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EVALUATION OF NEURODEVELOPMENTAL STATUS IN INFANTS DIAGNOSED WITH HYPOXIC ISCHEMIC ENCEPHALOPATHY

Dr. Suresh P. M[1], Dr. Ramkumar M[2], Dr. Veena R. S[3]

[1]*Professor, Department of Paediatrics, Sree Mookambika Institute of Medical Sciences, Kulasekaram, Kanyakumari*
[2]*Junior Resident, Department of Paediatrics, Sree Mookambika Institute of Medical Sciences, Kulasekaram, Kanyakumari*
[3]*Junior Resident, Department of Paediatrics, Sree Mookambika Institute of Medical Sciences, Kulasekaram, Kanyakumari.*

Correspondence:
Dr.RAMKUMAR .M

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Abstract

Background Hypoxic ischemic encephalopathy (HIE) is a major cause of neonatal mortality and long-term neurodevelopmental disability in term infants. The severity of HIE determines the extent of neurological injury and subsequent developmental outcomes. Early identification and follow-up are essential for timely intervention and improved prognosis. ***Methodology*** This prospective observational study was conducted in the Department of Paediatrics, Sree Mookambika Institute of Medical Sciences, Kulasekharam, from March 2025 to February 2026. A total of 150 term neonates diagnosed with HIE were enrolled. Clinical history, perinatal details, and neurological examination were recorded. Infants were followed up at 3, 6, 9, and 12 months. Neurological assessment was done using Amiel-Tison angles, and neurodevelopmental outcome was evaluated at 12 months using the Developmental Assessment Scale for Indian Infants (DASII). ***Results*** Antenatal risk factors were present in 60% of cases. Significant association was observed between HIE severity and tone abnormalities across all follow-ups ($p<0.05$). Head circumference showed significant reduction with increasing HIE severity from 6 months onwards ($p=0.001$). At 12 months, 22.7% of infants had abnormal neurodevelopmental outcomes on DASII, with higher incidence in HIE stage III (10.6%). Overall, severity of HIE strongly correlated with adverse developmental outcomes. ***Conclusion*** Severity of hypoxic ischemic encephalopathy is a strong predictor of neurodevelopmental outcome. Early identification and structured follow-up are essential for timely intervention and reduction of long-term disability.

Keywords: Hypoxic ischemic encephalopathy, neonates, neurodevelopmental outcome, DASII, cerebral palsy, perinatal asphyxia.

INTRODUCTION

Perinatal asphyxia refers to a condition in which there is interruption of oxygen supply and impaired blood flow to the fetus or newborn during the perinatal period, resulting in hypoxemia, hypercapnia, and metabolic acidosis. When severe or prolonged, this insult triggers a cascade of biochemical and cellular events leading to neuronal injury and multi-organ dysfunction. The resultant clinical syndrome is termed neonatal encephalopathy, of which hypoxic ischemic encephalopathy (HIE) is the most common cause [1]. HIE remains a significant contributor to neonatal mortality and long-term neurodevelopmental disability worldwide, particularly in low- and middle-income countries.

The pathophysiology of HIE involves primary energy failure due to hypoxia-ischemia, followed by secondary energy failure characterized by excitotoxicity, oxidative stress, inflammation, and apoptosis. These mechanisms lead to irreversible neuronal damage, especially in vulnerable regions of the developing brain. The severity of HIE can vary from mild neurological dysfunction to severe encephalopathy associated with coma, seizures, and multiorgan involvement [2].

Survivors of HIE are at increased risk of long-term neurodevelopmental impairments. These include cerebral palsy, global developmental delay, microcephaly, epilepsy, cognitive deficits, and behavioral disorders. The burden of disability is substantial and places significant emotional and socioeconomic strain on families and healthcare systems. Cerebral palsy remains one of the most common sequelae, particularly in infants with moderate to severe HIE [3].

