

Association between elevated intrauterine resting tone during labor and neonatal morbidity: A secondary analysis of a prospective cohort study

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Abstract

Objective: Internal contraction monitoring during the course of labor may identify elevated intrauterine resting tone. Our objective was to assess the association between elevated resting tone during labor and neonatal morbidity. **Design:** Secondary analysis of a prospective cohort study. **Setting and Population:** Term singleton patients with ruptured membranes and an intrauterine pressure catheter in place; Tertiary care hospital, United States of America **Methods.** Intrauterine resting tone was calculated as the average baseline pressure between contractions. The study group had elevated intrauterine resting tone, defined as intrauterine resting tone \geq 75th percentile. **Main Outcome Measures:** Composite neonatal morbidity: hypoxic ischemic encephalopathy, hypothermia treatment, intubation, seizures, umbilical arterial pH \leq 7.1, oxygen requirement, or death. **Results:** Of the 8580 patient in the cohort, 2210 (25.8%) were included. The median intrauterine resting tone was 9.7 mmHg (IQR 7.3-12.3 mmHg). Elevated resting tone was associated with shorter median duration of the first stage of labor (10.0 hrs vs 11.0 hrs, $p < 0.01$) and lower rates of labor induction ($p < 0.01$). Neonatal composite morbidity was higher among patients with elevated intrauterine resting tone (5.1% vs 2.9%, $p=0.01$). After adjusting for chorioamnionitis and amniocentesis, elevated intrauterine resting tone was associated with increased risk of neonatal morbidity (aOR 1.70, 95% CI 1.06-2.74). Compared to normal tone, elevated intrauterine resting tone was associated with mild acidemia and elevated lactate (aOR 1.81, 95% CI 1.38-2.37 and aOR 1.45, 95% CI 1.17-1.80, respectively). **Conclusion:** Elevated intrauterine resting tone is associated with increased risk of neonatal composite morbidity. **Funding:** None

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Short Title: Intrauterine resting tone and neonatal outcomes

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Design: Secondary analysis of a prospective cohort study.

Setting and Population: Term singleton patients with ruptured membranes and an intrauterine pressure catheter in place: Tertiary care hospital, United States of America

Methods . Intrauterine resting tone was calculated as the average baseline pressure between contractions. The study group had elevated intrauterine resting tone, defined as intrauterine resting tone [?]75th percentile.

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Results: Of the 8580 patient in the cohort, 2210 (25.8%) were included. The median intrauterine resting tone was 9.7 mmHg (IQR 7.3-12.3 mmHg). Elevated resting tone was associated with shorter median duration of the first stage of labor (10.0 hrs vs 11.0 hrs, $p < 0.01$) and lower rates of labor induction ($p < 0.01$). Neonatal composite morbidity was higher among patients with elevated intrauterine resting tone (5.1% vs 2.9%, $p=0.01$). After adjusting for chorioamnionitis and amnioinfusion, elevated intrauterine resting tone was associated with increased risk of neonatal morbidity (aOR 1.70, 95% CI 1.06-2.74). Compared to normal tone, elevated intrauterine resting tone was associated with mild acidemia and elevated lactate (aOR 1.81, 95% CI 1.38-2.37 and aOR 1.45, 95% CI 1.17-1.80, respectively).

Conclusion : Elevated intrauterine resting tone is associated with increased risk of neonatal composite morbidity.

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Keywords: Labor, Neonatal Outcomes, Intrauterine pressure, Intrauterine tone, Baseline tone

Tweetable Abstract

Elevated intrauterine resting tone is during labor associated with increased risk of neonatal morbidity

Introduction

Contraction monitoring during labor is critical to assessing the clinical response to labor induction. Evaluating uterine response to oxytocin allows for safe titration to achieve cervical dilation. There are three main strategies for contraction monitoring: manual palpation, external tocodynamometry and intrauterine pressure catheter (IUPC). Manual palpation can vary based on provider experience and maternal body habitus. An external tocometer allows for monitoring of contraction frequency and is non-invasive but does not provide an assessment of contraction magnitude which may be critical when determining need for cesarean delivery due to failure to progress. Internal contraction monitoring using an IUPC is more invasive and requires rupture of membranes prior to use. However, an IUPC offers additional advantages over tocodynamometry, most importantly, an objective measurement of intrauterine baseline and contraction-induced pressure, allowing for a more quantitative assessment of uterine contractility.

