Title:

Effect of oxytocin maximum dose and duration of exposure on postpartum hemorrhage following vaginal delivery

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morbidity composite in the unadjusted (OR 1.69, 95%CI 0.36 - 7.87) or adjusted models (aOR 0.25, 95%CI 0.02 - 3.85). There were no hysterectomies or maternal deaths in either group. Only one uterine rupture case was noted in the index CD group. Analyzed secondary maternal outcomes and subsequent neonatal outcomes were not significantly different between groups.

CONCLUSION: In our cohort, women who undergo a periviable CD do not have higher odds of severe maternal morbidity in subsequent pregnancies when compared to those with a prior periviable VD. Pooled multi-institutional data is necessary to further define the lifetime maternal risks of periviable birth for use in patient counseling.

Subsequent Pregnancy Obstetric Outcomes by Prior Periviable Mode of Delivery

Outcome	Index VD Group* (n = 74)	Index CD Group* (n = 60)	aOR†	95% CI
Primary Outcome				
Severe Maternal Morbidity Composite	1 (1.35)	6 (10.0)	0.25	0.02 - 3.85
Secondary Obstetric Outcomes				
Preterm Labor	21 (15.67)	10 (7.46)	2.49	0.52-11.98
Periviable Birth	5 (3.73)	0 (0.00)	N/A	N/A
PPROM	8 (5.97)	4 (2.99)	19.33	1.05-355.21
Abruption	5 (3.73)	2 (1.49)	0.47	0.04-6.07
Preeclampsia/ HELLP	4 (2.99)	4 (2.99)	0.21	0.02-3.28
Hemorrhage	6 (4.48)	4 (2.99)	0.25	0.02-3.47
Spontaneous Abortion	6 (4.48)	8 (5.97)	0.74	0.07-8.54
Pregnancy Termination	10 (7.46)	8 (5.97)	1.05	0.13-8.48
Intrauterine Demise	1 (0.75)	1 (0.75)	0.34	0.01-21.51

*All variables in Index CD and Index VD groups shown as n (%)
†OR adjusted for preterm labor in the index pregnancy, gestational age, previous classical hysterotomy and interconception interval

302 Maternal sense of control during childbirth and association with breastfeeding

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OBJECTIVE: To estimate whether maternal sense of control in labor is associated with breastfeeding at 4-8 weeks' postpartum.

STUDY DESIGN: This is a secondary analysis of data from a multicenter randomized controlled trial of elective induction of labor at 39 weeks gestation in low-risk nulliparous women. As part of this study, women completed the Labor Agentry Scale (LAS), a validated measure of women's feelings of control over the childbirth process, between 6-96 hours following delivery. The LAS score, which is higher with more perceived control during childbirth, was analyzed both as a continuous and categorical variable (quintiles). Breastfeeding by self-report at 4-8 weeks' postpartum was categorized as exclusive breast, breast and bottle, or exclusive bottle feeding. Women were included in this analysis if they labored, filled out a LAS questionnaire, had a neonate who survived until the postpartum visit, and provided information on feeding. Chi square and Kruskal-Wallis tests were used for bivariable analyses, and multinomial logistic regression was used to adjust for confounders.

RESULTS: Of 5,185 women included in this analysis, 32.9% (N=1,705) were exclusively breastfeeding, 31.2% (N=1,620) were breast and bottle feeding, and 35.9% (N=1,860) were exclusively bottle feeding 4-8 weeks after delivery. The overall LAS score ranged from 34 to 203 (median 167, interquartile range (IQR) 145-182). The median LAS score was 169 (IQR 151-183) for women exclusively breastfeeding, 166 (IQR 142-182) for women who were breast and bottle feeding, and 164 (IQR 142-181) for women bottle feeding only ($p < 0.001$).In the unadjusted multinomial model, women with LAS scores in the lowest two quintiles (i.e., those with lower perceived control during child birth) were less likely to be exclusively breastfeeding (as compared with those exclusively bottle feeding) than women in the highest LAS quintile (Table). When controlling for confounders, however, this association was no longer significant.