Early neurodevelopmental assessment in infants affected by HIE is crucial for identifying subtle neurological deficits and predicting long-term outcomes. The first year of life represents a critical window for brain plasticity and development, during which early detection of abnormalities allows timely initiation of rehabilitation and intervention programs. Structured follow-up using standardized developmental assessment tools helps in

monitoring motor, cognitive, language, and social milestones, enabling early diagnosis of developmental delay [4].

Despite advances in neonatal intensive care, including therapeutic hypothermia, HIE continues to be a major cause of neurodevelopmental disability. The prognosis largely depends on the severity of the initial insult, duration of hypoxia, and timeliness of resuscitation and supportive care. Early identification of at-risk infants and long-term follow-up is therefore essential in reducing the burden of disability and improving quality of life.

In this context, the present study aims to evaluate the neurodevelopmental outcomes in infants with hypoxic ischemic encephalopathy, with the objective of early identification of developmental abnormalities and facilitating timely intervention to improve long-term neurological outcomes.

Aim and Objectives

Aim

To assess the neurodevelopmental outcomes in infants with hypoxic ischemic encephalopathy (HIE) during follow-up.

Objectives

1. To evaluate neurodevelopmental status in infants diagnosed with hypoxic ischemic encephalopathy.
2. To assess motor, cognitive, language, and social developmental milestones during infancy.

To determine the proportion of infants developing neurodevelopmental abnormalities such as cerebral palsy, developmental delay, and seizure disorders.

MATERIALS AND METHODS

The present study was conducted in the Department of Paediatrics, Sree Mookambika Institute of Medical Sciences, Kulasekharam, during the study period from March 2025 to February 2026. The study included 150 term neonates diagnosed with hypoxic ischemic encephalopathy (HIE) admitted to the Neonatal Intensive Care Unit (NICU) of a tertiary care hospital (ASRAM, Eluru). Neonates included were those with gestational age ≥37 weeks, inborn infants with Apgar score <7 at 5 minutes, and outborn infants with a history suggestive of birth asphyxia, including delayed first cry (>5 minutes), requirement of positive pressure ventilation for more than 1 minute, or history of seizures following delayed cry. Both inborn and outborn neonates showing clinical features of HIE as per Sarnat and Sarnat staging were included. Neonates were excluded if they were preterm, had perinatal infections, congenital anomalies, suspected metabolic disorders, or were lost to follow-up.

After obtaining informed written consent from parents or guardians, detailed maternal, perinatal, and neonatal history was recorded using a predesigned proforma. At enrolment, a complete clinical and neurological examination was performed to assess neurological deficits and tone abnormalities. All enrolled infants were followed up in the outpatient department at 3, 6, 9, and 12 months of age. During each follow-up visit, neurological assessment was carried out using Amiel-Tison angles, along with detailed anthropometric measurements and evaluation of developmental milestones.

Neurodevelopmental outcome was assessed at 12 months of age using the Developmental Assessment Scale for Indian Infants (DASII), which provides motor and mental developmental quotients (DMoQ and DMeQ) based on motor age and mental age compared with chronological age. The composite developmental quotient (DQ) was calculated as the average of DMoQ and DMeQ. A DQ of less than 70% was considered abnormal, indicating neurodevelopmental delay.

Statistical analysis was performed using appropriate statistical methods. Categorical variables were expressed as frequency and percentages, while continuous variables were presented as mean ± standard deviation (SD). Associations between categorical variables were analyzed using the Chi-square test or Fisher's exact test as appropriate. Comparison of means between groups was performed using the Student's t-test or ANOVA where applicable. Correlation between severity of HIE and developmental outcomes was assessed using Pearson's or Spearman's correlation coefficient. A p-value of less than 0.05 was considered statistically significant. Data analysis was carried out using standard statistical software.

