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RESEARCH ARTICLE

NEURODEVELOPMENTAL OUTCOME AT ONE YEAR OF AGE IN NEONATES WITH HYPOXIC ISCHAEMIC ENCEPHALOPATHY TREATED WITH SERVO-CONTROLLED WHOLE BODY THERAPEUTIC HYPOTHERMIA: A PROSPECTIVE DESCRIPTIVE STUDY

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ABSTRACT

Background: Hypoxic ischaemic encephalopathy (HIE) is a significant cause of neonatal mortality and long-term neurodevelopmental morbidity. Therapeutic hypothermia (TH) is the established standard of care for neonates with moderate to severe HIE. **Aim:** To determine mortality and neurodevelopmental outcome at one year of age in neonates with HIE Grade II/III who underwent whole body therapeutic hypothermia using a servo-controlled device. **Methods:** A prospective descriptive study was conducted at a Level 3A NICU from June 2018 to May 2020. Neonates of gestational age ≥36 weeks admitted within 6 hours of birth, fulfilling TOBY trial-based physiological and neurological eligibility criteria, were enrolled (n=35). Whole body cooling was administered using Tecotherm Neo™ at a target rectal temperature of 33.5°C for 72 hours, followed by gradual rewarming. Neurodevelopmental assessment was performed using the modified Hammersmith neurological examination at discharge and the Trivandrum Developmental Screening Chart (TDSC) at one year of age. Statistical analysis was performed using Chi-square test; $p<0.05$ was considered significant. **Results:** Of 35 enrolled neonates, 30 (85.7%) survived to discharge. At one year follow-up, 25 of 30 survivors (83.3%) demonstrated normal neurodevelopmental outcome on TDSC. Requirement for invasive ventilation during cooling ($p=0.016$) and delayed establishment of direct breastfeeding beyond 48 hours ($p=0.003$) were significant predictors of adverse neurodevelopmental outcome. **Conclusion:** Therapeutic hypothermia using a servo-controlled device is associated with favorable survival and neurodevelopmental outcomes in neonates with HIE Grade II/III in an Indian tertiary NICU setting. Invasive ventilation requirement and delayed breastfeeding are clinically useful prognostic markers for adverse outcomes at one year.

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INTRODUCTION

Hypoxic ischaemic encephalopathy (HIE) remains one of the most devastating conditions encountered in neonatal medicine, contributing substantially to neonatal mortality and long-term neurodevelopmental disability worldwide. It occurs as a consequence of perinatal asphyxia, wherein a compromised oxygen supply to the neonatal brain triggers a cascade of cellular injury, culminating in neuronal death.[1,2] Globally, perinatal asphyxia accounts for approximately 23% of all neonatal deaths, and among surviving infants, a significant proportion sustain permanent neurological sequelae including cerebral palsy, cognitive impairment, epilepsy, and sensory deficits. In India, the burden is disproportionately higher, with perinatal asphyxia being among the leading contributors to neonatal mortality, particularly in outborn and resource-constrained settings.[3] The pathophysiology of HIE is characterised by a biphasic injury pattern. The primary phase occurs immediately following the hypoxic-ischaemic insult, with depletion of ATP, failure of ion pumps, cytotoxic oedema, and acute neuronal necrosis. This is followed by a latent phase of partial recovery, which transitions into a secondary phase of energy failure approximately 6–24 hours after the initial insult. The secondary phase is driven by excitotoxicity, oxidative stress, mitochondrial dysfunction, and activation of apoptotic pathways.[1] Crucially, the secondary phase represents a therapeutic window during which intervention can mitigate ongoing neuronal injury. Therapeutic hypothermia exploits this window by reducing cerebral metabolic rate, attenuating excitotoxic neurotransmitter release, suppressing free radical

production, and inhibiting apoptotic cascades, thereby limiting the extent of secondary neuronal death.[4,5] The evidence base for therapeutic hypothermia in moderate to severe HIE has been established through several landmark randomised controlled trials. The TOBY trial demonstrated that whole body cooling to 33–34°C for 72 hours significantly increased the rate of survival without neurodevelopmental disability at 18 months.

