BLOOD LACTATE KINETICS AS BIOMARKERS FOR MRI BRAIN INJURY IN NEWBORNS WITH HYPOXIC-ISCHEMIC ENCEPHALOPATHY

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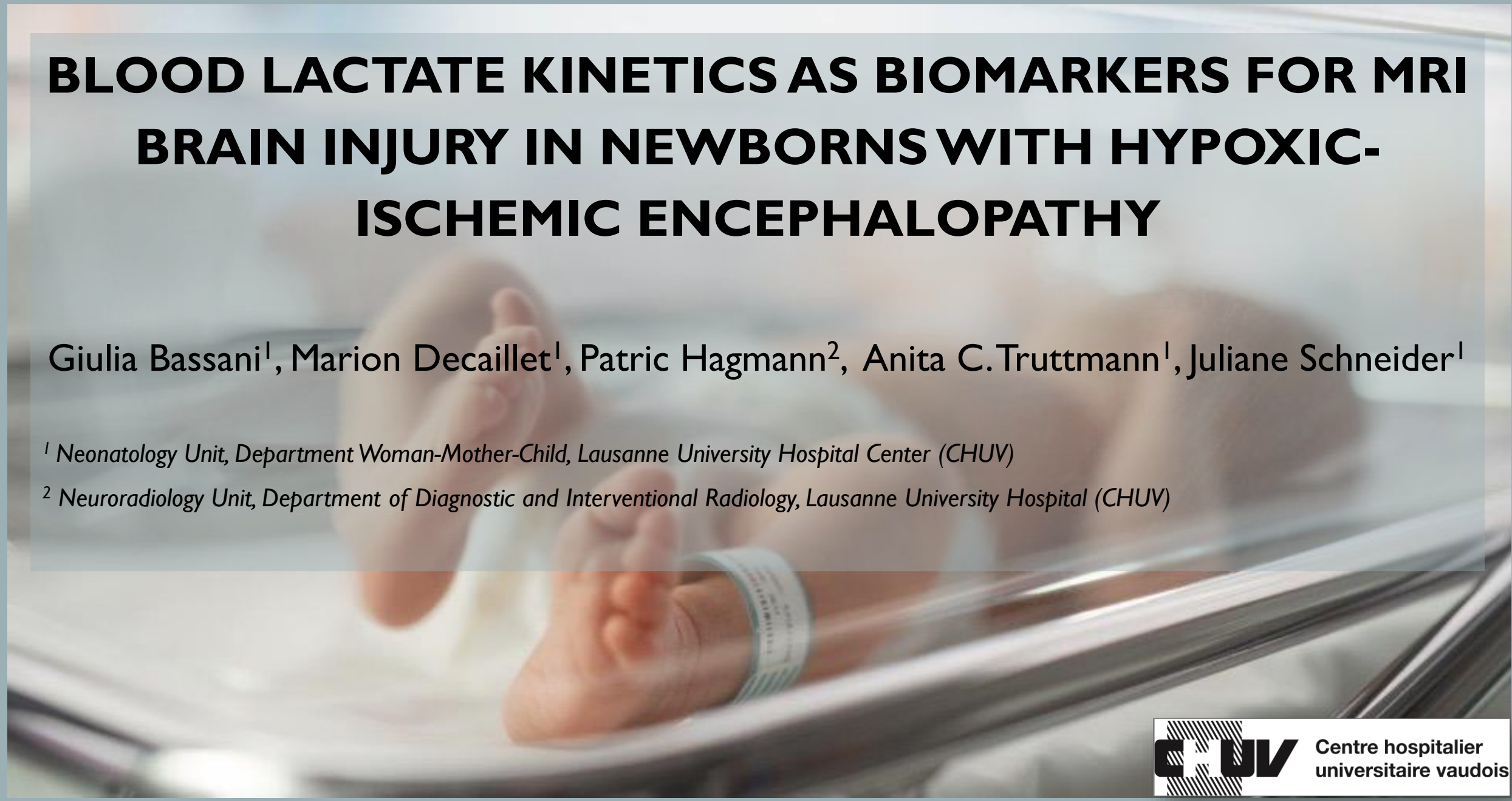

