

## INTRODUCTION

- Hypoxic ischemic encephalopathy (HIE) is the most common cause of neonatal acute symptomatic seizures – comprising 38% of neonatal seizures<sup>(7)</sup>
- Neonates treated with therapeutic hypothermia for HIE most commonly experience seizures on days 1-2 of cooling and during rewarming on day 4<sup>(6)</sup>
- Examination of intercenter variation in anti-seizure medication use amongst neonates with HIE demonstrated the following:
  - Phenobarbital: 97.6%
  - Levetiracetam: 16.9%
  - Phenytoin/Fosphenytoin: 15.6%
  - Oxcarbazepine, topiramate, and valproate: 2.4%<sup>(2)</sup>
- The World Health Organization (2011) recommends anti-seizure medication discontinuation in a neonate who has been seizure-free for 72 hours with a normal neurologic exam<sup>(1)</sup>
- In 2016, a study of 6245 neonates demonstrated a rate of anti-seizure medication continuation at discharge to be 68.6%<sup>(3)</sup>
- Seizures in neonates with acute acquired brain injury are unlikely to recur soon after resolution of the acute phase<sup>(1)</sup>
- There is currently no consensus regarding medication<sup>(2,3)</sup> and EEG<sup>(4)</sup> management for acute symptomatic seizures in neonates with HIE

## METHODS

- Single center retrospective study of infants with HIE who underwent therapeutic hypothermia from 2017-2021
- Only subjects with EEG data were included
- Recorded demographic data, clinical course, clinical and electrographic seizures, anti-seizure medication use, and anti-seizure medication discontinuation upon discharge

## OBJECTIVES

- Primary objective:** Determine electrographic seizure frequency in neonates undergoing therapeutic hypothermia for HIE during initial admission
- Secondary objective:** Determine the rate of seizure recurrence in neonates following initial anti-seizure medication discontinuation

## RESULTS

### DEMOGRAPHICS

Race/Ethnicity	
African American	25
Caucasian	29
Unknown	39
American Indian/Native Alaskan	2
Asian	3
Hispanic/Latino	1
Delivery Location	
Inborn	21
Outborn	78
Delivery Method	
Vaginal	34
Cesarean section	65

### CLINICAL COURSE

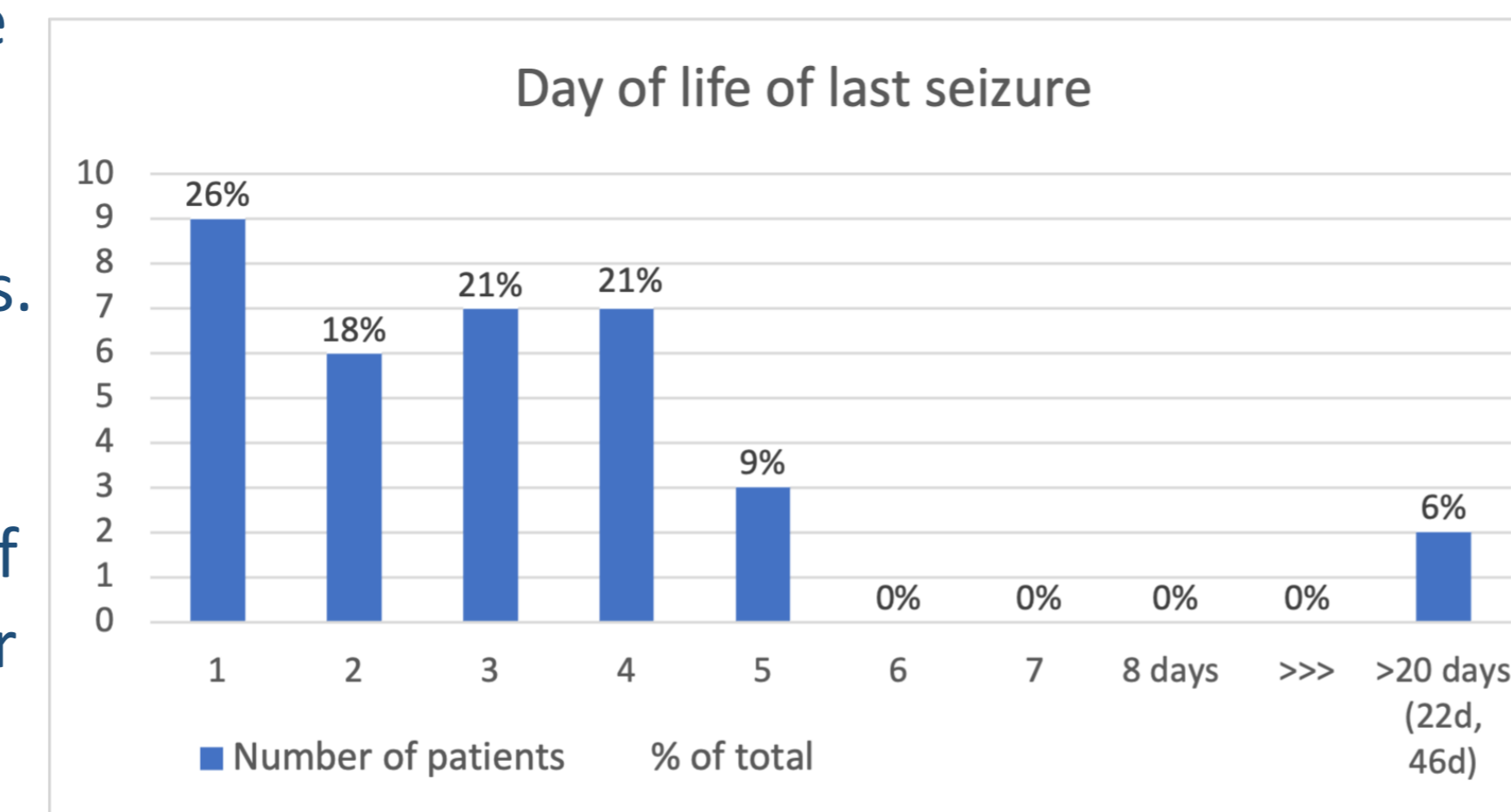
APGAR < 5 at 5 minutes	75
Cord blood with pH < 7	49
Intubation/Mechanical ventilation	88
Chorioamnionitis	8
Sepsis (confirmed positive culture)	6
Positive CSF culture	0
Necrotizing enterocolitis	3
Abnormal EEG	83