Prior to placement, the IUPC is calibrated outside the uterus, with external atmospheric pressure set as baseline or zero. Once placed inside the uterus, the IUPC will report a baseline pressure within the uterus between contractions (resting tone) and a peak intrauterine pressure when the uterus is maximally contracted. The difference between these two values calculated over a ten-minute period is considered the contraction pressure and is measured in Montevideo units (MVU)[1]. Prior research has focused on the impact of maximum tone and MVUs on labor duration and cervical dilation [2-4]. The potential neonatal effects of elevated baseline intrauterine pressure are unknown, but prior studies have shown that uterine contractions compress the spiral arteries, resulting in placental and fetal hypoxia [5, 6]. We hypothesized that elevated intrauterine resting tone could lead to compression of the spiral arteries, thus limiting uterine blood flow and resulting in neonatal compromise. Therefore, our objective was to assess the association between elevated resting tone during labor and neonatal morbidity.

Methods

This was a secondary analysis of a prospective cohort study of singleton term deliveries from 2010-2014. Patients were included in the analysis if they were [?]37 weeks gestation, had ruptured membranes and an IUPC in place for at least 30 minutes prior to delivery. Individual clinician decision making determined which patients received an IUPC for contraction monitoring. The patients were not involved in the study design. The Institutional Review Board and Human Research Protection Office approved this study. Patients with multiple gestations and those presenting for scheduled cesarean delivery were excluded. Trained obstetric research nurses blinded to outcomes abstracted intrauterine pressure measurements in 10 minute segments. Intrauterine resting tone was defined as the average baseline pressure between contractions during the 30 minutes prior to delivery. Elevated intrauterine resting tone was defined as intrauterine resting tone [?]75th percentile within this cohort. No established cut offs for defining elevated intrauterine resting tone have been published therefore the upper quartile was chosen.

The primary outcome was composite neonatal morbidity which included: Hypoxic ischemic encephalopathy, hypothermia treatment, intubation, seizures, umbilical arterial (UA) pH [?] 7.1, neonatal respiratory support, and neonatal death. Secondary outcomes included lactate [?] 4 mmol/l, NICU admission, 5 min Apgar <7 and mild acidemia defined as UA pH <7.2.[7, 8]. Mild acidemia was defined as UA pH < 7.2 as it has been associated with increased neonatal morbidity compared to neonates with UA pH [?] 7.2[7]. Our institution performs universal umbilical artery cord gases. These outcomes were compared between patients with and without elevated intrauterine resting tone.

Baseline demographics and outcomes were compared using χ^2 for categorical variables and the student t test or Mann-Whitney U test for continuous variables, as appropriate. Normality was tested using the Shapiro-Francia test. Multivariable logistic regression was used to estimate odds ratios (OR) while adjusting for potential confounders. Initial confounders included in the models were selected based on the results of univariate analyses and those that had biologic plausibility [9-13] [14]. Initial models included obesity, amniocentesis, tachysystole, induction, parity and fetal growth restriction. A backwards step-wise selection was then performed, keeping only covariates that remained significant ($P < 0.1$). Regression models assessing

the association between neonatal outcomes and elevated intrauterine resting tone included amnioinfusion as this has been previously associated with changes in uterine tone and neonatal outcomes, however, this covariate was not significant in the final model [13, 15]. Model fit was confirmed with the Hosmer-Lemeshow goodness of fit test[16].

A sub-group analysis was performed to evaluate the association between persistent elevated intrauterine pressure and primary and secondary outcomes. Persistent elevated intrauterine pressure was defined as present at both 30 and 120 min prior to delivery. Multivariable regression models were used to estimate the OR for primary and secondary outcomes for patients with normal uterine pressure, elevated resting tone only for the last 30 minutes prior to delivery and for patients with persistently elevated intrauterine pressure were performed. To account for elevated tone related to tachysystole, we performed an additional sensitivity analysis excluding those with uterine tachysystole during the monitoring period. We also performed a sensitivity analysis of patients who had elevated resting intrauterine pressure only in the second stage of labor.