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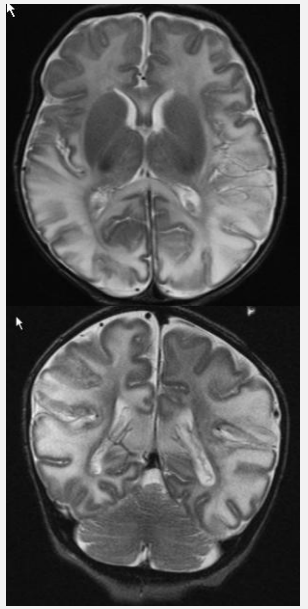
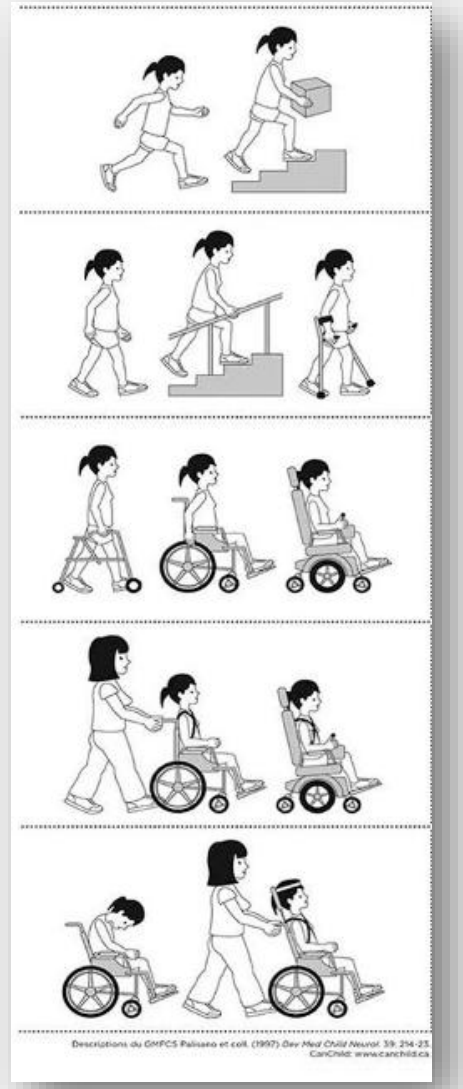
BACKGROUND

- **What is HIE?:** Hypoxic-ischemic encephalopathy (HIE) is clinical syndrome of neurologic dysfunction caused by a perinatal event of diminished blood and oxygen supply.
- **Global Impact:** HIE affects 0.5 to 1.5 per 1000 live births in high-income countries[1]; it's a major cause of death or neurologic morbidity.
- **Current Gaps:** Despite neuroimaging advances, there is a need of accessible biochemical markers to support early prognostication. Lactate as been studied with conflicting results [2].





GMFCS score edition 2

[1] McIntyre et al. 2021, *Semin Fetal Neonatal Med.*
[2] Boerger et al. 2024, *Neonatology*

OBJECTIVES AND HYPOTHESIS

Primary Outcome:

Correlation between lactate kinetics and MRI- assessed brain injury, using the Weeke severity score, a predictor of neurologic outcomes at 2-years and at school age [3].

Hypothesis: positive correlation between lactate parameters and MRI brain injury

Secondary outcome:

Relationship between lactate kinetics and seizures or neurologic exam at discharge

[3] Weeke et al. 2018, *J Pediatr.*

METHODS
STUDY DESIGN AND PARTICIPANTS

Study Design

Single-center, prospective observational study - Lausanne University Hospital NICU.

Inclusion criteria

Term/near-term neonates (≥ 35 weeks GA) with HIE (mild to severe, treated or not with TH), born between Feb 2022 to Dec 2024.

Exclusion criteria

Major malformations, metabolic or genetic disorders, lack of consent, or inability to obtain it.