CONCLUSION: After adjustment for confounders, perceived control during childbirth was not associated with breastfeeding at 4-8 weeks postpartum.

Table: Labor agentry score and breastfeeding at 4-8 weeks' postpartum

		Labor Agentry Score[1]				
		Quintile 1 N = 1,024	Quintile 2 N = 1,077	Quintile 3 N = 982	Quintile 4 N = 1,024	Quintile 5 N = 1,078
N (%)	Exclusive breastfeeding	259 (25.3)	354 (32.9)	326 (33.2)	370 (36.1)	396 (36.7)
	Breast and bottle feeding,	359 (35.1)	322 (29.9)	308 (31.4)	306 (29.9)	325 (30.2)
	Exclusive bottle feeding	406 (39.7)	401 (37.2)	348 (35.4)	348 (34.0)	357 (33.1)
Unadjusted OR (95% CI)[2]	Exclusive breastfeeding	0.58 (0.47 0.71)	0.80 (0.65 0.97)	0.85 (0.69 1.04)	0.96 (0.78 1.18)	(reference)
	Breast and bottle feeding	0.97 (0.79 1.19)	0.88 (0.72 1.09)	0.97 (0.78 1.21)	0.97 (0.78 1.20)	(reference)
Adjusted OR (95% CI)[2,3]	Exclusive breastfeeding	0.95 (0.74 1.21)	1.02 (0.81 1.28)	0.95 (0.75 1.20)	1.01 (0.81 1.27)	(reference)
	Breast and bottle feeding	1.07 (0.86 1.34)	0.96 (0.77 1.20)	1.03 (0.82 1.29)	1.00 (0.80 1.25)	(reference)

[1] Hodnett ED, Simmons-Tropea DA. The Labour Agentry Scale: psychometric properties of an instrument measuring control during childbirth. Res Nurs Health 1987;10:301-10.
[2] Versus exclusive bottle feeding
[3] Adjusted for maternal age, race/ethnicity, BMI, marital status, insurance type, smoking, delivery type, neonatal NICU admission. Adjustment for center did not change the results.

303 Effect of oxytocin maximum dose and duration of exposure on postpartum hemorrhage following vaginal delivery

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OBJECTIVE: Recent data suggest rising rates of postpartum hemorrhage (PPH) secondary to uterine atony in developed countries. Oxytocin (OT) use is associated with increased rates of PPH as a result of uterine atony. We sought to determine the effect of prolonged use or high doses of OT on risk of PPH and transfusion.

STUDY DESIGN: This was a secondary analysis of a prospective cohort study of all women who had a vaginal delivery of a singleton gestation at ≥37 weeks gestation within a single institution from 2010-2014. Women with a prior cesarean delivery and with multiple gestations were excluded. The cohort was stratified by duration of OT exposure < or ≥15 hours from initiation to delivery (≥15 hours OT duration represented the 90th percentile) and by maximum dose of OT (<20mU/min vs ≥20mU/min). The primary outcomes were rates of PPH (estimated blood loss >500cc), severe PPH (estimated blood loss >1000cc), and need for blood transfusion. Multivariable logistic regression was used to account for confounders, including prolonged labor duration, obesity and nulliparity. Receiver operating characteristic (ROC) curves were used to examine the predictive value of OT duration and maximum dose on PPH.

RESULTS: Among 4,202 patients, maximum OT dose ≥20mU/min or OT exposure ≥15hrs was associated with an increased risk of PPH

(aOR 2.48, 95%CI 1.72-3.59 and aOR 2.10, 95%CI 1.34-3.29, respectively; Table 1). OT ≥15hrs was also associated with an increased risk of blood transfusion (aOR 2.62, 95%CI 1.08-6.34; Table 1). Although OT duration and maximum dose were modest predictors of PPH at best, OT duration was a better predictor of PPH than maximum OT dose (AUC 0.70 vs 0.66, p = 0.02; Graph 1). In the stratified analysis by low or high dose OT, OT exposure >15 hours was associated with PPH, severe PPH and need for blood transfusion only among women exposed to low dose OT (<20mU/min) but not among women exposed to high dose OT.