All patients meeting inclusion criteria were included and an *a priori* sample size estimation was not performed. STATA Version 16 (STATA Corp., College Station, TX) was used to perform all analyses. STROBE guidelines were followed throughout the study [17].

Results

Of the 8580 patients in the cohort, 2210 (25.8%) had an IUPC with at least 30 minutes of pressure data prior to delivery and were included in this analysis. The median intrauterine resting tone was 9.7 mmHg (IQR 7.3-12.3 mmHg; Figure 1). A total of 567 patients had an average elevated resting intrauterine tone [?] 12.3 mmHg ([?]75th percentile).

Admission body mass index was higher for patients with elevated resting tone (33 mmHg [IQR 29-39] vs 32 mmHg [28-38], $p < 0.01$.) Patients with elevated resting tone were also older and more likely to be nulliparous (Table 1). Incidence of maternal comorbidities including chronic hypertension, pregnancy associated hypertension, and pregestational diabetes were not significantly different between groups ($p < 0.05$). Neonatal birth weight and incidence of intrauterine growth restriction did not differ for patients with elevated resting tone (Table 1).

Patients with elevated resting tone were less likely to undergo induction of labor (52.9 vs 60.4%, $p < 0.05$) and were less likely to deliver by cesarean (0.4% vs 2.4%, $p < 0.05$). Oxytocin use (84.0 vs 89.9%, $p < 0.01$) and maximum oxytocin dose achieved (12 mu/min [IQR 6-18] vs 14 mu/min [8-20], $p < 0.01$) were lower for patients with elevated resting tone compared to those with normal resting tone. Chorioamnionitis was more common among patients with high resting tone (6.2% vs 3.7%, $p = 0.01$). While the median durations of 1st and 2nd stage of labor differed slightly between patients with elevated and normal resting tone, overall prolonged labor duration > 24 hrs and prolonged 2nd stage [?] 3hrs were similar (Table 2). Incidence of tachysystole is more common for patients with elevated resting tone then patients with normal tone (15.3% vs 1.3%, $p < 0.01$).

Composite neonatal morbidity was significantly higher in the group with elevated resting tone (5.1% vs 2.9%, $p = 0.01$; Table 3). After adjusting for amnioinfusion and chorioamnionitis, elevated intrauterine resting tone was associated with increased odds of neonatal morbidity (aOR 1.70 95% [CI 1.06-2.74]; Table 3). Elevated intrauterine resting tone was associated with mild acidemia and elevated lactate (aOR 1.81 [95%CI 1.38-2.37] and aOR 1.45 [95% CI 1.17-1.80] respectively; Table 3). The incidence of low Apgar score at 5 minute and NICU admission was similar between groups (Table 3). Among women without evidence of tachysystole, high intrauterine resting tone remained significantly associated with increased risk of neonatal composite morbidity (aOR 1.64 [95%CI 1.01-2.78]).

A sub-group analysis stratified patients with intrauterine pressure for 30 minutes and 120 minutes prior to delivery. Persistently elevated intrauterine tone for 120 minutes prior to delivery was seen in 234 patients, representing 41% of all patients with elevated intrauterine resting tone. Increasing duration of elevated

resting tone was associated with increased risk of composite neonatal morbidity (2.9% for normal resting tone vs 3.9% for 30 minutes elevated resting tone vs 6.8% for 120 minutes elevated resting tone; p for trend 0.03). After adjusting for amnioinfusion and chorioamnionitis, persistently elevated intrauterine tone was associated with increased risk of neonatal morbidity while elevated tone for only 30 minutes did not (aOR 2.21 [95% CI 1.22-4.01] and aOR 1.34 [95% CI 0.71-2.50], respectively). A similar pattern was noted for lactate ≥ 4 mmol/l, 5-minute Apgar score < 7 , and umbilical artery pH < 7.2 (Table 4). The majority of patients included in the analysis were in the second stage of labor (98.1%). In a sensitivity analysis excluding those who delivered in the first stage of labor, elevated intrauterine resting tone remained significantly associated with composite neonatal morbidity (aOR 1.77 [95% CI 1.09-2.86]).