The CoolCap trial, utilising selective head cooling, similarly reported a reduction in death or severe neurodisability in neonates with less severe amplitude-integrated EEG changes.[6] The NICHD trial by Shankaran *et al*. demonstrated a significant reduction in the combined outcome of death or moderate-to-severe disability at 18–22 months in cooled infants. Subsequent meta-analyses have consistently confirmed that therapeutic hypothermia reduces the risk of death or major neurodevelopmental disability with a number needed to treat of approximately 7–8, making it one of the most effective neonatal neuroprotective interventions available.[7]

The technology for delivering therapeutic hypothermia has evolved considerably. Early methods of passive and manually regulated cooling were associated with temperature instability and overcooling, which carry independent risks of adverse outcomes including cardiac arrhythmias, coagulopathy, and pulmonary hypertension. Servo-controlled automated devices, such as the Tecotherm Neo™, allow precise and consistent maintenance of target core body temperature, reducing temperature variability and associated risks.

The adoption of such devices in Indian tertiary NICUs has grown steadily; however, outcome data from these settings remain sparse compared to high-income countries.[6,8] Neurodevelopmental follow-up beyond the neonatal period is essential for a comprehensive understanding of TH outcomes. The modified Hammersmith neurological examination provides a standardised assessment of neurological integrity at discharge, while tools such as the Trivandrum Developmental Screening Chart (TDSC) offer a validated, culturally appropriate, and resource-friendly means of assessing developmental milestones at follow-up visits in the Indian context. The TDSC has demonstrated robust sensitivity and specificity for identifying developmental delay in Indian children and is well-suited for use in outpatient follow-up settings.[7,9]

Despite the established efficacy of therapeutic hypothermia in high-income settings, outcome data from Indian NICUs, particularly regarding long-term neurodevelopmental trajectories remain limited. Variables that may influence outcome in the Indian context, including severity of encephalopathy, outborn status, timing of cooling initiation, requirement for respiratory support, and post-cooling recovery milestones such as establishment of breastfeeding, have not been systematically evaluated. Understanding these predictors is vital for risk stratification, parental counselling, and optimisation of follow-up services. In view of these gaps, the present study was undertaken to determine mortality and neurodevelopmental outcome at one year of age in neonates with HIE Grade II/III who underwent whole body therapeutic hypothermia using a servo-controlled device at a tertiary care NICU in Karnataka, India, and to identify perinatal and clinical variables that significantly predict neurodevelopmental outcome at one year.

MATERIALS AND METHODS

This was a prospective descriptive study conducted over a period of two years, from June 2018 to May 2020. The study was conducted in the Neonatal Intensive Care Unit (NICU) of a tertiary care hospital in a second-tier city of Karnataka, India. The unit is accredited at Level 3A by the National Neonatology Forum (NNF) and holds NABH accreditation. The NICU is equipped for advanced neonatal management including servo-controlled therapeutic hypothermia, mechanical ventilation, and continuous physiological monitoring. A structured protocol for recording perinatal risk factors, clinical events, and neurodevelopmental follow-up has been in place since 2012.

Study Population: Neonates of gestational age ≥36 weeks admitted to the NICU within 6 hours of birth and fulfilling eligibility criteria for therapeutic hypothermia were considered for inclusion.

Inclusion and Exclusion Criteria: Eligibility was based on the TOBY trial protocol, requiring fulfillment of at least 2 of 3 physiological criteria and at least 1 of 2 neurological criteria. Physiological criteria included: (i) 10-minute APGAR score ≤5; (ii) need for assisted ventilation at birth for ≥5 minutes; and (iii) metabolic or mixed acidosis with pH ≤7.1 and/or base deficit ≥16 mmol/L in cord blood or blood gas within the first hour of life. Neurological criteria included: (i) presence of clinical seizures; or (ii) physical examination consistent with moderate to severe encephalopathy as per modified Sarnat staging. Neonates fulfilling physiological but not neurological criteria at admission were reassessed every 30 minutes up to 6 hours of life; cooling was initiated if neurological criteria were subsequently fulfilled. Neonates were excluded if they had: birth weight <2000 grams; gestational age <36 weeks; inability to initiate cooling by 6 hours of life; life-threatening congenital cardiovascular or respiratory anomalies (including complex congenital heart disease confirmed by echocardiography, congenital diaphragmatic hernia, CCAM, esophageal atresia, and TEF); or major congenital malformations, neuromuscular disorders, or lethal chromosomal anomalies.