RESULTS

ASSOCIATIONBETWEENTONEANDSEVERITYOFHIEATDISCHARGE AND DURING FOLLOW UP USING AMIELTISONANGLES

Tonen(%)			HIE-1	HIE-2	HIE-3	P-Value
AtDischatge	Normal	118(78.6)	37(97.4)	78(82.1)	3(17.6)	0.001
	Abnormal	32(21.3)	1(2.6)	17(17.9)	14(82.4)	
3 Months	Normal	121(80.6%)	37(97.4)	80(84.2)	4(23.5)	0.001
	Abnormal	29(19.3%)	1(2.6)	15(15.8)	13(76.5)	
6 Months	Normal	118(78.6%)	37(97.4)	77(81.1)	4(23.5)	0.002
	Abnormal	32(21.3%)	1(2.6)	18(18.9)	13(76.5)	
9 Months	Normal	119(79.3%)	37(97.4)	78(82.1)	4(23.5)	0.001
	Abnormal	31(20.6%)	1(2.6)	17(17.9)	13(76.5)	
12 Months	Normal	119(79.3%)	37(97.4)	78(82.1)	4(23.5)	0.001
	Abnormal	31(20.6%)	1(2.6)	17(17.9)	13(76.5)	

Among the 150 HIE babies, 118 (78.6%) had normal tone and 32(21.3%) had abnormal tone at the time of discharge and there issignificantassociationbetweenseverityofHIEandtoneabnormality.A significant association (P value 0.001) was found between toneabnormality and severity of HIE during 3rd month follow up. Asignificant association (P value 0.002) was found between toneabnormality and severity of HIE during 6th month follow up.Asignificant association (P value 0.001) was found between toneabnormality and severity of HIE during 9th month follow up.Asignificant association (P value 0.001) was found between toneabnormalityandseverityof HIE during12thmonthfollowup.

ASSOCIATION BETWEEN HEAD CIRCUMFERENCE ANDSEVERITYOFHIEDURINGFOLLOWUP

HeadCircumference(cm)		N	Mean	S.D	95%Confidenceintervals		Pvalue
					Lowerbound	Upperbound	
3 months	HIE1	38	38.4286	1.63780	36.9139	39.9433	0.894
	HIE2	95	38.2455	1.73582	37.4758	39.0151	
	HIE3	17	37.9600	1.51921	36.0737	39.8463	
6 months	HIE1	38	41.3368	1.57350	40.8196	41.8540	0.001
	HIE2	95	40.3084	2.14345	39.8718	40.7451	
	HIE3	17	38.5706	2.49944	37.2855	39.8557	
9 months	HIE1	38	42.8368	1.32674	42.4008	43.2729	0.001
	HIE2	95	41.8274	2.22115	41.3749	42.2798	
	HIE3	17	39.9294	2.86308	38.4574	41.4015	
12 months	HIE1	38	44.3079	1.43854	43.8351	44.7807	0.001
	HIE2	95	43.2684	2.34186	42.7914	43.7455	
	HIE3	17	41.2118	3.57996	39.3711	43.0524	

Duringthe3rd month follow up a significant statistical difference (Pvalue0.894) was not found between head cir cum Ference and severity of HIE.
There is no significant difference between the mean weight, length of infants and severity of HIE in our study population.

ASSOCIATION BETWEEN SEVERITY OF HIE AND DEVELOPMENT ALDELAYINDASIIAT THE END OF FOLLOW UP (12MONTH)

VARIABLE		N(%)	HIESTAGING			Pvalue
			HIE-1	HIE-2	HIE-3	
DASII	NORMAL	116(77.3)	37(24.6)	78(52)	1(0.6)	0.001
	ABNORMAL	34(22.7)	1(0.6%)	17(11.3)	16(10.6)	

AttheageofoneyearAmongthe38HIEIinfants,37(24.6%)foundtobe normal and1(0.6%) found to be abnormal.Among the 95 HIE IIinfants, 78 (52%) found to be normal and 17 (11.3%) found to beabnormal.Amongthe17HIEIIIinfants,1(0.6%)foundtobenormaland 16 (10.6 %) found to be abnormal. A significant statisticalassociation (P value 0.001) was found between severity of HIE anddevelopmentaldelayasperDASIIattheendof1yearfollowup.