Discussion

Main Findings

Our findings indicate that higher intrauterine resting tone is associated with a significantly increased risk of composite neonatal morbidity, and evidence of neonatal acidemia with higher incidence of umbilical arterial pH < 7.2 and a lactate > 4 mmol/l. Additionally, increasing duration of elevated resting tone was associated with increased risk of composite neonatal morbidity.

Strengths and Limitations

Strengths of this study include use of a large diverse cohort, allowing for subgroup analysis and larger generalization of the results. Assessment of resting intrauterine tone is novel and addresses a quandary that is identified in clinical practice. There are several limitations to this study. First, placement of IUPC at our institution is not universal and thus the cohort is subject to selection bias. Additionally, our database only included the last 120 minutes of IUPC data, limiting our analysis to this timepoint. Due to a paucity of data on the average or “normal” resting intrauterine tone there is no established definition of elevated tone. We chose $\geq 75\%$, however, further investigations with larger sample sizes should be used to determine a possible threshold resting tone that is associated with uterine hypoperfusion and neonatal morbidity. The majority of patients delivered vaginally and were primarily in the second stage of labor for the duration of available IUPC data. Thus, we were unable to assess the effects of elevated resting tone throughout the first stage of labor. Lastly, while the number of patients included in the study was sizable it remains underpowered for individual analysis of rare adverse events leading to the need for a composite outcome with the potential bias associated with pooling outcomes.

Interpretation

Numerous studies have shown that uterine contractions result in compression of the uterine spiral arteries, decreased placental perfusion and intermittent fetal hypoxia [5, 18-21]. Peebles et al. additionally indicated that an interval of 2-3 minutes between contractions resulted in stable fetal cerebral hemoglobin saturations, while shorter intervals resulted in decreased oxyhemoglobin:deoxyhemoglobin ratios [22]. Thus, the time between contractions allows for maternal-fetal gas exchange, fetal metabolic recovery, and maintenance of normal fetal acid base status. In cases of uterine tachysystole, when this recovery time is decreased, accumulation of cord blood lactate is seen [23]. Our data suggest that higher intrauterine pressure during this recovery phase is associated with increased risk of fetal acidemia (as evidenced by low pH and elevated lactate in the umbilical artery). We suspect that the increased uterine resting tone results in decreased recovery in utero-placental perfusion between contractions, similar to the effect seen with tachysystole. In our sub-group analysis, excluding women with evidence of tachysystole prior to delivery, we observed the same relationship between intrauterine resting tone and neonatal morbidity, suggesting an independent effect.

Conclusion

Clinical Implications and practical recommendations

Elevated baseline intrauterine tone noted during labor prompts questions regarding subsequent labor management. Our data show that elevated intrauterine resting tone is associated with neonatal compromise.

We propose that this be considered during management of labor close to delivery. While the impact of this finding is not robust enough for us to suggest immediate or emergent delivery due to fetal concerns, the study should be used to interpret IUPC data in the context of labor progress, duration, and fetal tolerance.

Elevated intrauterine tone among patients in the second stage provides a context for potential intervention. Oxytocin augmentation is commonly continued from the first stage of labor into the second stage, however, it remains unclear if additional increased expulsion “power” is necessary to effect vaginal delivery following complete dilation. Oxytocin has known risks including fetal acidemia especially when used during the second stage [24]. Vlachos et al investigated the impact of stopping oxytocin infusions once active labor has been achieved and found that less cases of non-reassuring fetal heart rates were observed [25]. However, literature specifically evaluating need for oxytocin during the second stage is needed to determine the potential safety of continuing a common obstetrical practice. Similarly, we were unable to assess effects of elevated resting tone specifically during the first stage and cannot make conclusions regarding effects on neonatal morbidity outside the context of second stage of labor.

