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## Elevated umbilical cord arterial lactate at birth and electronic fetal monitoring characteristics on admission and in the active phase

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### Abstract

**Objective:** To investigate the association between elevated umbilical arterial lactate at birth and electronic fetal monitoring (EFM) characteristics at admission and in the beginning of the active phase of labor.

**Study Design:** Nested case-control study within a prospective cohort of laboring patients at term who achieved active labor. Neonates with umbilical arterial lactate  $\geq 4$  mmol/L (cases, n=119), were matched 1:1 to controls with lactate  $<4$  mmol/L. EFM patterns were compared with multivariable logistic regression.

**Result:** There were no differences in EFM parameters in the first 60 minutes after admission. At the beginning of active labor, 13.5% of cases and 26.1% of controls had always category I tracings, adjusted odds ratio 0.48, 95% confidence interval 0.24-0.94). Cases were less likely to have an always category I tracing from admission into the active phase.

**Conclusion:** Elevated umbilical arterial lactate at birth is associated with distinct EFM patterns early in the labor course.

### Keywords

electronic fetal monitoring; umbilical arterial lactate; term infants; acid-base status

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**Conflict of Interest:** The authors report no conflict of interest.

## Introduction

Despite unclear efficacy, electronic fetal monitoring (EFM) is used clinically to establish fetal wellbeing and to predict fetal oxygenation and acid-base status with the ultimate goal of preventing neonatal morbidity [1]. Given its widespread adoption, it is critical to optimize use of EFM despite its known limitations. A large prospective cohort study on the association between EFM parameters in the 120 minutes prior to delivery and acidemia recently demonstrated that total deceleration area was most predictive for neonatal acidemia [2]. However, moderate variability alone was not predictive of normal neonatal acid-base status [2].

Other studies on EFM and neonatal acid-base status have similarly focused on the period just before delivery [3-5]. However, the association between acidemia at birth and EFM parameters earlier in the labor course is not well defined. Since the final acid-base status of the neonate may be based on the entire labor course and not just the minutes preceding delivery, it is important to understand how EFM parameters earlier in labor may be associated with neonatal outcomes [6]. Therefore, we investigated the association between elevated umbilical cord arterial lactate at birth and EFM characteristics at admission and in the beginning of the active phase of labor. We hypothesized that there would be significant associations between elevated lactate at birth and EFM parameters at admission and at the beginning of the active phase.

## Materials and Methods

This is a nested case-control study within a prospective cohort study of 8,580 consecutive term, vertex, non-anomalous singleton pregnancies admitted for labor and delivery [2]. Neonates with <10 minutes of EFM in the 30 minutes before delivery, who were <37 weeks' gestational age, who did not achieve the active phase of labor (defined as 6 cm dilation) [1], or who had a postnatal anomaly diagnosis were excluded. At our institution EFM is used universally during labor with either external or internal monitoring as clinically appropriate. Umbilical artery cord gas values including pH and lactate are obtained routinely. The DXC-800 Automated Chemistry Analyser (Beckman Coulter) was used for lactate assays. The coefficient of variation of the lactate assay from regular quality control testing in our laboratory is approximately 2.9%.

Cases were defined as the neonates with the highest umbilical cord arterial lactate  $\geq 4$  mmol/L ( $n=119$ ), who were selected from the cohort and temporally matched 1:1 based on mode of delivery with controls ( $n=119$ ), defined as neonates with umbilical cord arterial lactate  $<4$  mmol/L. In case of more than one possible matched control, the control was randomly selected from the potential controls. The cutoff of  $\geq 4$  mmol/L was chosen based on our prior work which showed that lactate at this level is most discriminatory for neonatal morbidity [7]. Although many clinicians use umbilical cord arterial pH as an assessment of neonatal acid-base status, cord blood arterial or venous lactate have been shown to be superior to pH or base deficit in predicting short-term neonatal morbidity [7, 8].