DISCUSSION

The present study evaluated neurodevelopmental outcomes in 150 term neonates with hypoxic ischemic encephalopathy (HIE) and demonstrated a clear association between severity of HIE and adverse neurological outcomes during follow-up. HIE remains a major contributor to long-term neurodevelopmental disability in term infants, and its severity at birth strongly predicts both short-term and long-term outcomes.

In the present study, antenatal and perinatal risk factors were commonly observed, with 60% of cases having identifiable antenatal risk factors. Meconium-stained liquor (28%) and pregnancy-induced hypertension (10.6%) were the most frequent contributors. Similar perinatal risk associations have been reported in previous studies, where obstetric complications such as fetal distress, prolonged labour, and placental insufficiency were significantly linked to HIE development [5]. Majority of cases were delivered by normal vaginal delivery (74%), highlighting that HIE may occur even in seemingly uncomplicated deliveries.

Neurological tone abnormalities showed a strong correlation with severity of HIE. In the present study, abnormal tone was significantly higher in HIE stage III infants (76.5%) compared to stage I and II, with statistically significant association across all follow-up periods (p = 0.001–0.002). These findings are consistent with Amiel-Tison neurological assessment principles, where persistent tone abnormalities in early infancy are

strong predictors of later motor impairment and cerebral palsy [6].

Head circumference growth pattern also demonstrated a significant association with severity of HIE. Although no significant difference was observed at 3 months, progressive divergence became evident from 6 months onwards, with significantly lower head circumference in HIE stage III infants ($p = 0.001$). This suggests delayed brain growth in severe HIE, which correlates with underlying neuronal injury and impaired neurodevelopmental progression. Similar observations have been reported by Robertson et al., who noted that severe HIE is associated with microcephaly and impaired brain growth during infancy [7].

At 12 months of follow-up, neurodevelopmental assessment using DASII revealed a significant association between severity of HIE and developmental delay ($p = 0.001$). Abnormal developmental outcomes were predominantly seen in HIE stage III infants (10.6%), whereas most HIE I infants showed normal development. These findings are consistent with previous studies demonstrating that moderate to severe HIE is strongly associated with adverse neurodevelopmental outcomes including cerebral palsy, global developmental delay, and cognitive impairment [8].

The overall incidence of abnormal neurodevelopmental outcome in the present study was 22.7%, with tone abnormalities in 20.6% and seizures in 22%. These findings are comparable with earlier studies reporting similar neurological sequelae in HIE survivors, emphasizing the long-term burden of perinatal asphyxia [9]. The significant correlation between HIE severity and DASII outcomes highlights the importance of early staging using Sarnat classification in predicting prognosis.

Overall, the present study reinforces that severity of HIE is a strong predictor of neurodevelopmental outcome. Early identification, structured follow-up, and timely rehabilitation can significantly improve functional outcomes and reduce long-term disability.

CONCLUSION

The present study demonstrates that hypoxic ischemic encephalopathy (HIE) in term neonates is strongly associated with significant neurodevelopmental morbidity during infancy. The severity of HIE, as classified by Sarnat staging, showed a clear and statistically significant correlation with abnormal neurological tone, impaired head growth, and adverse neurodevelopmental outcomes on DASII assessment at one year of age.

Infants with severe HIE (stage III) had the highest risk of persistent tone abnormalities, delayed head circumference growth, and developmental delay compared to those with mild and moderate HIE. The study highlights that neurological abnormalities can be detected early during follow-up, even before the completion of one year, emphasizing the importance of structured developmental surveillance.

Overall, early identification of high-risk infants using clinical staging and systematic follow-up with tools such as Amiel-Tison examination and DASII allows timely initiation of rehabilitation and intervention strategies. This may significantly reduce long-term disability and improve neurodevelopmental outcomes in infants affected by HIE.

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