Incidence of lower umbilical cord pH has been associated with longer second stage. A meta-analysis from 2020 found a RR 2.00 (95% CI 1.30-3.07) [26]. Our data suggest that longer exposure to elevated resting tone is also associated with fetal acidemia and may compound the effects of prolonged second stage. Therefore, practice patterns to shorten the second stage of labor such as immediate pushing, manual rotation of occiput posterior position, and traditional coached pushing may also be employed to reduce time the fetus spends exposed to elevated pressure [27-30].

Research Implications and recommendations

Our data are among the first to suggest a link between intrauterine resting tone during labor and neonatal outcomes. We hypothesize that this is a result of persistent utero-placental hypoperfusion during labor due to limited recovery of uterine and spiral artery blood flow between contractions. However, this hypothesis will need to be tested with future clinical and mechanistic studies. The most relevant and urgent research directions to consider are whether duration of elevated intrauterine resting tone affects neonatal outcomes and to determine a more precise definition of “elevated” resting tone, rather than our empiric cutoff of $>75^{\text{th}}$ percentile. Additionally, studies examining whether any interventions, such as positional changes or intermittent pushing during second stage of labor, can decrease intrauterine resting tone and subsequently fetal morbidity, are needed.

We found that induction of labor, which applied to 58% of patients in the cohort, was less common among women with elevated resting tone. Similarly, women with elevated resting tone were less likely to receive oxytocin and had lower maximum doses of oxytocin during their labor. Despite fewer interventions, women with elevated resting tone were more likely to have a vaginal delivery. These findings suggest that higher resting tone may be a surrogate for more efficient uterine contractility and labor. However, since women in this cohort had an indication for IUPC placement, most likely due to dysfunctional labor, these findings need further assessment in a non-biased cohort. Further research is needed to determine the association between elevated resting tone, uterine contractility and labor progress.

Conclusions

Our findings suggest that elevated intrauterine resting tone is associated with increased risk of neonatal composite morbidity and may compound with time. Further investigation is needed to guide management of patients who experience elevated intrauterine resting tone during labor.

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Disclosure of Interests

The authors report no conflicts of interest

Contribution to authorship

All authors were involved in study conception and design. Dr. Alison Cahill specifically assisted with acquisition of data and drafting and revising the manuscript. Dr. Nandini Raghuraman was instrumental in conception, design, statistical analysis and drafting the manuscript. Dr. Ebony Carter assisted with acquisition of data and revising critically important manuscript drafts. Dr. Jeannie Kelly assisted with data collection and revising of critically important manuscript and intellectual content. Dr. Antonina Frolova was critical in conception, analysis and interpretation of data, and revising the manuscript for critically important intellectual content.

Details of Ethics Approval

The Institutional Review Board and Human Research Protection Office approved this study. IRB #202008034. Initial approval on August 6th, 2020 and reapproved on February 19th, 2021.

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Figure Caption: Average resting tone in the 30 minutes prior to delivery.

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Table 1: Maternal demographics and characteristics between patients with and without elevated intrauterine resting tone

| | Elevated resting tone ^a N= 567 | Normal resting tone N= 1643 | p-value |
|-----------------------|--|--------------------------------|---------|
| Maternal demographics | | | |
| Age (y) | 24.3 ± 5.34 | 26.0 ± 5.9 | <0.01 |