### Among the 99 infants included in this study:

- 53 patients had seizures (clinical, subclinical, or both)
- The mean day of life of the last seizure was 2.65 days
- 53 infants received ASM's, only 11% continued ASM on discharge
- 21 infants had a second EEG after initial monitoring during three days of therapeutic hypothermia
  - 18/21 - the 2<sup>nd</sup> EEG did not show seizure activity
  - 3/21 - the 2<sup>nd</sup> EEGs showed seizures

One had the last seizure on the 5<sup>th</sup> day of life.

Two patients had continued seizures for 22 and 46 and days. One was diagnosed with medication-resistant genetic epilepsy (congenital disorder of glycosylation type Ij). The other etiology diagnosis not reached



### EVALUATION AND TREATMENT

	MRI BRAIN		SEIZURES		
	Completed	Presence of Injury	Clinical seizures	Clinical seizures confirmed on EEG	Subclinical seizures
<b>No</b>	9	27	55 (3 unknown)	80	67 (2 unknown)
<b>Yes</b>	90	63	41	19	30
	ANTI-SEIZURE MEDICATION		REPEAT EEG		
	During admission	Continued upon discharge	Additional study completed	Presence of seizures	
<b>No</b>	46	42	78	18	
<b>Yes</b>	53	11	21	3	
<b>Day of life on last seizure (mean)</b>	2.65 days (SD of 1.35)				

## CONCLUSIONS

- Clinical and electrographic seizures in this retrospective study of acute HIE resolve by day of life five, except for two patients with likely neonatal-onset genetic epilepsy
- The rate of discontinuing anti-seizure medications prior to discharge was higher in our study than reported in a recent practice survey
- Our data suggest that it may be reasonable to consider discontinuing anti-seizure medications after seizures have resolved, and after day of life 5 in neonates with seizures secondary to HIE who are treated with therapeutic hypothermia.

## REFERENCES

- Glass HC, Soul JS, Chang T, Wusthoff CJ, Chu CJ, Massey SL, et al. Safety of Early Discontinuation of Antiseizure Medication After Acute Symptomatic Neonatal Seizures. *JAMA Neurol.* 2021;78(7):817-25.
- Dizon MLV, Rao R, Hamrick SE, Zaniletti I, DiGeronimo R, Natarajan G, et al. Practice variation in anti-epileptic drug use for neonatal hypoxic-ischemic encephalopathy among regional NICUs. *BMC Pediatr.* 2019;19(1):67.
- Le VT, Abdi HH, Sanchez PJ, Yossef L, Reagan PB, Slaughter LA, et al. Neonatal Antiepileptic Medication Treatment Patterns: A Decade of Change. *Am J Perinatol.* 2021;38(5):469-76.
- Shellhaas RA, Chang T, Tsuchida T, Scher MS, Riviello JJ, Abend NS, et al. The American Clinical Neurophysiology Society's Guideline on Continuous Electroencephalography Monitoring in Neonates. *J Clin Neurophysiol.* 2011;28(6):611-7.
- Medications in Neonates with Hypoxic-Ischemic Encephalopathy." *Epilepsia*, vol. 58, no. 6, 12 Apr. 2017, pp. 1047–1053.
- Fitzgerald, M. P., Sudha Kilaru Kessler, & Abend, N. S. (2017) Early discontinuation of antiseizure medications in neonates with hypoxic-ischemic encephalopathy. *Epilepsia*, 58(6), 1047–1053.
- Carrasco, M., Bonifacio, S. L., deVeber, G., & Chau, V. (2023). Early Discontinuation of Phenobarbital After Acute Symptomatic Neonatal Seizures in the Term Newborn. *Neurology: Clinical Practice*, 13(2), e200125