Intervention: Whole body cooling was administered using the Tecotherm Neo™ (Inspiration Healthcare), a fully automated servo-controlled device, targeting a rectal temperature of 33.5°C. Following an induction phase of rapid cooling over 1 hour, the target temperature was maintained for 72 hours. Rewarming was subsequently performed at a rate of 0.5°C per hour over 7 hours until a core body temperature of 37°C was achieved. Cooling was discontinued prematurely in cases of life-threatening coagulopathy or haemodynamic instability with arrhythmias (HR <80/min).

Outcome Assessment: Neurodevelopmental assessment was performed using the modified Hammersmith neurological examination at discharge and the Trivandrum Developmental Screening Chart (TDSC) at 4 months, 8 months, and 1 year of age. Clinical, laboratory, and imaging variables recorded before, during, and after therapeutic hypothermia were correlated with TDSC outcomes at 1 year.

Sample Size: Based on an expected proportion of 54.6% from a comparable study by Sowjanya *et al*. and an absolute precision of 18%, a minimum sample size of 31 was

calculated; 35 neonates were enrolled to account for potential dropouts.[10]

Statistical Analysis: Data were entered in Microsoft Excel and analyzed using SPSS version 21.0 for Windows. Descriptive statistics including mean and standard deviation were used for continuous variables. Categorical variables were expressed as frequencies and percentages. Chi-square test was applied to assess associations between clinical variables and neurodevelopmental outcome. A p-value of <0.05 was considered statistically significant.