| | Elevated resting tone ^a N= 567 | Normal resting tone N= 1643 | p-value |
|---|---|---|---|
| Advanced maternal age ^b | 29 (5.1) | 157 (9.6) | <0.01 |
| Race Black White Latina Other | 422 (75.1) 94 (16.7) 30 (5.3) 16 (2.9) | 1164 (71.2) 321 (16.7) 101 (6.2) 48 (2.9) | 0.35 |
| Body mass index (kg/m ²) | 33 (29, 39) | 32 (28, 38) | <0.01 |
| Maternal weight (kg) | 89.0 (74.5-106.1) | 85.3 (73.5-101.6) | 0.02 |
| Pregnancy characteristics | | | |
| Gestational age (Weeks) | 39.3 ± 1.2 | 39.1 ± 1.3 | 0.04 |
| Gestational age <39 weeks | 218 (38.5) | 706 (43.0) | 0.06 |
| Nulliparity | 87 (50.6) | 622 (37.9) | <0.01 |
| Prior cesarean delivery | 51 (9.0) | 166 (10.1) | 0.44 |
| Maternal comorbidities | | | |
| Chronic hypertension | 37 (6.5) | 109 (6.6) | 0.93 |
| Hypertensive disorder of pregnancy | 125 (22.1) | 334 (20.3) | 0.39 |
| Pregestational diabetes | 13 (2.3) | 20 (1.2) | 0.07 |
| Fetal Characteristics | | | |
| Fetal growth restriction | 90 (15.9) | 272 (16.6) | 0.71 |
| Birthweight (g) | 3165 ± 472 | 3164 ± 471 | 0.17 |
| Male sex | 286 (50.4) | 817 (49.7) | 0.77 |
| ^a Elevated tone defined as > 75 th percentile | ^a Elevated tone defined as > 75 th percentile | ^a Elevated tone defined as > 75 th percentile | ^a Elevated tone defined as > 75 th percentile |
| ^b Defined as maternal age [?] 35 at time of delivery *Data presented as N(%), Mean ± SD, or Median (IQR) | ^b Defined as maternal age [?] 35 at time of delivery *Data presented as N(%), Mean ± SD, or Median (IQR) | ^b Defined as maternal age [?] 35 at time of delivery *Data presented as N(%), Mean ± SD, or Median (IQR) | ^b Defined as maternal age [?] 35 at time of delivery *Data presented as N(%), Mean ± SD, or Median (IQR) |

Table 2: Labor characteristics and mode of delivery between patients with and without elevated intrauterine resting tone

| | Elevated resting tone ^a N= 567 | Normal resting tone N= 1643 | p-value |
|---------------------------------|--|--------------------------------|-----------------|
| Labor characteristics | | | |
| Induction of labor | 300 (52.9) | 992 (60.4) | <0.01 |
| Artificial rupture of membranes | 391 (69.0) | 1,161 (70.7) | 0.44 |
| Oxytocin use | 476 (84.0) | 1475 (89.8) | <0.01 |

| | Elevated resting tone ^a N= 567 | Normal resting tone N= 1643 | p-value |
|---|---|---|---|
| Maximum oxytocin dose | 12 (6-18) | 14 (8-20) | <0.01 |
| High dose oxytocin (>20 mu/min) | 100 (21.0) | 395 (25.8) | 0.01 |
| Prostaglandin use | 124 (21.9) | 363 (22.1) | 0.91 |
| Magnesium use | 50 (8.8) | 143 (8.7) | 0.93 |
| Chorioamnionitis | 35 (6.2) | 61 (3.7) | 0.01 |
| Terbutaline | 25 (4.4) | 85 (5.2) | 0.47 |
| Labor Length (hrs) | 12.1 (8.2-16.8) | 12.5 (8.7-18.3) | 0.07 |
| Duration of 1 st stage (hrs) | 10.0 (6.4-15.0) | 11.0 (7.3-16.4) | <0.01 |
| Duration of 2 nd stage (min) | 29 (16-54) | 26 (13-51) | 0.02 |
| Labor duration >24hrs | 57 (10.1) | 182 (11.1) | 0.51 |
| Prolonged 2nd stage ([?]3hrs) | 19 (3.4) | 36 (2.2) | 0.15 |
| Tachysystole in last 30 minutes | 87 (15.3) | 22 (1.3) | <0.01 |
| Mode of delivery | 527 (93.0) 38 (6.7) 2 (0.4) | 1490 (90.7) 113 (6.9) 40 (2.4) | <0.01 |
| Spontaneous vaginal | | | |
| Operative vaginal | | | |
| Cesarean delivery | | | |
| ^a Elevated tone defined as > 75 th percentile | ^a Elevated tone defined as > 75 th percentile | ^a Elevated tone defined as > 75 th percentile | ^a Elevated tone defined as > 75 th percentile |
| *Data presented as N(%), Mean ± SD, or Median (IQR) | *Data presented as N(%), Mean ± SD, or Median (IQR) | *Data presented as N(%), Mean ± SD, or Median (IQR) | *Data presented as N(%), Mean ± SD, or Median (IQR) |

