S32-S44. https://doi.org/10.5152/TurkPediatriArs.2018.01805
5. Sandoval Karamian AG, Mercimek-Andrews S, Mohammad K, Molloy EJ, Chang T, Chau V, et al. Neonatal encephalopathy: Etiologies other than hypoxic-ischemic encephalopathy. Semin Fetal Neonatal Med. 2021;26(5):101272. https://doi.org/10.1016/j.siny.2021.101272
6. Cornet M-C, Kuzniewicz M, Scheffler A, Forquer H, Hamilton E, Newman TB, et al. Perinatal hypoxic-ischemic encephalopathy: incidence over time within a modern US birth cohort. Pediatr Neurol. 2023;149:145-50. https://doi.org/10.1016/j.pediatrneurol.2023.08.037
7. Ristovska S, Stomnaroska O, Danilovski D. Hypoxic Ischemic Encephalopathy (HIE) in Term and Preterm Infants. Pril (Makedon Akad Nauk Umet Odd Med Nauki). 2022;43(1):77-84. https://doi.org/10.2478/prilozi-2022-0013
8. Pisani F, Fusco C, Nagarajan L, Spagnoli C. Acute symptomatic neonatal seizures, brain injury, and long-term outcome: the role of neuroprotective strategies. Expert Rev Neurother. 2021;21(2):189-203. https://doi.org/10.1080/14737175.2021.1848547
9. Park J, Park SH, Kim C, Yoon SJ, Lim JH, Han JH, et al. Growth and developmental outcomes of infants with hypoxic ischemic encephalopathy. Sci Rep. 2023;13(1):23100. https://doi.org/10.1038/s41598-023-50187-0
10. Lee BL, Glass HC. Cognitive outcomes in late childhood and adolescence of neonatal hypoxic-ischemic encephalopathy. Clin Exp Pediatr. 2021;64(12):608. https://doi.org/10.3345/cep.2021.00164
11. Trivedi SB, Vesoulis ZA, Rao R, Liao SM, Shimony JS, McKinstry RC, et al. A validated clinical MRI injury scoring system in neonatal hypoxic-ischemic encephalopathy. Pediatric Radiol. 2017;47:1491-9. https://doi.org/10.1007/s00247-017-3893-y
12. Perez JMR, Golombek SG, Sola A. Clinical hypoxic-ischemic encephalopathy score of the Iberoamerican Society of Neonatology (Siben): a new proposal for diagnosis and management. Rev Assoc Méd Bras. 2017;63(1):64-9. https://doi.org/10.1590/1806-9282.63.01.64
13. Mendler MR, Mendler I, Hassan MA, Mayer B, Bode H, Hummler HD. Predictive value of Thompson-score for long-term neurological and cognitive outcome in term newborns with perinatal asphyxia and hypoxic-ischemic encephalopathy undergoing controlled hypothermia treatment. Neonatology. 2018;114(4):341-7. https://doi.org/10.1159/000490721
14. Sarnat HB, Flores-Sarnat L, Fajardo C, Leijser LM, Wusthoff C, Mohammad K. Sarnat grading scale for neonatal encephalopathy

after 45 years: an update proposal. Pediatr Neurol. 2020;113:75-9. https://doi.org/10.1016/j.pediatrneurol.2020.08.014

15. Proietti J, Boylan GB, Walsh BH. Regional variability in therapeutic hypothermia eligibility criteria for neonatal hypoxic-ischemic encephalopathy. Pediatr Res. 2024;96(5):1153-61. https://doi.org/10.1038/s41390-024-03184-6
16. Bayley N. Bayley-III: Bayley Scales of infant and toddler development: Giunti OS Florence, Italy; 2009.
17. Bayley N. Manual fort he Bayley Scales of Infant Development. 2nd ed. San Antonio, TX: The Psychological Corporation; 1993.
18. Goswami I, Guillot M, Tam EW, editors. Predictors of long-term neurodevelopmental outcome of hypoxic-ischemic encephalopathy treated with therapeutic hypothermia. Semin Neurol. 2020;40(3):322-34. https://doi.org/10.1055/s-0040-1702939
19. Cainelli E, Vedovelli L, Mastretta E, Gregori D, Suppiej A, Bisiacchi PS. Long-term outcomes after neonatal hypoxic-ischemic encephalopathy in the era of therapeutic hypothermia: a longitudinal, prospective, multicenter case-control study in children without overt brain damage. Children. 2021;8(11):1076. https://doi.org/10.3390/children8111076
20. Çelik P. Hipoksik İskemik Ensefalopati Nedeniyle Terapötik Hipotermi Uygulanan Bebeklerin Nörogelişimsel Sonuçları. Turkish J Pediatr Dis. 2021;15(5):359-64. https://doi.org/10.12956/tchd.788065
21. Edmonds CJ, Helps SK, Hart D, Zatorska A, Gupta N, Cianfaglione R, et al. Minor neurological signs and behavioural function at age 2 years in neonatal hypoxic ischaemic encephalopathy (HIE). Eur J Paediatr Neurol. 2020;27:78-85. https://doi.org/10.1016/j.ejpn.2020.04.003
22. Al Amrani F, Kwan S, Gilbert G, Saint-Martin C, Shevell M, Wintermark P. Early Imaging and Adverse Neurodevelopmental Outcome in Asphyxiated Newborns Treated With Hypothermia. Pediatr Neurol. 2017;73:20-7. https://doi.org/10.1016/j.pediatrneurol.2017.04.025
23. Jary S, Whitelaw A, Walløe L, Thoresen M. Comparison of Bayley-2 and Bayley-3 scores at 18 months in term infants following neonatal encephalopathy and therapeutic hypothermia. Dev Med Child Neurol. 2013;55(11):1053-9. https://doi.org/10.1111/dmcn.12208
24. Moore T, Johnson S, Haider S, Hennessy E, Marlow N. Relationship between test scores using the second and third editions of the Bayley Scales in extremely preterm children. J Pediatr. 2012;160(4):553-8. https://doi.org/10.1016/j.jpeds.2011.09.047
25. Çelik P, Sucakli IA, Yakut HI. Which Bayley-III cut-off values should be used in different developmental levels? Turk J Med Sci. 2020;50(4):764-70. https://doi.org/10.3906/sag-1910-69