CONCLUSION: Prolonged OT exposure during labor is associated with increased rates of PPH and transfusion following a vaginal delivery. This trend remains after controlling for prolonged labor duration and is strongest among women receiving lower doses of OT. This suggests that long exposure to low doses of OT may be an important factor to consider in active labor management as it may predict or contribute to PPH.

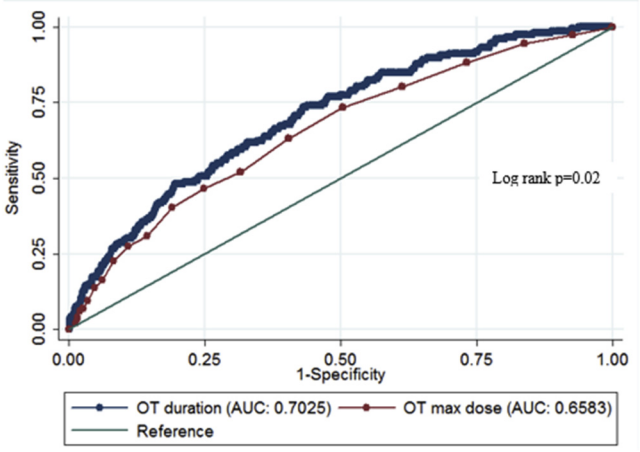
Table 1: Risk of postpartum hemorrhage, severe postpartum hemorrhage and transfusion following a vaginal delivery by maximum OT dose and duration of OT use.

	<20mU/min (N=3,376)	≥20mU/min (N=826)	OR (95%CI)	aOR (95%CI)
PPH	87 (2.58)	59 (7.14)	2.91 (2.03-4.13)	**2.48 (1.72-3.59)**
Severe PPH	10 (0.30)	5 (0.61)	2.05 (0.55-6.60)	1.54 (0.48-4.88)
Transfusion	22 (0.65)	13 (1.57)	2.44 (1.12-5.08)	2.01 (0.95-4.22)

	<15hrs (N=3,700)	≥15hrs (N=502)	OR (95%CI)	aOR (95%CI)
PPH	102 (2.76)	44 (8.76)	3.38 (2.35-4.89)	**2.10 (1.34-3.29)**
Severe PPH	12 (0.32)	3 (0.60)	1.81 (0.33-6.75)	0.83 (0.18-3.76)
Transfusion	24 (0.65)	11 (2.19)	3.43 (1.67-7.04)	**2.62 (1.08-6.34)**

Table values are n (%), unless indicated otherwise.
Odds ratio adjusted for obesity, nulliparity, induction, and labor duration >24hrs.

Figure 1: Receiver operating curve for postpartum hemorrhage.



304 Cluster analysis of preterm birth and neonatal adverse outcomes in low-risk nulliparous women

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OBJECTIVE: To use unsupervised learning approaches to detect mechanistic clusters associated with preterm birth (PTB) and adverse neonatal outcome among nulliparous women.

STUDY DESIGN: Secondary analysis of a multicenter prediction study embedded within a randomized trial to prevent preeclampsia in nulliparous women. The trial result was negative so treatment groups were combined for this analysis. Patients had blood drawn during the first trimester and uterine artery Doppler (UAD) performed before 21 weeks of gestation. Outcomes were ascertained by trained research coordinators. The primary outcome for this analysis was PTB < 37 weeks. The secondary outcome was an adverse neonatal outcome composite (ANC) defined as either perinatal death, a 5-minute Apgar score < 4, seizures, intubation in the delivery room, intraventricular hemorrhage, necrotizing enterocolitis, sepsis, or NICU admission > 48 hours. Cellular fibronectin, CRP, endoglin, IGFBP-1, leptin, PlGF, sFLT-1, ADAM12, PAPP-A, and PP13 were determined for selected women, and combined with UAD measures, as well as with clinical characteristics in a principal component analysis followed by a hierarchical clustering analysis to identify potential mechanistic clusters associated with PTB and ANC.