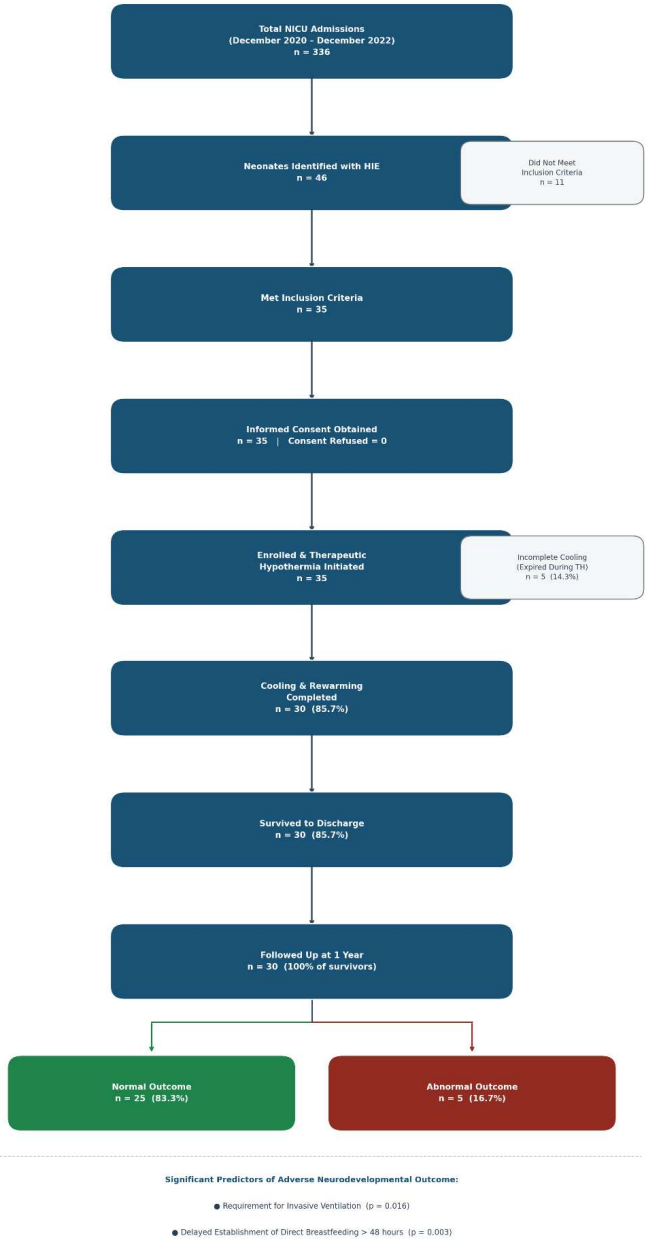

Figure 1. Study Recruitment and outcome flowchart

The majority of enrolled neonates were outborn (97.1%), with only one inborn case, reflecting the referral-dependent tertiary care context of the study unit (Table 1).Therapeutic hypothermia was initiated within 3 hours of birth in 5 neonates (14.3%) and between 3 and 6 hours in the remaining 30 neonates (85.7%). All 35 enrolled neonates received TH within the prescribed 6-hour eligibility window. The predominance of later initiation (>3 hours) is attributable to the time elapsed during inter-facility transport, as 97.1% of neonates were outborn. Moderate HIE (Grade II) was the predominant encephalopathy grade (85.7%); ABG within the first hour of birth was unavailable in 91.4% of cases due to outborn status (Table 1). Coagulopathy was the most frequent complication (71.4%), followed by liver enzyme derangement (60.0%) and thrombocytopenia (51.5%; Table 3). Invasive ventilation was required by 37.1% of neonates. Of 30 survivors followed up at 1 year, 25 (83.3%) demonstrated normal neurodevelopmental status on the Trivandrum Developmental Screening Chart (TDSC). The modified Hammersmith neurological examination at discharge identified 10 (33.3%) as abnormal; however, this did not correlate significantly with TDSC at 1 year (p=0.233), suggesting neurological recovery occurred in a subset of neonates. The requirement for invasive ventilation during the cooling period was a statistically significant predictor of adverse neurodevelopmental outcome at 1 year (p=0.016). Among neonates requiring invasive ventilation, 50% had abnormal TDSC at 1 year, compared to 0% in those who required no assisted breathing or hood oxygen only. Time taken to achieve direct breastfeeding after therapeutic hypothermia was a highly significant predictor of neurodevelopmental outcome (p=0.003). All 19 neonates who achieved direct breastfeeding within 48 hours had a normal TDSC at 1 year, while 66.7% of those who took >7 days to establish breastfeeding had abnormal outcomes. Duration of hospital stay and Hammersmith scores at discharge did not significantly predict 1-year neurodevelopmental outcome (p=0.276 and p=0.233, respectively).

DISCUSSION

The present study was a prospective descriptive study conducted at a Level 3A NICU in Karnataka, India, over June 2018 to May 2020. Thirty-five neonates with HIE Grade II/III fulfilling TOBY trial-based eligibility criteria underwent whole body therapeutic hypothermia (TH) using the Tecotherm Neo™ servo-controlled device at a target rectal temperature of 33.5°C for 72 hours, followed by gradual rewarming at 0.5°C per hour. Neurodevelopmental outcome was assessed using the modified Hammersmith neurological examination at discharge and the Trivandrum Developmental Screening Chart (TDSC) at one year of age. The aim was to determine mortality, neurodevelopmental outcomes at one year, and to identify perinatal and clinical predictors of adverse outcome in this cohort. In the present study, 51.4% of neonates were male and 48.6% female. Catherine *et al.* similarly reported male preponderance among TH-treated neonates with moderate to severe HIE in a randomised controlled trial at JIPMER, Puducherry.[11] A striking demographic feature was that 97.1% of neonates were outborn, reflecting the referral-dependent nature of neonatal care in second-tier Indian cities. Thayyil *et al.* in the HELIX trial reported 67–70% outborn rates across seven South Asian tertiary NICUs, noting that referred neonates had a significantly higher proportion of severe HIE compared to inborns.[12] Identifiable maternal risk factors were present in 37.1% while 62.9% had no identifiable antenatal risk factors. The majority (85.7%) had moderate HIE at admission, closely mirroring the HELIX trial population where 80% had moderate encephalopathy.[12] A specific challenge arising from the predominantly outborn cohort (97.1%) was the unavailability of cord blood gas analysis or ABG within the first hour of birth in 91.4% of cases, and incomplete resuscitation documentation in a significant proportion of referred neonates. TH eligibility in these cases was determined using the clinical neurological criteria component of the

Table 1. Baseline Demographic, Perinatal, and Clinical Characteristics (n=35)