Table 3: Neonatal outcomes among patients with elevated intrauterine tone

| | Elevated resting tone ^a N=567 | Normal resting tone N=1643 | P value | OR (95% CI) | aOR (95% CI) ^b |
|---|--|----------------------------|---------|------------------|---------------------------|
| Composite neonatal morbidity ^c | 29 (5.1) | 48(2.9) | 0.01 | 1.79 (1.16-2.87) | 1.70 (1.06-2.74) |
| Hypoxic ischemic encephalopathy | 1 (0.2) | 1 (0.1) | 0.43 | | |
| Hypothermia treatment | 2 (0.4) | 3 (0.2) | 0.46 | | |
| Intubation | 3 (0.5) | 9 (0.6) | 0.96 | | |
| Seizures | - | 3 (0.2) | 0.31 | | |
| Neonatal death | 1 (0.2) | 1 (0.1) | 0.43 | | |
| Umbilical artery pH < 7.1 | 10 (1.8) | 17 (1.0) | 0.17 | | |

| | Elevated resting tone ^a N=567 | Normal resting tone N=1643 | P value | OR (95% CI) | aOR (95% CI) ^b |
|--|--|--|--|--|--|
| Oxygen therapy | 15 (2.7) | 30 (1.8) | 0.23 | | |
| NICU admission ^d | 9 (1.6) | 14 (0.9) | 0.14 | 1.88 (0.81-4.36) | 1.79 (0.77-4.18) |
| 5-minute Apgar score <7 | 16 (2.8) | 26 (1.6) | 0.06 | 1.81 (0.96-3.39) | 1.73 (0.92-3.26) |
| Umbilical artery pH <7.2 | 97 (17.1) | 165 (10.2) | <0.01 | 1.83 (1.39-2.40) | 1.81 (1.38-2.37) |
| Lactate [?] 4 mmol/l | 178 (31.5) | 382 (23.7) | <0.01 | 1.48 (1.20-1.83) | 1.45 (1.17-1.80) |
| ^a Elevated tone defined as > 75 th percentile | ^a Elevated tone defined as > 75 th percentile | ^a Elevated tone defined as > 75 th percentile | ^a Elevated tone defined as > 75 th percentile | ^a Elevated tone defined as > 75 th percentile | ^a Elevated tone defined as > 75 th percentile |
| ^b Adjusted for chorioamnioni- tis, amnioinfusion | ^b Adjusted for chorioamnioni- tis, amnioinfusion | ^b Adjusted for chorioamnioni- tis, amnioinfusion | ^b Adjusted for chorioamnioni- tis, amnioinfusion | ^b Adjusted for chorioamnioni- tis, amnioinfusion | ^b Adjusted for chorioamnioni- tis, amnioinfusion |
| ^c Composite Neonatal Morbidity: Hypoxic Ischemic en- cephalopathy, hypothermia treatment, intubation, seizures, UA pH[?]7.1, oxygen requirement, and neonatal death | ^c Composite Neonatal Morbidity: Hypoxic Ischemic en- cephalopathy, hypothermia treatment, intubation, seizures, UA pH[?]7.1, oxygen requirement, and neonatal death | ^c Composite Neonatal Morbidity: Hypoxic Ischemic en- cephalopathy, hypothermia treatment, intubation, seizures, UA pH[?]7.1, oxygen requirement, and neonatal death | ^c Composite Neonatal Morbidity: Hypoxic Ischemic en- cephalopathy, hypothermia treatment, intubation, seizures, UA pH[?]7.1, oxygen requirement, and neonatal death | ^c Composite Neonatal Morbidity: Hypoxic Ischemic en- cephalopathy, hypothermia treatment, intubation, seizures, UA pH[?]7.1, oxygen requirement, and neonatal death | ^c Composite Neonatal Morbidity: Hypoxic Ischemic en- cephalopathy, hypothermia treatment, intubation, seizures, UA pH[?]7.1, oxygen requirement, and neonatal death |
| ^d Neonatal intensive care admission | ^d Neonatal intensive care admission | ^d Neonatal intensive care admission | ^d Neonatal intensive care admission | ^d Neonatal intensive care admission | ^d Neonatal intensive care admission |