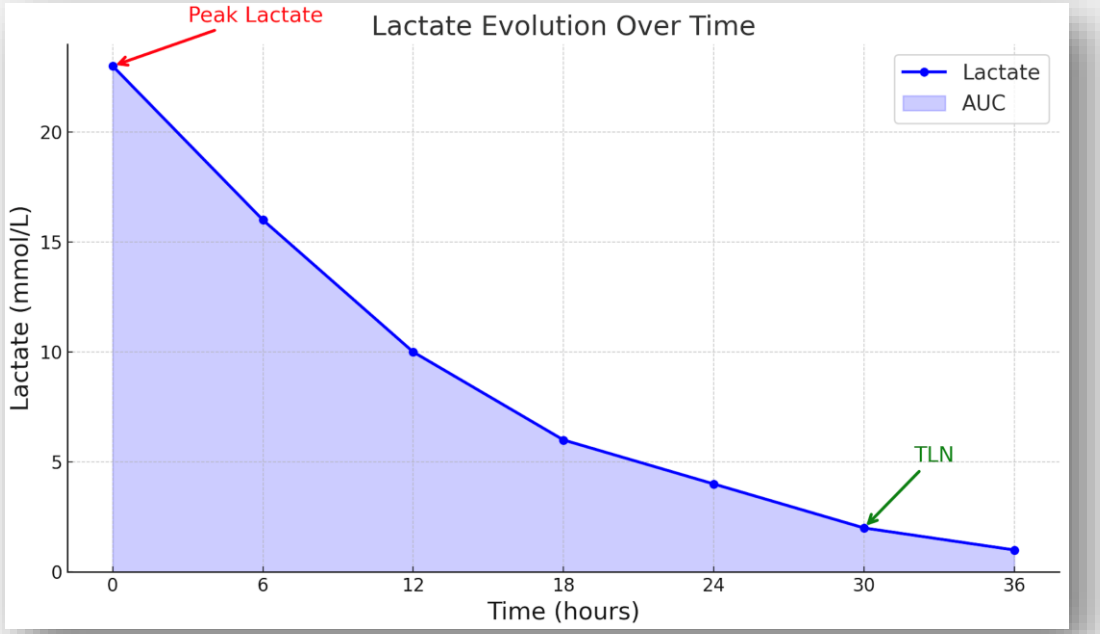
METHODS
LACTATE MONITORING AND MRI PROTOCOL

- *Predictor variables* = **Lactate Kinetics:**

  1) Time for lactate to normalize (**TLN**) = time from birth until the lactate level was ≤ 2.5 mmol/l

  2) **Peak lactate**

  3) **Lactate AUC** (Area Under the Curve)