	Characteristic	Category	Frequency (%)
Baseline Demographic and Perinatal Characteristics	Gender	Male	18 (51.4%)
		Female	17 (48.6%)
	Birth Weight	>2500 g	31 (88.6%)
		<2500 g	4 (11.4%)
	Place of Birth	Outborn	34 (97.1%)
		Inborn	1 (2.9%)
	Mode of Delivery	Normal vaginal delivery	20 (57.1%)
		LSCS	14 (40.0%)
		Assisted vaginal delivery	1 (2.9%)
	Identifiable maternal risk factors	Present	13 (37.1%)
		Absent	22 (62.9%)
Clinical Profile at Admission and During Therapeutic Hypothermia	Stage of Encephalopathy	Moderate (Grade II)	30 (85.7%)
		Severe (Grade III)	5 (14.3%)
	Abnormal ABG at admission	Yes	11 (31.4%)
		No	24 (68.6%)
	Seizures on clinical assessment	Present	28 (80.0%)
		Absent	7 (20.0%)
	Need for resuscitation – PPV (bag & mask)	Yes	16 (45.7%)
		Intubation & resuscitation	11 (31.4%)
		Extensive resuscitation	8 (22.9%)
	Cooling & Rewarming	Complete	30 (85.7%)
		Incomplete	5 (14.3%)

Table 2. Complications During Therapeutic Hypothermia

Complication	**Category**	**Frequency (%)**
Assisted Breathing	None required	9 (25.7%)
	Oxygen with hood	10 (28.6%)
	Non-invasive ventilation (NIV)	3 (8.6%)
	Invasive ventilation	13 (37.1%)
Coagulopathy	Present	25 (71.4%)
	Absent	10 (28.6%)
Liver enzyme derangement	Present	21 (60.0%)
	Absent	14 (40.0%)
Thrombocytopenia	None	17 (48.6%)
	Thrombocytopenia	15 (42.9%)
	Severe (requiring platelet transfusion)	3 (8.6%)
Sepsis	No sepsis	29 (82.9%)
	CRP+, culture negative	3 (8.6%)
	CRP+, culture positive	2 (5.7%)
	Culture positive with meningitis	1 (2.9%)

Table 3. Primary Outcome - Mortality and Neurodevelopmental Status at 1 Year

Outcome Measure	**Category**	**Frequency (%)**
Survival to discharge	Survived	30 (85.7%)
	Expired	5 (14.3%)
Stage of HIE in expired babies	Severe encephalopathy	4 (80.0%)
	Moderate encephalopathy	1 (20.0%)
Modified Hammersmith at discharge *(n=30)*	Normal	20 (66.7%)
	Abnormal	10 (33.3%)
Neurodevelopmental outcome at 1 year (TDSC) *(n=30)*	Normal	25 (83.3%)
	Abnormal	5 (16.7%)
Antiepileptic drug use at 1 year	Yes	4 (13.3%)
	No	26 (86.7%)

Table 4: Secondary Outcome - Correlation of Variables with Neurodevelopmental Outcome at 1 Year

Variable	Normal TDSC n (%)	Abnormal TDSC n (%)	Total n (%)	p-value
Age at TH initiation				
<3 hours	4 (80.0%)	1 (20.0%)	5 (100%)	0.956
>3 hours	16 (66.7%)	8 (33.3%)	24 (100%)	
Need for resuscitation				
PPV bag & mask	14 (87.5%)	2 (12.5%)	16 (100%)	0.787
Intubation & resuscitation	8 (80.0%)	2 (20.0%)	10 (100%)	
Extensive resuscitation	3 (75.0%)	1 (25.0%)	4 (100%)	
Assisted breathing				
None	9 (100%)	0 (0%)	9 (100%)	0.016*
Oxygen with hood	10 (100%)	0 (0%)	10 (100%)	
NIV	2 (66.7%)	1 (33.3%)	3 (100%)	
Invasive ventilation	4 (50.0%)	4 (50.0%)	8 (100%)	
Neurosonogram findings				
Normal	16 (88.8%)	2 (11.1%)	18 (100%)	0.381
Abnormal	6 (66.7%)	3 (33.3%)	9 (100%)	

**Statistically significant ($p<0.05$)*

Table 5. Post-Hypothermia Recovery Variables and Neurodevelopmental Outcome at 1 Year