EFM patterns were extracted by trained obstetric research nurses who were blinded to clinical data including outcomes, using the National Institute of Child Health and Human Development system for two distinct periods: in the first 60 minutes after admission and in the first 60 minutes after achieving the active phase of labor. If there was overlap between these two time periods, the EFM data was analyzed at the latest phase for that patient. Heart rate patterns were characterized by fetal heart rate baseline, variability (absent, minimal, moderate, marked), presence and number of accelerations, and presence, number, and type of decelerations (variable, early, late, prolonged). Within each of the two 60-minute periods, we defined “always” (e.g. “always moderate variability”) as present for all 60 minutes of that period. We also examined “severe” decelerations, defined as decelerations with nadir below 60 beats per minute [3]. Finally, in accordance with previous studies we examined the total area of decelerations [2, 3]. EFM patterns were interpreted in 10-minute epochs by trained obstetric research nurses with high interobserver and intraobserver reliability. The readers underwent blind rereading of 30 EFM tracings after every 500 patients over the entire study period, with a range of Spearman correlation coefficients of 0.83–0.95, mean differences in deceleration area of  $108 \pm 248$  (intra-observer) and  $154 \pm 424$  (inter-observer). These nurses were blinded to all outcome and clinical data as well as group assignment.

Maternal and neonatal demographic data included obstetric and gynecologic history, use and types of labor augmentation, type of labor, delivery mode, complications, regional anesthesia, and neonatal birthweight. Neonatal outcomes were ascertained from the neonatal medical record as diagnosed by the attending neonatologist. Neonatal outcomes included death, requirement for therapeutic hypothermia, mechanical ventilation, respiratory distress, meconium aspiration syndrome, suspected sepsis, hypoxic-ischemic encephalopathy, or seizures. Composite neonatal morbidity was defined as having at least one of those conditions, and composite neurological morbidity included hypoxic-ischemic encephalopathy, requirement for therapeutic hypothermia, or seizures.

Baseline characteristics of women who delivered infants with and without elevated lactate were compared. Continuous variables were tested for normality with the Shapiro-Francia test. The Student *t* test and Mann-Whitney *U* test were used for continuous variables;  $\chi^2$  and Fisher exact tests were used for dichotomous variables as appropriate. Crude odds ratios (cOR) and odds ratios and 95% confidence intervals (CI) adjusted for oxytocin use (aOR) were calculated for each of the EFM characteristics at admission and in the first 60 minutes of the active phase.

To determine the association between elevated umbilical arterial lactate at delivery and change in EFM parameters between admission and the active phase, the proportion of fetuses with changes in EFM parameters was determined for each parameter. These changes were characterized as present on admission but no longer present in the active phase, present on admission and still present in the active phase, not present on admission and then present in the active phase, or neither present on admission nor in the active phase.

A two-sided *p*-value of  $< 0.05$  was considered statistically significant. There was no adjustment for multiple comparisons. Analyses were performed using SAS software

(Version 9.2; SAS Institute Inc, Cary, NC). The study was conducted after approval from the Washington University School of Medicine Human Research Protection Office.

## Results

Characteristics of the study participants are shown in Table 1. There were no significant differences between the cases and controls with the exception of maternal age which was higher in the group with elevated lactate ( $p < 0.01$ ), and oxytocin use which was more common in the controls ( $p = 0.04$ ). The median lactate (interquartile range) in the cases was 8.3 mmol/L (interquartile range [IQR] 7.2-9.6) and in the controls was 2.5 mmol/L (IQR 2.2-3.1). There were no differences among other characteristics including obesity, birthweight, or hypertensive disorders of pregnancy. Neonatal outcomes by group are shown in Table 2. Notably, neonates with umbilical cord arterial lactate  $\geq 4$  mmol/L were significantly more likely to have neurologic morbidity as well as more likely to have overall composite neonatal morbidity (49 (41.2% of cases) vs. 14 (11.8%) of controls, aOR for overall composite morbidity (95% CI) 4.94 (2.52, 9.68).

There were no differences in EFM parameters in the first 60 minutes of admission between cases and controls (Table 3). There were also no associations between elevated umbilical arterial lactate at delivery and deceleration patterns or total deceleration area.

However, there were significant differences in EFM parameters in cases and controls in the first 60 minutes of the active phase of labor (Table 4). In particular, cases were less likely to have always category I tracings (26.1% of controls and 13.5% of cases, aOR 0.48, 95% CI 0.24, 0.94). Cases were also less likely to have always moderate variability. Notably, there were no differences in deceleration patterns, and presence of late decelerations were similar in the two groups (21.0% in the controls and 18.5% in the cases,  $p = 0.72$ ).

