

5 DOES THE HUMAN FETUS RUPTURE THE MEMBRANES IN PRETERM PROM? ROBERTO ROMERO¹, TINNAKORN CHAIWORAPONGSA¹, RICARDO GOMEZ², BO HYUN YOON³, MOSHE MAZOR⁴, ELI MAYMON², STANLEY BERRY⁵; ¹Perinatology Research Branch, NICHD/NIH, Detroit, MI; ²Perinatology Research Branch, NICHD/NIH, Detroit, MI; ³Seoul National University, Seoul; ⁴Soroka University Medical Center, Beer-Sheva; ⁵Wayne State University, Ob/Gyn, Detroit, MI

OBJECTIVE: The fetus plays a central role in the onset of preterm labor in the context of infection. We propose that the human fetus ruptures the chorio-amniotic membranes to accelerate its exit from a hostile intrauterine environment. To test this hypothesis, we measured fetal plasma concentrations of matrix metalloproteinase-9 (MMP-9), an enzyme implicated in the mechanisms of rupture of membranes and interleukin-1 beta (IL-1β), a cytokine that stimulates uterine contractility and MMP-9 expression.

STUDY DESIGN: Fetal plasma MMP-9 and IL-1β were measured in fetuses presenting with preterm labor and intact membranes (PTL) (n = 96) and preterm PROM (n = 43). Fetal blood and amniotic fluid were obtained by cordocentesis and amniocentesis under an IRB approved protocol. MMP-9 and IL-1β concentrations were determined by immunoassays.

RESULTS: 1) The median fetal plasma MMP-9 concentration was significantly higher in fetuses with preterm PROM than in those with PTL (median 128.6 ng/ml; range 18.8-1690 vs. median 93.7 ng/ml; range 13.2-738.5, P = .035); 2) In contrast, fetal plasma IL-1β was significantly higher in patients with PTL than in those with preterm PROM (median 3.75 pg/ml; range 0.5-99.1 vs median 2.61 pg/ml; range 0.14-252, P = .01); 3) The median amniotic fluid concentration of MMP-9 was higher in patients with preterm PROM than in those with PTL (median 16.8 ng/ml; range 0.4-1088 vs median 1.7; range 0.3-2160, P < .001); 4) There were no differences in the maternal plasma MMP-9 concentrations between patients in these two groups (P = .16).

CONCLUSION: Fetuses presenting with preterm PROM have increased concentrations of an enzyme implicated in the mechanism of membrane rupture (MMP-9) but lower concentrations of IL-1β than fetuses with PTL. These findings support the concept that the fetus plays a role in determining whether preterm labor begins with intact or rupture of membranes. We propose that rupture of membranes is a mechanism used by the fetus to accelerate its exit from a hostile intrauterine environment.

6 REASSESSING THE LABOR CURVE JIM ZHANG¹, JAMES TROENDLE², MICHAEL YANCEY³; ¹National Institute of Child Health and Human Development, NI, Bethesda, MD; ²National Institute of Child Health and Human Development, Bethesda, MD; ³Tripler Army Medical Center, TAMC, HI

OBJECTIVE: The Friedman curve has dictated the obstetric practice for half a century. However, the validity of this curve has never undergone rigorous tests.

STUDY DESIGN: We extracted detailed labor data from 1329 nulliparous parturients who were 18-34 years old undergoing term delivery of singleton, vertex fetus following spontaneous labor. 12.6% had c-section (excluded); 49% used epidural analgesia; 53% used oxytocin with a median maximum dose of 6mU/min. We used repeated measures regression with a ninth order polynomial function to discover the contemporary labor curve. To calculate the normal range of labor progression by cervical dilation, a two-stage modeling was conducted. Based on the speed of overall labor progression and current cervical dilation, we calculated the expected traverse time in order for the cervix to reach the next centimeter and the expected rate of cervical dilation at each phase of labor.

RESULTS: Our average labor curve of the first stage differs markedly from the Friedman curve. The transition from the latent phase to the active phase was more gradual. It took 5 h on average from 4cm to 9cm, comparing to <2 h under the Friedman curve. We observed no deceleration phase. The median duration of the second stage was 53 min, the same as Friedman's data. Several factors that may affect labor progression were examined.

CONCLUSION: Labor curve has a profound impact on the diagnosis of protraction and arrest disorders and the decision on C-section. Our results suggest that the pattern of labor progression in contemporary obstetrics differs significantly from the Friedman curve. The diagnostic criteria of <1.2 cm/h for protraction and >2 h of cessation for arrest disorders appear too stringent in nulliparas.

Table

Expected transverse time and rate of cervical dilation

CERVICAL DILATION (CM)		TRAVERSE TIME (H)			RATE OF CERVICAL DILATION (CM/H)		
FROM	TO	MEDIAN	5TH %	95TH %	MEDIAN	5TH %	95TH %
2	3	2.5	0.4	13.8	0.4	0.07	2.5
3	4	2.2	0.5	9.5	0.5	0.10	2.0
4	5	1.5	0.3	6.5	0.7	0.15	3.3
5	6	0.8	0.2	3.1	1.3	0.32	5.0
6	7	0.6	0.2	2.2	1.7	0.45	6.7
7	8	0.5	0.1	1.5	2.0	0.66	7.7
8	9	0.4	0.1	1.6	2.5	0.63	9.0
9	10	0.4	0.1	1.5	2.5	0.66	8.3