Variable	Normal TDSC n (%)	Abnormal TDSC n (%)	Total n (%)	p-value
Time to achieve direct breastfeeding				
<48 hours	19 (100%)	0 (0%)	19 (100%)	0.003*
48 hours – 7 days	5 (62.5%)	3 (37.5%)	8 (100%)	
>7 days	1 (33.3%)	2 (66.7%)	3 (100%)	
Duration of hospital stay				
<48 hours	19 (90.5%)	2 (9.5%)	21 (100%)	0.276
48 hours – 7 days	4 (66.7%)	2 (33.3%)	6 (100%)	
>7 days	2 (66.7%)	1 (33.3%)	3 (100%)	
Hammersmith at discharge vs TDSC at 1 year				
Normal Hammersmith	20 (66.7%)	—	20	0.233
Abnormal Hammersmith	10 (33.3%)	—	10	

**Statistically significant (p<0.05)*

TOBY-based protocol; specifically, the presence of seizures or physical examination findings consistent with moderate to severe encephalopathy on modified Sarnatstaging, which are assessable at any referral point independent of blood gas data or APGAR documentation. ABG performed at the time of NICU admission (>1 hour of birth) was abnormal in 31.4% of cases, corroborating the clinical encephalopathy assessment. While this pragmatic approach reflects the reality of neonatal referral networks in resource-limited Indian settings, it introduces an inherent selection risk: neonates with biochemical HIE but minimal clinical signs may have been missed, and conversely, encephalopathic neonates with non-hypoxic-ischaemic aetiology may have been included. Standardised transport documentation systems and point-of-care lactate testing at referring centres would strengthen eligibility ascertainment in future studies.

Coagulopathy was the most frequent complication during TH, observed in 71.4% of neonates. The HELIX trial reported coagulation derangement in 39% of the hypothermia group, with the higher rate in the present study likely reflecting delayed referral presentations in the outborn-heavy cohort.[12] Mascarenhas *et al*. in a retrospective observational study of 155 neonates at KEM Hospital, Mumbai, similarly reported clinically significant bleeding and notable thrombocytopenia as key TH complications in an Indian NICU setting.[13] Thrombocytopenia was present in 42.9% of neonates, liver enzyme derangement in 60%, and sepsis in 17.1%. Invasive ventilation was required by 37.1% compared to 60% in the HELIX trial, reflecting the moderate HIE predominance in the present cohort.[12] Saraswat *et al*. from Bapuji NICU, Davangere, similarly documented multi-organ complications including haematological disturbances as central features of the NICU course during TH.[14] Of 35 enrolled neonates, 5 (14.3%) expired, yielding a survival rate of 85.7%; four deaths occurred in neonates with severe HIE. Saraswat *et al*. reported a strikingly consistent mortality of 14% in their TH cohort from Davangere, providing direct regional validation of the present study's outcomes.[14] In contrast, the HELIX trial reported mortality of 42% in the TH group, paradoxically higher than the control group's 31% leading investigators to question TH safety in LMICs without optimal supportive care.[12] The markedly better survival in the present study reflects the structured institutional cooling protocol, rigorous multi-organ supportive care, and predominantly moderate HIE profile of the enrolled cohort. Of 30 survivors, 25 (83.3%) had normal neurodevelopmental outcome on TDSC at one year. Catherine *et al*. reported 65% normal outcomes at 18 months in their South Indian RCT TH arm, a lower proportion attributable to longer follow-up and a greater proportion of severe HIE.[11] Veeraiah *et al*. reported that 81.2% of followed-up neonates showed mild delay or normal development on BSID-IV at 18–24 months in Shivamogga, closely comparable to the present study's 83.3%, with geographic proximity and identical device use strengthening this comparison.[15] Kachhwaha *et al*. similarly reported 85.7% normal neurodevelopmental outcomes in the TH arm of their Indian hospital-based study, directly comparable to the present findings.[16]When both mortality and neurodevelopmental disability are considered together, the composite adverse outcome rate was 28.6% (10 of 35 enrolled neonates: 5 deaths and 5 with abnormal TDSC at one year). Without a concurrent normothermic control group, it is not possible to determine whether this combined rate differs significantly from what would have been observed with supportive care alone in the same population — an inherent limitation shared by all single-arm observational TH studies conducted after TH became standard of care. Timing of cooling initiation and resuscitation method were not significantly associated with neurodevelopmental outcome (p=0.956 and p=0.787). The absence of a significant outcome difference between neonates cooled within 3 hours versus 3–6 hours (p=0.956) may reflect the small sample size in the earlier-initiation group (n=5), rather than a true lack of benefit from early cooling. All neonates in the present study received TH within the 6-hour window, indicating that the referral and triage system successfully preserved the therapeutic window despite a predominantly outborn population. Requirement for invasive ventilation during cooling was a statistically significant predictor of adverse outcome (p=0.016); neonates requiring invasive ventilation had a 50% abnormal TDSC rate versus 0% in those requiring no respiratory support. Boo *et al*. in their Malaysian National Neonatal Registry analysis identified systemic severity as a key mortality risk factor, validating respiratory compromise as an adverse outcome predictor in LMIC HIE cohorts.[17] Time to direct breastfeeding was the strongest predictor of adverse neurodevelopmental outcome (p=0.003); all 19 neonates achieving breastfeeding within 48 hours had normal TDSC at one year, while 66.7% of those taking more than 7 days had abnormal outcomes, identifying breastfeeding latency as a novel bedside proxy for residual brainstem injury not evaluated in major global TH trials.[12] The modified Hammersmith at discharge identified 33.3% as abnormal, yet only 16.7% were abnormal on TDSC at one year (p=0.233), confirming neurological recovery in a subset and underscoring the importance of serial longitudinal follow-up, consistent with observations by Saraswat *et al*.[14] The study is limited by a small sample size (n=35) at a single tertiary centre, restricting statistical power and generalisability. The absence of a concurrent normothermic control group, ethically unjustifiable once TH became the established standard of care prevents direct efficacy comparison, and the predominance of

