## 43 Elevated mid-trimester maternal serum cytokines are associated with spontaneous preterm birth in women undergoing cerclage

**Angelica V. Glover, Robert A. Strauss, William H. Goodnight, Tracy A. Manuck**

University of North Carolina at Chapel Hill, Chapel Hill, NC

**OBJECTIVE:** To examine the role of maternal serum inflammatory biomarkers in the mid-trimester in women undergoing cerclage and assess the differences in serum cytokines between women destined to deliver preterm versus those who deliver at term after cerclage placement.

**STUDY DESIGN:** Prospective cohort study of singleton, non-anomalous pregnancies from 2016-2018 at a single tertiary institution who underwent a history-indicated, ultrasound-indicated (mid-trimester CL <25mm), or exam-indicated (asymptomatic cervical dilation) cerclage <24 weeks. Maternal blood was collected in the perioperative period. A custom magnetic bead Luminex cytokine assay was used to measure serum inflammatory cytokines (IL-1b, IL-6, IL-8, GCSF, MCP-1, TNF-a, MMP-8). Cytokine levels were compared between women with spontaneous preterm birth (SPTB) <37 weeks and those with term births. A statistical cut point was calculated for each cytokine to determine the optimal sensitivity and specificity of the cytokine in SPTB prediction. Women were classified as having a 'high' or 'low' result for each cytokine based on this cut point. Data were analyzed using t-test, $chi^2$, Cox regression, and Kaplan-Meier curves.

**RESULTS:** 42 women met inclusion criteria; 20 (47.6%) had SPTB and delivered at a median 29.6 (IQR 27.3-34.1) weeks. Samples were collected at a median of 0 (IQR -2 to 20) days after cerclage, at a median 17.6 (IQR 12.9-21.1) weeks' gestation. Baseline characteristics were similar between SPTB and term births (Table). Maternal serum levels of IL-6, MCP-1, and MMP-8 were higher in women with SPTB (Table). Overall, 10 women (24%) had 0-1 high cytokine results, 15 (35%) had 2 or 3, and 17 (41%) had $^3$4 high cytokine results. A greater number of high inflammatory cytokines [Hazard Ratio (HR) 3.4, 95% CI 2.0-5.7)] and ultrasound- or exam-indication for cerclage (HR 3.5, 95% CI 1.7-7.4) were associated with earlier delivery GA. Increasing numbers of high cytokine results were associated with preterm delivery (Figure). Presence of $^3$4 high cytokine results was 75% sensitive and 91% specific for SPTB (AUC 0.84, 95% CI 0.71-0.97; PPV=88%, NPV=80%).

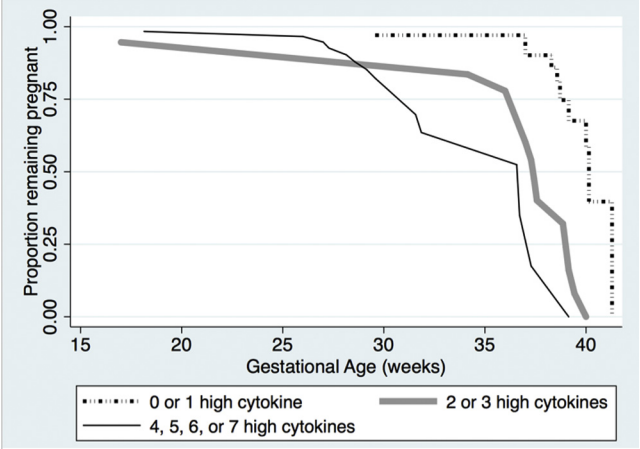
**CONCLUSION:** Among women who undergo cerclage and lack signs or symptoms of labor or intra-amniotic infection, an elevated maternal serum cytokine profile drawn in the perioperative period is associated with SPTB. Confirmation and refinement of this panel may provide insight into improved selection of patients who may benefit from cervical cerclage.