7 DO OUTCOMES DIFFER IN SPONTANEOUS VS ASSISTED-CONCEIVED TWINS? B LUKE¹, E ANDERSON¹, R MISIUNAS¹, D MARTIN², VH GONZALEZ-QUINTERO², L TOLAYMAT², MJ O'SULLIVAN², FR WITTER³, J MAULDIN⁴, RB NEWMAN⁴, M D'ALTON⁵, EA REECE⁶, GVD HANKINS⁷; ¹University of Michigan, Obstetrics & Gynecology, Ann Arbor, MI; ²University of Miami, Obstetrics and Gynecology, Miami, FL; ³Johns Hopkins University, Gynecology and Obstetrics, Baltimore, MD; ⁴Medical University of South Carolina, Department of Obstetrics and Gynecology, Charleston, SC; ⁵Columbia University, Obstetrics and Gynecology, New York, NY; ⁶Temple University, Obstetrics, Gynecology & Reproductive Science, Philadelphia, PA; ⁷University of Texas Medical Branch at Galveston, Obstetrics & Gynecology, Galveston, TX

OBJECTIVE: To evaluate differences in the course and outcome of twin pregnancies by spontaneous versus assisted-conception.

STUDY DESIGN: As part of an ongoing collaborative study of twins, data was obtained on 2,938 pregnancies (2,523 spontaneous + 415 assisted-conception) from seven medical centers in Baltimore, MD (510+66), Miami, FL (1,098+61), Ann Arbor, MI (377+214), Charleston, SC (329+47), Galveston, TX (67+2), New York, NY (68+24), and Philadelphia (74+1). Multiple and logistic regression modeling was used, controlling for confounding factors, to evaluate the effect of assisted conception on outcomes.

RESULTS: Women with assisted conceptions were significantly older (33.0 yrs vs 26.4 yrs), more likely to be primiparas (68% vs 36%), of normal or underweight before conception (75% vs 66%), and less likely to be smokers (3% vs 13%) or to have a monochorionic placentation (4% vs 23%). In models controlling for maternal race, age, insurance, height, pregravid weight, smoking, placental membranes, fetal reduction, and fetal gender, assisted conception was associated with significantly shorter gestations (-5.1 ± 1.6 days) and higher risks of delivering preterm (<36 wks, AOR 1.35, 1.03-1.79; <32 wks, AOR 1.50, 1.02-2.21), lower average birthweight (-110 ± 41g) and a higher risk of low birthweight (<2,500 g, AOR 1.40, 1.06-1.86) but not very low birthweight (<1,500 g, AOR 1.34, 0.89-2.07); and higher risks for cerclage (AOR 8.70, 4.32-17.51) and preterm labor (AOR 1.45, 1.08-1.95), but not preeclampsia or preterm premature rupture of membranes. Controlling for all factors listed above plus infertility indicated that fetal reduction is associated with significantly lower birthweights (-212 ± 41g) and higher risks for early preterm birth (<32 wks, AOR 1.97, 1.03-3.75; <30 wks, AOR 2.52, 1.14-5.60).

CONCLUSION: These findings indicate that twin pregnancies achieved through assisted conception are at higher risk for lower birthweights and shorter gestations, even after controlling for other factors.

8 VENOUS DOPPLER IN FETAL GROWTH RESTRICTION (IUGR): WHICH VESSEL? WHICH PARAMETER? CHRISTOPHER HARMAN¹, AHMET BASCHAT¹, ULRICH GEMBRUCH²; ¹University of Maryland at Baltimore, Obstetrics, Gynecology and Reproductive Sciences, Baltimore, MD; ²Medical University Lübeck, Obstetrics & Gynecology, Lübeck

OBJECTIVE: New data suggest adding precordial venous Dopplers may be crucial to completely evaluate IUGR. This study was designed to find the venous Doppler parameter(s) which best delineate critical outcomes.

STUDY DESIGN: 212 fetuses met entry criteria of IUGR (Birthweight <10%, elevated umbilical artery (UA) Doppler Pulsatility Index >2SD above gestational age mean) with normal karyotype and normal anatomy. Waveform pattern analysis of the ductus venosus (DV) and inferior vena cava (IVC) for presence of retrograde atrial-wave flow (RAV), and of the free umbilical vein for pulsatile flow (UV-P) was performed within one week of delivery. Numerical analysis used peak velocity index (PVIV) for DV and IVC; 2SD above gestational mean was considered abnormal. Indices were converted to z-scores to eliminate the effect of gestational age. Correlation of this set of Doppler parameters with critical outcomes (acidemia, defined by gestational norms, controlling for mode of delivery, stillbirth (SB), neonatal death (ND), total perinatal mortality (PM) and major neonatal morbidity (NM)) used stepwise logistic regression.

RESULTS: There were 17 SB and 12 ND (PM 13.7%). Acidemia complicated 63 (32%) liveborn. 47 neonates had NM, including the 12 ND. Several Doppler indices were statistically associated with SB, but only DV-RAV predicted ND. Thus, DV-RAV was the only venous Doppler parameter statistically significant in predicting PM (P < .001, Pearson coefficient 0.548). 14/19 fetuses with DV-RAV died (sensitivity 48%, specificity 97%, PPV 73%, NPV 93%). Conversely, in predicting acidemia among survivors, only UV-P was significant (P < .015, Pearson coefficient 0.395). In no vessel was PVIV elevation (either categorical or z-score) a significant predictor of PM, acidemia, or NM.

CONCLUSION: There is growing interest in adding venous Doppler to IUGR surveillance. This outcome-based study shows that DV and UV waveform pattern are the best venous markers. Numerical analysis provides little additional information.