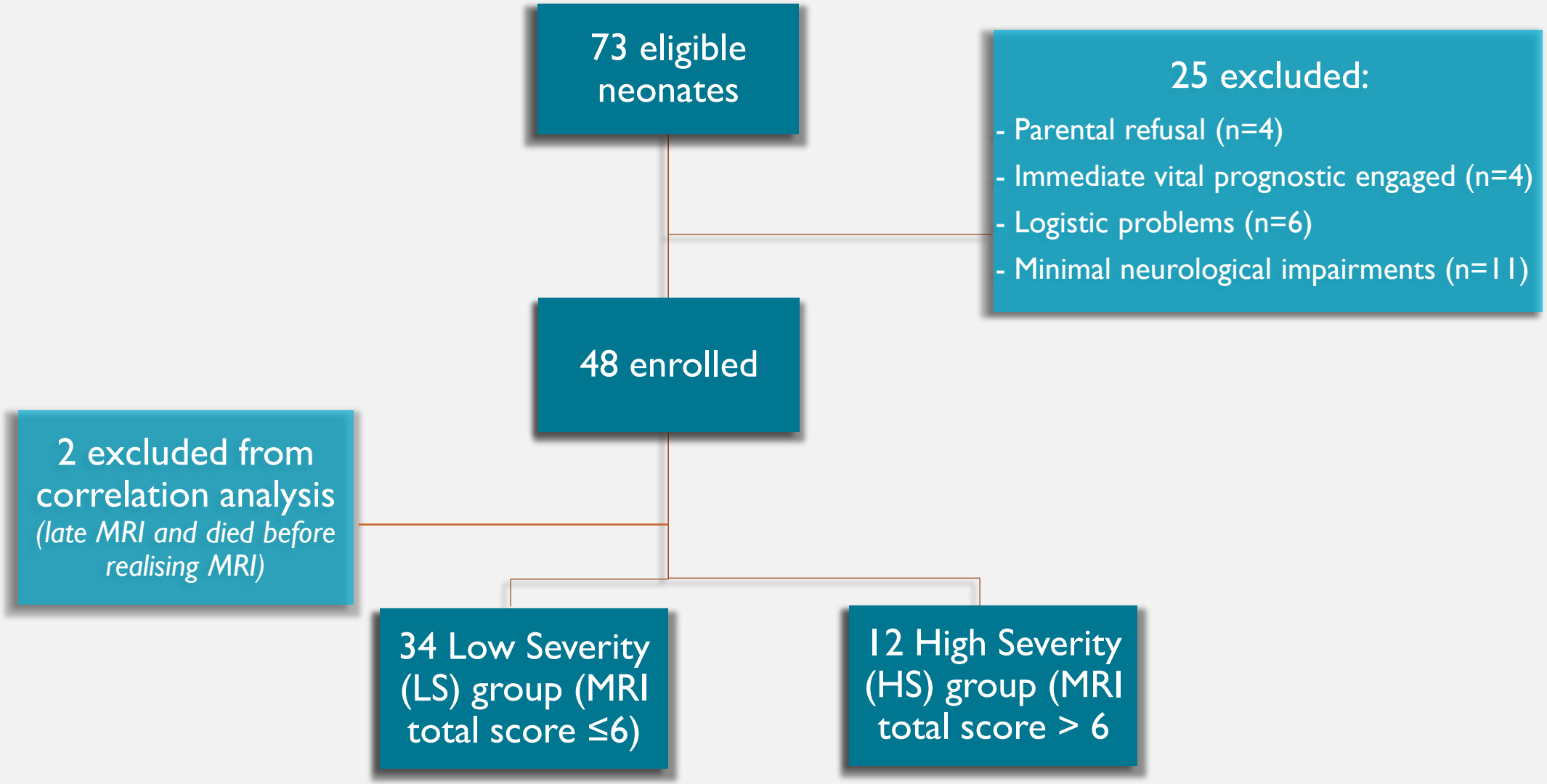
- *Outcome variable* = **Brain MRI:**

Performed on DOL 4-7 using a 3T MRI.

The extent of brain injury was evaluated using the scoring system by Weeke et al. [3]
(Total score = grey matter, white matter, cerebellum, additional subscores; maximum score, 55)

[3] Weeke et al. 2018, *J Pediatr.*

RESULTS
FLOWCHART



RESULTS
PATIENTS' CHARACTERISTICS

Demographic characteristics	Total (N=48)	Low Severity (LS) group (N=34)	High Severity (HS) group (N=12)	p-value
Sex- male, n, (%)	22 (45)	14 (41)	8 (66)	0.12
Outborn, n, (%)	26 (54)	18 (52)	7 (58)	0.74
Gestational age, median (IQR)	39.8 (1.9)	40 (1.5)	38.7 (2.3)	0.08
Primiparous, n, (%)	33 (68)	23 (67)	8 (66)	0.42
Fœtal and delivery characteristics				
Pathological obstetrical contexte, n, (%)	10 (20)	7 (20)	3 (25)	0.75
Fetal distress, n, (%)	29 (60)	20 (58)	7 (58)	0.97
Emergency C-section, n, (%)	24 (50)	15 (44)	9 (75)	0.06
Delivery complication n, (%)	45 (93)	16 (47)	5 (41)	0.74