Table 4: Neonatal outcomes among patients with elevated intrauterine tone 30 minutes and 120 minutes prior to delivery

| | Normal resting tone N=1643 | Elevated ^a resting tone 30 min prior to delivery N=333 | Persistent elevated resting tone 120 min prior to delivery N=234 | aOR (95% CI) ^b Normal vs 30min | aOR (95% CI) ^b Normal vs 120min | P for trend |
|--|--|--|--|--|--|-------------|
| Composite neonatal morbidity ^c | 48(2.9) | 13 (3.9) | 16 (6.8) | 1.34 (0.71-2.50) | 2.21 (1.22-4.01) | 0.03 |
| NICU admission ^d | 14 (0.9) | 4 (1.2) | 5 (2.1) | 1.39 (0.45-4.26) | 2.33 (0.82-6.62) | 0.28 |
| 5-minute Apgar Score <7 | 26 (1.6) | 4 (1.2) | 12 (5.1) | 0.74 (0.26-2.15) | 3.14 (1.55-6.37) | <0.01 |
| Umbilical artery pH <7.2 | 165 (10.2) | 56 (16.8) | 41 (17.5) | 1.79 (1.29-2.48) | 1.84 (1.26-2.67) | <0.01 |
| Lactate [?] 4 mmol/l | 382 (23.7) | 93 (28.0) | 85 (36.3) | 1.25 (0.96-1.63) | 1.78 (1.33-2.39) | <0.01 |
| ^a Elevated tone defined as > 75 th percentile ^b Adjusted for chorioam- nionitis, amnioinfu- sion ^c Composite Neonatal Morbidity: Hypoxic Ischemic en- cephalopa- thy, hypothermia treatment, intubation, seizures, UA pH[?]7.1, oxygen requirement, and neonatal death ^d Neonatal intensive care admission | ^a Elevated tone defined as > 75 th percentile ^b Adjusted for chorioam- nionitis, amnioinfu- sion ^c Composite Neonatal Morbidity: Hypoxic Ischemic en- cephalopa- thy, hypothermia treatment, intubation, seizures, UA pH[?]7.1, oxygen requirement, and neonatal death ^d Neonatal intensive care admission | ^a Elevated tone defined as > 75 th percentile ^b Adjusted for chorioam- nionitis, amnioinfu- sion ^c Composite Neonatal Morbidity: Hypoxic Ischemic en- cephalopa- thy, hypothermia treatment, intubation, seizures, UA pH[?]7.1, oxygen requirement, and neonatal death ^d Neonatal intensive care admission | ^a Elevated tone defined as > 75 th percentile ^b Adjusted for chorioam- nionitis, amnioinfu- sion ^c Composite Neonatal Morbidity: Hypoxic Ischemic en- cephalopa- thy, hypothermia treatment, intubation, seizures, UA pH[?]7.1, oxygen requirement, and neonatal death ^d Neonatal intensive care admission | ^a Elevated tone defined as > 75 th percentile ^b Adjusted for chorioam- nionitis, amnioinfu- sion ^c Composite Neonatal Morbidity: Hypoxic Ischemic en- cephalopa- thy, hypothermia treatment, intubation, seizures, UA pH[?]7.1, oxygen requirement, and neonatal death ^d Neonatal intensive care admission | ^a Elevated tone defined as > 75 th percentile ^b Adjusted for chorioam- nionitis, amnioinfu- sion ^c Composite Neonatal Morbidity: Hypoxic Ischemic en- cephalopa- thy, hypothermia treatment, intubation, seizures, UA pH[?]7.1, oxygen requirement, and neonatal death ^d Neonatal intensive care admission | |