RESULTS: 620 women were included in this analysis. Of these, 63 (10.2%) had PTB and 88 (14.3%) had the ANC. Three clusters (subgroups) of patients were identified; patient characteristics among clusters are summarized in the Table. All characteristics were significantly different among clusters except cellular fibronectin, CRP and ADAM12. Additionally, there were significant differences in the frequency of PTB (8.6%, 8.4%, 16.1%; p-value=0.035), but not of ANC, among these clusters.

CONCLUSION: Using an unsupervised learning approach, we were able to stratify 3 clusters of nulliparous women with differing PTB characteristics and risks. Further studies are needed to elucidate the relevant biological pathways, and to improve stratification and phenotyping of patients at risk for PTB.

Table. Demographic and clinical characteristics across PTB clusters

	Cluster 1 (N=232)	Cluster 2 (N=251)	Cluster 3 (N=137)	P value*
PTB<37 weeks (%)	8.6	8.4	16.1	0.035
Continuous attribute, within cluster mean (SD)				
Maternal age	26.31±4.47	20.94±3.79	21.30±4.17	<0.0001
Total years of schooling	14.86±1.56	11.75±2.00	10.69±2.49	<0.0001
BMI at enrollment	24.88±4.83	27.20±7.00	26.03±5.71	0.0038
Baseline systolic BP	110.85±10.01	107.47±9.71	107.02±9.46	0.0001
Baseline diastolic BP	66.95±7.27	62.87±7.27	64.66±7.58	<0.0001
Waist to hip ratio	0.82±0.07	0.84±0.08	0.87±0.07	<0.0001
White blood count	8.83±2.02	8.22±2.12	8.61±2.09	0.006
Red blood count	4.35±0.33	4.14±0.39	4.29±0.29	<0.0001
Hemoglobin	13.32±0.90	12.20±0.89	12.76±0.94	<0.0001
Hematocrit	38.44±2.51	35.62±2.83	37.31±2.52	<0.0001
Platelet count	264.58±54.25	270.75±62.17	253.53±53.95	0.026
Mean platelet volume	8.66±1.06	9.57±1.37	10.33±1.56	<0.0001
Cellular fibronectin (ug/ml)	18.95±12.58	18.50±10.86	21.26±15.98	0.73
C-reactive protein (ug/ml)	6.10±6.75	7.04±7.89	5.75±5.72	0.84
Endoglin (ng/ml)	5.06±1.74	4.48±1.24	4.71±1.76	0.001
IGFBP-1 (ng/ml)	78.53±49.24	56.48±48.34	64.15±51.91	<0.0001
Leptin (ng/ml)	22.79±15.68	28.12±20.70	25.63±14.90	0.02
PlGF (pg/ml)	30.37±17.22	30.81±16.80	26.60±21.16	0.0008
sFLT-1 (pg/ml)	1509.42±931.77	1536.37±1141.30	1224.85±783.17	0.0008
ADAM12 (ng/mL)	517.63±232.08	492.79±243.33	467.35±204.43	0.10
PAPP-A (mU/mL)	2488.27±3105.37	2478.56±2594.14	1713.36±1407.74	0.007
PP13 (pg/mL)	72.36±40.10	66.07±31.88	58.85±26.29	0.0003
Mean RI	0.59±0.09	0.59±0.08	0.70±0.07	<0.0001
Mean PI	1.06 ± 0.30	1.08±0.29	1.55±0.39	<0.0001
Categorical attribute, percentage of cluster, % (N)				
Race African American	3.5 (8)	52.6 (132)	13.9 (19)	<0.0001
Hispanic	6.5 (15)	28.3 (71)	67.9 (93)	<0.0001
Married	87.1 (202)	16.3 (41)	23.4 (32)	<0.0001
Private insurance	86.6 (201)	5.6 (14)	10.2 (14)	<0.0001
Obstetrician as prenatal caregiver	91.8 (213)	31.1 (78)	34.3 (47)	<0.0001
Presence of notch (uterine artery Doppler)	11.6 (27)	5.2 (13)	34.3 (47)	<0.0001
Presence of bilateral notch (uterine artery Doppler)	3.9 (9)	0.4 (1)	16.1 (22)	<0.0001

* Kruskal-Wallis or Chi-square Test