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Delayed Initiation of Therapeutic Hypothermia for Outborn Infants is Associated with Adverse Outcomes

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Background/Aims

tal Encephalopathy (NE) is a clinical syndrome
ıg between 2-5 per 1000 live births. Therapeutic
ermia (TH) is a neuroprotective treatment for NE

ıe, the majority of infants who meet eligibility
for TH are born in community hospitals
rn) and must be transferred to a tertiary care
for treatment

Characterize time to TH initiation for infants born
ary care centers (inborn) versus outborn infants
termine if delayed initiation is associated with
e short-term outcomes

Methods

spective study of infants treated with TH between
and 2018 in two NICUs excluding infants older
hours at TH initiation (14), less than 35 weeks
ional age (5), early termination of TH (1),
ce of encephalopathy (2), and no MRI (11)

scored by blinded neuroradiologist using the
e* scoring system with severe injury defined as
natter score >9.5 * Weeke et al (2018), doi:10.1016/j.jpeds.2017.09.043

ry outcome: Time to initiation of TH compared
en inborn and outborn infants

ıdary outcome: In-hospital mortality, severe MRI
and/or severe seizure on EEG defined as use of
barbital, fosphenytoin and midazolam drip

ical analysis: Baseline differences between
and outborn infants were compared using chi
e or Fisher's exact tests for categorical variables
tests or their non-parametric equivalents for
uous variables. Logistic regression was used to
l for confounding

Table 1. Clinical/Demographic Characteristics*

	Inborn n= 69	Outborn n= 153	p-value
Maternal Characteristics			
Gestational Diabetes (n, %)	14 (20%)	15 (10%)	0.05
Mean Maternal Age (SD)	30.4 (5.9)	27.6 (5.9)	0.001
Delivery Characteristics			
Cesarean section (n, %)	41 (59%)	79 (52%)	0.35
Chest compressions performed (n, %)	10 (15%)	56 (37%)	0.001
Infant Characteristics			
Female Sex (n, %)	31 (45%)	70 (46%)	0.99
Mean birth weight in kg (SD)	3.3 (0.7)	3.4 (0.6)	0.19
Mean Gestational Age in Weeks (SD)	38.5 (2.0)	39.6 (1.7)	<0.001
Median Apgar Score 1 min (# obtained, IQR)	1 [69, 1, 2]	2 [151, 1, 3]	0.06
Median Apgar Score 5 min (# obtained, IQR)	4 [69, 3, 6]	4 [150, 3, 5]	0.70
Median Apgar Score 10 min (# obtained, IQR)	6 [55, 4, 7]	6 [135, 4, 7]	0.53
Cord Gases			
Number of arterial gases obtained (n, %)	55 (80%)	88 (58%)	0.002
Mean arterial pH (SD)	7.04 (0.16)	7.06 (0.18)	0.48
Number of venous gases obtained (n, %)	52 (75%)	82 (54%)	0.003
Mean venous pH (SD)	7.10 (0.17)	7.13 (0.20)	0.47

*Statistically insignificant differences in characteristics not shown here include maternal fever, GBS positive, pre-eclampsia/eclampsia, vacuum assistance, shoulder dystocia, nuchal cord, cord prolapse, placental abruption, uterine rupture, late decelerations on fetal heart monitoring, chorioamnionitis, and prolonged rupture of membranes

Grey Matter Injury on MRI

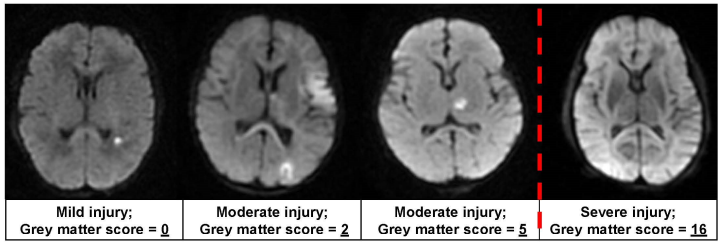

Table 2. Outcomes

All infants	Inborn n= 69	Outborn n= 153	p-value
Median Hour of Life TH Initiated (IQR)	1 (1,3)	4 (3,5)	<0.001
Mortality (n, %)	3 (4.3)	21 (13.7)	0.038
Any seizure (n, %)	16 (23.2)	57 (37.5)	0.045
Severe seizure (n, %)	3 (4.3%)	14 (9.2%)	0.28
Severe grey matter injury (n, %)	2 (3)	8 (5.7)	0.62
Mortality, severe seizure, and/or severe grey matter injury (n, %)	7 (10.1)	34 (22.2)	0.039

Results: Encephalopathy Tree Diagr

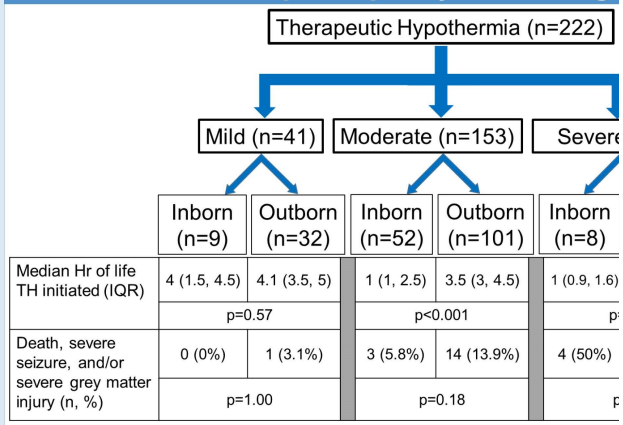

Table 3. Logistic Regression Analys

Assessing Effect of Confounding on Combined Outc Mortality, Severe Seizure, or Severe Grey Matter Injur

	Predictor Variable	Odds Ratio
Parent Model	Outborn infant	2.53
Extended Model*	Outborn infant	4.95

*Extended model is controlling for confounding from encephalopathy gestational age, gestational diabetes and sex

Conclusions

- There is significant delay in TH initiation for outborn and an associated increase in the odds of death, s neonatal seizures and/or severe grey matter injury.
- The relationship between delayed TH initiation and adverse outcomes is strongest for those with symp severe encephalopathy.
- Investigation into factors contributing to severe encephalopathy prior to and immediately following urgently needed.

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