When changes between EFM on admission and in the active phase were compared, fetuses with elevated lactate at delivery were less likely to have a category I tracing at both time points (aOR 0.36, 95% CI 0.14, 0.94) and less likely to have persistent moderate variability (aOR 0.46, 95% CI 0.22, 0.96). They were also more likely to have always category II tracings across both time points (aOR 2.37 (1.06, 5.31)). There were no significant changes in deceleration patterns (Table 5).

## Discussion

In patients who entered active labor, we found no differences in EFM characteristics at admission to labor and delivery between fetuses with normal arterial lactate at birth and those with elevated lactate at delivery. However, in the first 60 minutes of the active phase, fetuses with elevated lactate at delivery were less likely to have moderate variability and category I tracings. Significantly, there were differences in the EFM characteristics at the two time points taken together: fetuses with elevated lactate at birth were less likely to have moderate variability and category I tracings both at admission and in the first 60 minutes of the active phase.

In our previous work, we observed that in the last 120 minutes prior to delivery, deceleration area was most predictive of acidemia, and moderate variability alone was not protective against acidemia [2]. The findings in this study suggest that there is an evolution in EFM patterns over the labor course associated with abnormal acid-base status at birth. This difference suggests that as the labor course progresses EFM parameters may have different associations with eventual neonatal outcome and thus differences in clinical meaning.

Multiple randomized controlled trials specifically of EFM at admission to labor and delivery have demonstrated that universal EFM at admission does not improve neonatal outcomes and indeed increases cesarean delivery rates[9-11]. We found no differences in EFM parameters on admission between fetuses with and without elevated umbilical arterial lactate at birth, suggesting that in these fetuses admission EFM lacked clinical utility. However, our study only included patients who achieved active labor. Therefore, patients with abnormal admission EFM precipitating delivery in the latent phase were excluded. Although universal EFM on admission has not been shown to improve neonatal outcomes, the results of our study can only be extrapolated to patients who achieved the active phase. This finding does not hold true in the active phase, at which point there were significant differences between the two groups of fetuses.

Strengths of our study included examining time periods remote from delivery. A recent editorial discussed the importance for obstetric providers to consider the entire EFM tracing and not just a short period of time proximal to delivery [6]. By examining EFM on admission and in the beginning of the active phase we were able to better contextualize delivery outcomes. An additional strength of our study is the rigorous approach to interpretation of EFM and the prospective nature of the data collection including robust clinical and demographic data. EFM patterns were analyzed by trained clinical obstetric research nurses trained in the NICHD criteria and blinded to outcome. They also underwent formal inter- and intraobserver reliability testing to reduce reduced inter- and intraobserver variability [3]. At the same time, the use of human, and not computerized, interpretation presented a more real-world scenario since in daily practice EFM is subject to human interpretation. Unlike previous studies, we were able to examine umbilical cord arterial lactate which has been shown previously to have a higher correlation with neonatal morbidity than pH, but is comparable to base deficit [7]. In the present study, there was a strong association between elevated umbilical artery lactate and neonatal morbidity, lending validity to the use of this marker as a surrogate. Finally, we used universal umbilical cord gas collection, which eliminates selection bias when selective cord gas assessment is performed based on the neonatal status at birth.

That the study was restricted to patients with at least 60 minutes of EFM on admission and at the beginning of active labor may introduce bias as patients with clinically concerning EFM tracings may have been delivered before active labor or before 60 minutes of active labor, thus excluding them from the study. However, patients such as these were included in our recent cohort study of all laboring patients with at least 30 minutes of EFM data in the last 120 minutes prior to delivery [2]. This study was conducted among women who were at least 37 weeks gestation, potentially limiting extrapolation to the preterm population.

Finally, our study is further limited in that we do not have data on long-term neonatal outcomes.