moderate HIE (85.7%) makes it difficult to independently attribute the favourable outcomes to TH rather than the natural history of moderate encephalopathy. Arterial blood gas analysis within the first hour of birth was available in only 8.6% of enrolled neonates, limiting objective metabolic eligibility assessment. Follow-up was confined to one year of age, and late-emerging cognitive, behavioural, and scholastic deficits may not be captured by TDSC at this time point; longer follow-up using comprehensive assessments such as BSID-III is recommended. Neuroimaging was restricted to neurosonogram in the majority due to resource constraints, precluding MRI-based characterisation of injury patterns. Amplitude-integrated EEG was unavailable,limiting seizure quantification and electrographic prognostication. An important interpretive limitation of the present study warrants explicit acknowledgment. Of the 30 surviving neonates, 29 (96.7%) had moderate HIE (Grade II), with only 1 having severe HIE. Pre-TH-era historical data from India and globally consistently demonstrate that 75–85% of neonates with moderate HIE achieve normal neurodevelopmental outcomes with supportive care alone, without active neuroprotective intervention. The observed 83.3% normal outcome rate in the present study is therefore consistent with and not clearly superior to the expected natural history of moderate HIE. In the absence of a concurrent control group, it is not possible to attribute the favourable outcomes directly to TH rather than to the underlying encephalopathy grade distribution. The combined adverse outcome rate (death or neurodisability) in the present study was 33.3% (10/30 survivors at risk of adverse outcome, plus 5 deaths from 35 enrolled = 10/35 = 28.6%), which falls within the range reported for untreated moderate HIE in historical cohorts. These observations do not diminish the clinical value of establishing TH delivery capacity in Indian NICUs, but they underline the urgent need for controlled trials in the Indian LMIC setting, such as the ongoing HELIX-2 trial to definitively establish the incremental benefit of TH over optimised supportive care in this population.

The favourable survival and neurodevelopmental outcomes achieved in a second-tier Indian NICU demonstrate that servo-controlled TH within a structured protocol can deliver results comparable to high-income country benchmarks, directly contrasting with the HELIX trial and emphasising optimal supportive care as the critical determinant of TH success.[12,18] Invasive ventilation requirement and delayed breastfeeding should prompt early identification for intensive neurodevelopmental surveillance and structured parental counselling. The discordance between discharge neurological findings and one-year TDSC outcomes reinforces the mandatory role of longitudinal follow-up for all TH-treated neonates across Indian NICU settings.

CONCLUSION

The present study demonstrates that whole body therapeutic hypothermia using a servo-controlled device is associated with favourable survival (85.7%) and neurodevelopmental outcomes (83.3% normal at one year) in neonates with HIE Grade II/III in a tertiary Indian NICU setting. Requirement for invasive ventilation and delayed establishment of direct breastfeeding beyond 48 hours are significant predictors of adverse neurodevelopmental outcome at one year. Serial longitudinal follow-up using validated tools such as the TDSC is essential for all TH-treated neonates.

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