RESULTS
PATIENTS' CHARACTERISTICS

Neonatal clinical characteristics	Total (N=48)	Low Severity (LS) group (N=34)	High Severity (HS) group (N=12)	p-value
Resuscitation needs, n, (%)	46 (95)	33 (97)	11 (91)	0.43
Apgar 5 min, median (IQR)	3 (3)	3 (2)	4 (4)	0.39
Apgar 10 min, median (IQR)	5 (4)	5 (3.7)	5.5 (4.2)	0.73
Lowest pH, median (IQR)	6.09 (0.2)	6.9 (0.18)	6.9 (0.37	0.6
Thompson, median (IQR)	8 (2.2)	8 (3)	10.5 (2.5)	0.009
Sarnat, median (IQR)	1.5 (1)	1 (1)	2 (0.25)	0.04
Sarnat I, n (%)	24 (50)	21 (61)	3 (25)	0.02
Sarnat II, n, (%)	21 (43)	12 (35)	8 (66)	0.059
Sarnat III, n, (%)	3 (6)	1 (2)	1 (8)	0.45
Invasive ventilation, n, (%)	27 (56)	17 (50)	8 (66)	0.31
Sepsis, n, (%)	3 (6)	1 (2)	1 (8)	0.45
Renal failure, n, (%)	25 (52)	15 (44)	9 (75)	0.06
Hepatic failure, n, (%)	24 (50)	16 (47)	6 (50)	0.86
Hypothermia, n, (%)	40 (83)	28 (82)	10 (83)	0.93
Seizures, n, (%)	8 (16)	2 (5)	5 (41)	0.003
Pathological neurologic exam at discharge, n (%)	14 (29)	5 (14)	8 (66)	<0.001
Death before discharge, n, (%)	3 (6)	0 (0)	2 (16)	0.06
Total MRI score, median (IQR) *(46 patients)*	4 (4.7)	3 (3)	15.5 (12)	< 0.001

RESULTS
PRIMARY OUTCOME: LACTATE AND MRI CORRELATIONS

- **Positive correlations *(Spearman):***

  lactate AUC associated with :

  ~ MRI total score (p=0.06)

  ~ GM subscore (p<0.001)

  ~ WM subscore (p=0.03)

  TLN ~ GM subscore (p= 0.004)

  peak blood lactate ~ GM subscore (p=0.02)

- **GLM (*General Linear model*) Analyses:**
  - lactate AUC or TLN:
    - ~ total MRI score
    - ~ GM subscore

positive correlation (all p< 0.01), after adjusting for confounders *(sex, gestational age, Thompson score, 5min Apgar and seizures)*.

RESULTS
SECONDARY OUTCOMES

Neurologic Exam at Discharge

TLN was significantly longer in patients with pathological neurologic exam at discharge (p=0.02).

Seizures

No significant differences in lactate parameters between seizure and non-seizure groups.

CONCLUSIONS AND DISCUSSION
CLINICAL IMPACT AND FUTURE PERSPECTIVES

- **Clinical Relevance:**
  - Blood lactate kinetics are associated with the severity of MRI brain injury
  - Lactate measurement is a readily available bedside tool in clinical setting
  - Analyzing its kinetics may improve prognostic accuracy
- **Study limitations**: small cohort, majority of mild HIE
- **Next steps:**
  - Integration of hemodynamic data (cardiac function, inotropic support..)
  - Explore the relationship between persistent lactate elevation, hemodynamic status, and long-term neurological outcomes

MERCI DE VOTRE ATTENTION

DIAGNOSIS OF HIE – INCLUSION CRITERIA

- Clinical signs of neonatal **encephalopathy** (per Sarnat classification) AND criteria for **perinatal asphyxia**:
  - evidence of **fetal distress**:
    - Acute perinatal event
    - Cord pH < 7.0 or base deficit < –16 mmol/L
  - evidence of **neonatal distress**:
    - Apgar score < 5 at 10 minutes of life
    - Blood pH < 7.0 or base deficit < –16 mmol/L or Lactate > 12 mmol/L (within 1st hour of life)
    - Resuscitation > 10 min (bag-mask ventilation