Despite these potential limitations, the widespread adoption of EFM deserves evidence-based attention. EFM has never been shown in randomized studies to have a positive impact on significant neonatal outcomes [12]. However, it seems unlikely that obstetric providers will abandon this monitoring modality, and therefore it is essential to maximize its utility to improve neonatal outcomes and to reduce unnecessary interventions including cesarean delivery [12, 13]. Our results suggest that changes in EFM patterns at transition from early labor into active labor may have clinical significance at delivery. Still, future work is needed to fully optimize the use of EFM in modern obstetrics.

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Table 1.

## Clinical characteristics

	Lactate $\geq$ 4 mmol/L (N= 119)	Lactate < 4 mmol/L (N= 119)	P <sup>a</sup>
Maternal age, yrs	27.5 $\pm$ 7.3	24.9 $\pm$ 6.2	<0.01
Maternal age $\geq$ 35, yrs	21 (17.7)	9 (7.6)	0.02
Maternal race <sup>b</sup>			
African American	75 (63.0)	78 (65.5)	
Caucasian	31 (26.1)	25 (21.0)	0.79
Latina	7 (5.9)	7 (5.9)	
Other	5 (4.2)	7 (5.9)	
Body mass index (BMI)	34.2 $\pm$ 8.7	34.0 $\pm$ 7.6	0.89
Obese, BMI $\geq$ 30 kg/m <sup>2</sup>	76 (63.9)	78 (65.6)	0.79
Any gestational hypertension or preeclampsia	23 (19.3)	24 (20.2)	0.87
Gestational diabetes	5 (4.2)	1 (0.8)	0.21
Pregestational diabetes	5 (4.2)	2 (1.7)	0.45
Intrapartum fever	7 (5.9)	6 (5.0)	0.78
Nulliparous	63 (52.9)	63 (52.9)	1.00
Labor type			
Spontaneous	36 (30.1)	24 (20.2)	
Augmented	29 (24.4)	34 (28.6)	0.20
Induction	54 (45.4)	61 (51.3)	
Regional anesthesia <sup>c</sup>	108 (90.8)	113 (95.0)	0.21
Prostaglandin	25 (21.0)	26 (21.9)	0.87
Foley bulb	19 (16.0)	19 (16.0)	1.00
Oxytocin	75 (63.0)	90 (75.6)	0.04
Time in active labor (hours)	7.3 (3.1, 11.1)	5.7 (2.5, 9.4)	0.09
Gestational age at delivery, wks	39.2 $\pm$ 1.23	39.1 $\pm$ 1.18	0.87
Birthweight, g	3276 $\pm$ 513	3381 $\pm$ 502	0.11
Birthweight > 4000, g	9 (7.6)	12 (10.1)	0.49
Mode of delivery			
Vaginal delivery	36 (30.3)	36 (30.3)	
Operative vaginal	10 (8.4)	10 (8.4)	----
Cesarean	73 (61.3)	73 (61.3)	

<sup>a</sup>  $\chi^2$ , Fisher exact tests, or Student's t test

<sup>b</sup> missing=3

<sup>c</sup> Regional anesthesia considered to be an epidural, spinal, or a combination of epidural and spinal anesthesia



**Table 2:**

## Neonatal Outcomes

	Lactate $\geq 4$	Lactate $< 4$	cOR	aOR <sup>c</sup>
	(n= 119)	(n= 119)	(95% CI)	(95% CI)
Composite neonatal morbidity <sup>a</sup>	49 (41.2)	14 (11.8)	5.25 (2.60, 11.03)	4.94 (2.52, 9.68)
Composite neurologic morbidity <sup>b</sup>	20 (16.8)	0 (0.0)	--	--
Neonatal death	2	0	--	--
Respiratory distress	35	4	4.61 (1.11, 22.38)	5.62 (1.44, 21.84)
Mechanical ventilation	10	2	1.36 (0.24, 14.39)	1.86 (0.32, 10.90)
Meconium aspiration syndrome	4	2	0.48 (0.06, 5.96)	0.50 (0.08, 3.07)
Suspected sepsis	37	12	0.36 (0.04, 1.94)	0.37 (0.08, 1.90)
Hypoxic-ischemic encephalopathy	14	0	--	--
Therapeutic hypothermia	18	0	--	--
Seizures	7	0	--	--

cOR: crude odds ratio, aOR, adjusted odds ratio, CI confidence interval

N (%) for categorical outcomes

<sup>a</sup>Includes death, therapeutic hypothermia, mechanical ventilation, respiratory distress, meconium aspiration syndrome, suspected sepsis, hypoxic-ischemic encephalopathy, seizures

<sup>b</sup>Includes hypoxic-ischemic encephalopathy, therapeutic hypothermia, seizures

<sup>c</sup>Adjusted for oxytocin

**Table 3.**

Electronic fetal monitoring patterns in the first 60 minutes of admission

	Lactate $\geq 4$ mmol/L (N= 119)	Lactate $< 4$ mmol/L (N= 119)	cOR (95%CI)	aOR <sup>a</sup> (95%CI)
<b>EFM Parameters</b>				
Always Category I	41 (34.5)	53 (44.5)	0.65 (0.37, 1.14)	0.75 (0.43, 1.30)
Ever Category II	45 (37.0)	39 (32.8)	1.20 (0.68, 2.13)	1.12 (0.65, 1.93)
Ever Category III <sup>b</sup>	--	--	--	--
<b>Baseline</b>				
Always tachycardic	1 (0.8)	0 (0.0)	--	--
Ever tachycardic	5 (4.2)	4 (3.4)	1.65 (0.26, 6.52)	1.33 (0.35, 5.15)
Always bradycardic <sup>†</sup>	--	--	--	--
Ever bradycardic	2 (1.7)	2 (1.7)	1.00 (0.07, 14.01)	1.04 (0.14, 7.60)
<b>Variability</b>				
Always minimal	1 (0.8)	0 (0.0)	--	--
Always moderate	64 (53.8)	75 (63.0)	0.68 (0.39, 1.18)	0.75 (0.44, 1.28)
<b>Decelerations</b>				
Any severe decelerations	3 (2.5)	3 (2.5)	1.00 (0.13, 7.62)	0.98 (0.19, 5.06)
Any early decelerations	--	--	--	--
Any late decelerations	8 (6.7)	6 (6.7)	1.36 (0.40, 4.90)	1.26 (0.42, 3.81)
Any prolonged decelerations	7 (5.9)	6 (5.0)	1.18 (0.33, 4.38)	1.17 (0.38, 3.67)
Total deceleration area	1676 (759, 4673)	1555 (1044, 3629)	--	--

EFM: electronic fetal monitoring, cOR: crude odds ratio, aOR, adjusted odds ratio, CI confidence interval

Median (p25, p75) for continuous outcomes, N (%) for categorical outcomes

<sup>a</sup>Adjusted for oxytocin<sup>b</sup>No tracings were observed in either those with a lactate  $\geq 4$  mmol/L or a lactate  $< 4$  mmol/L

**Table 4.**

Electronic fetal monitoring patterns in the first 60 minutes of the active phase

	Lactate $\geq 4$ mmol/L (N= 119)	Lactate $< 4$ mmol/L (N= 119)	cOR (95%CI)	aOR (95%CI) <sup>a</sup>
<b>EFM Parameters</b>				
Always Category I	16 (13.5)	31 (26.1)	0.44 (0.21, 0.89)	0.48 (0.24, 0.94)
Ever Category II	52 (43.7)	41 (34.5)	1.50 (0.86, 2.63)	1.86 (1.06, 3.26)
Ever Category III <sup>b</sup>	--	--	--	--
<b>Baseline</b>				
Always tachycardic <sup>b</sup>	--	--	--	--
Ever tachycardic	6 (5.0)	1 (0.8)	6.21 (0.73, 87.99)	5.99 (0.70, 51.08)
Always bradycardic <sup>b</sup>	--	--	--	--
Ever bradycardic	1 (0.8)	1 (0.8)	0.99 (0.02, 76.49)	1.20 (0.07, 19.56)
<b>Variability</b>				
Always minimal	1 (0.8)	0 (0.0)	--	--
Always moderate	38 (31.9)	57 (47.9)	0.51 (0.29, 0.89)	0.57 (0.33, 0.98)
<b>Decelerations</b>				
Any severe decelerations	10 (8.4)	5 (4.2)	2.09 (0.63, 8.03)	2.27 (0.74, 6.93)
Any early decelerations	3 (2.5)	1 (0.8)	3.05 (0.24, 161.52)	3.21 (0.32, 31.75)
Any late decelerations	22 (18.5)	25 (21.0)	0.69 (0.35, 1.70)	0.96 (0.50, 1.84)
Any prolonged decelerations	12 (10.1)	14 (11.8)	0.84 (0.34, 2.06)	0.88 (0.39, 2.01)
Total deceleration area	5913 (3289, 12098)	6446 (1716, 13371)	--	--

EFM: electronic fetal monitoring, cOR: crude odds ratio, aOR, adjusted odds ratio, CI confidence interval

Median (p25, p75) for continuous outcomes, N (%) for categorical outcomes

<sup>a</sup>Adjusted for oxytocin<sup>b</sup>No tracings were observed in either those with a lactate  $\geq 4$  mmol/L or a lactate  $< 4$  mmol/L

**Table 5.**

Electronic fetal monitoring pattern changes from admission to active phase

	Lactate ≥ 4 mmol/L (N= 119)	Lactate < 4 mmol/L (N= 119)	P <sup>a</sup>	cOR	aOR <sup>b</sup>
<b>EFM Parameters</b>					
Always Category I			0.05		
No to no	69 (58.0)	52 (43.7)		<i>Ref</i>	<i>Ref</i>
No to yes	9 (7.6)	14 (11.8)		0.48 (0.19, 1.21)	0.54 (0.22, 1.35)
Yes to no	34 (28.6)	36 (30.3)		0.71 (0.39, 1.28)	0.82 (0.44, 1.52)
Yes to yes	7 (5.9)	17 (14.3)		0.31 (0.12, 0.80)	0.36 (0.14, 0.94)
Ever Category II			0.30		
No to no	46 (38.7)	52 (43.7)		<i>Ref</i>	<i>Ref</i>
No to yes	29 (24.4)	28 (23.5)		1.12 (0.61, 2.25)	1.42 (0.72, 2.80)
Yes to no	21 (17.7)	26 (21.9)		0.91 (0.45, 1.84)	0.76 (0.37, 1.58)
Yes to yes	23 (19.3)	13 (10.9)		2.00 (0.91, 4.39)	2.37 (1.06, 5.31)
<b>Variability</b>					
Always moderate			0.04		
No to no	40 (33.6)	29 (24.4)		<i>Ref</i>	<i>Ref</i>
No to yes	15 (12.6)	15 (12.6)		0.73 (0.31, 1.71)	0.85 (0.35, 2.06)
Yes to no	41 (34.5)	33 (27.7)		0.90 (0.46, 1.75)	0.99 (0.50, 1.96)
Yes to yes	23 (19.3)	42 (35.3)		0.40 (0.20, 0.79)	0.46 (0.22, 0.96)
<b>Decelerations</b>					
Any late decelerations			0.68		
No to no	90 (75.6)	90 (75.6)		<i>Ref</i>	<i>Ref</i>
No to yes	12 (10.1)	9 (7.6)		1.33 (0.54, 3.32)	1.55 (0.61, 3.92)
Yes to no	3 (2.5)	2 (1.7)		1.50 (0.24, 9.19)	1.25 (0.20, 7.92)
Yes to yes	1 (0.8)	0 (0.0)		--	--
Any prolonged decelerations			0.57		
No to no	101 (84.9)	99 (83.2)		<i>Ref</i>	<i>Ref</i>
No to yes	6 (5.0)	10 (8.4)		0.59 (0.21, 1.68)	0.70 (0.24, 2.03)
Yes to no	5 (4.2)	4 (3.4)		1.23 (0.32, 4.70)	1.22 (0.31, 4.75)
Yes to yes	--	--		--	--

The parameters are categorized as present neither upon admission nor in the first 60 minutes of the active phase (“no to no”), not present on admission but present in the first 60 minutes of the active phase (“no to yes”), present on admission but no longer present in the first 60 minutes of the active phase (“yes to no”) or present at both time points (“yes to yes”)

EFM: electronic fetal monitoring, cOR: crude odds ratio, aOR, adjusted odds ratio, CI confidence interval

<sup>a</sup>  $\chi^2$  or Fisher exact tests

<sup>b</sup> Adjusted for oxytocin