**Table.** Antenatal characteristics and cytokines, by GA at delivery. Data are n(%) unless specified.

| Characteristic | PTB N=20 | Term Birth N=22 | p-value |
|---|---|---|---|
| Black race | 6 (30.0) | 10 (45.5) | 0.303 |
| Married | 12 (63.2) | 15 (68.2) | 0.735 |
| ≥1 prior term birth* | 8/17 (47.1) | 9/20 (45.0) | 0.900 |
| ≥ 1 prior SPTB* | 13/17 (70.6) | 18/20 (90.0) | 0.212 |
| Received 17P** | 13/13 (100) | 19/19 (100) | >0.99 |
| Delivery GA of earliest delivery, mean weeks ± SD* | 25.4 ± 7.9 | 23.8 ± 5.9 | 0.495 |
| Ultrasound- or physical-exam indicated cerclage | 13/20 (65.0) | 10/22 (45.5) | 0.204 |
| Shortest vaginal cervical length, median mm (IQR) | 15 (2-27) | 21 (9.5-36) | 0.141 |
| Time between sample and delivery, median weeks (IQR) | 10.0 (6.7 – 16.1) | 20.2 (16.1 – 26.2) | <0.001 |
| **Serum Cytokine Results – Median values (IQR)** | | | |
| **Cytokine** | **PTB N=20** | **Term Birth N=22** | **p-value** |
| Interleukin-1-β (IL-1β) | 2.44 (0.58 – 5.12) | 0.02 (0.0 – 1.11) | 0.162 |
| Interleukin-6 (IL-6) | 6.00 (3.04 – 13.80) | 2.15 (1.70 – 2.86) | 0.015 |
| Interleukin-8 (IL-8) | 10.33 (3.83 – 14.47) | 2.53 (1.29 – 3.59) | 0.251 |
| Granulocyte colony stimulating factor (G-CSF) | 41 (28 – 49) | 60 (47 – 88) | 0.237 |
| Monocyte chemoattractant protein-1 (MCP-1) | 145 (68 – 219) | 109 (70 – 125) | 0.026 |
| Tumor necrosis factor-α (TNF-α) | 1.34 (0.05 – 3.86) | 0.99 (0.89 – 2.22) | 0.154 |
| Matrix metallo-proteinase-8 (MMP-8) | 6163 (2163–13295) | 1073 (763 – 2404) | 0.032 |

* Among multiparous women

**Figure.** Probability of remaining pregnant by number of 'high' cytokines.




* Adjusted for cerclage indication (ultrasound or exam indicated vs. prophylactic cerclage)

## 44 Randomized controlled trial of intrapartum glucose management in women with gestational diabetes: NCT02596932

**Maureen S. Hamel, Lindsey Kanno, Phinnara Has, Michael Beninati, Dwight J. Rouse, Erika F. Werner**
Alpert Medical School, Brown University, Providence, RI

**OBJECTIVE:** To assess the effect of tight compared to liberalized intrapartum maternal blood glucose management for women with gestational diabetes mellitus (GDM) on neonatal blood glucose concentrations.

**STUDY DESIGN:** Randomized controlled trial of women with singleton gestations and GDM attempting vaginal delivery. After written informed consent, women were randomly allocated to one of two intrapartum maternal glucose management protocols: tight control (hourly blood glucose measurements and treatment for maternal blood glucose <60 mg/dL or >100 mg/dL) or liberalized control (blood glucose measurements every four hours and treatment for maternal blood glucose <60 mg/dL or >120 mg/dL). The pediatric team assessing and treating the neonates were blinded to study group. The primary study outcome was the first neonatal blood glucose concentration (assessed within 2 hours of birth); the study was powered to have 80% power to detect a mean difference of 10 mg/dL between groups. Secondary outcomes included neonatal blood glucose concentrations within the first 24 hours of life, number of glucose treatments (IV or PO) that neonates received to improve their glucose, NICU admission, and neonatal hyperbilirubinemia.

**RESULTS:** From February 2016 to April 2018, 76 women were enrolled and all were included in the analysis: 38 in the tight control group and 38 in the liberalized group. Baseline characteristics of the two groups were comparable for all relevant obstetric variables; mean gestational age was 39 weeks in both groups. Antepartum, two thirds of women in each group were managed medically (almost exclusively with insulin). The primary outcome was similar between tight and liberalized groups: 53 mg/dL compared to 58 mg/dL, P=0.6. However, within the first 24 hours of life, mean neonatal glucose concentrations were lower in the tight control group: 54 mg/dL compared to 58 mg/dL, P=0.049. Other secondary outcomes were similar between groups.

**CONCLUSION:** A protocol aimed at tight maternal glucose management in labor, compared to liberalized management for women with GDM did not result in better initial neonatal glucose values and was associated with lower mean neonatal blood glucose concentrations in the first 24 hours of life. This study supports raising the upper threshold for intrapartum maternal glucose concentration and decreasing the frequency of intrapartum glucose assessment for women with GDM.

| Variable | Tight Control n=38 | Liberalized Control n=38 | P value |
|---|---|---|---|
| Maternal | | | |
| Labor duration (hours) | 9 (0-28) | 10 (0-42) | 0.33 |
| Any glucose value exceeding upper protocol threshold | 17 (45) | 3 (8) | 0.01 |
| Plasma glucose values | 85 (52-138) | 87 (68-121) | 0.84 |
| Insulin for maternal hyperglycemia | 12 (32) | 1 (3) | 0.01 |
| Insulin units administered | 5 (2-22) | 3 (-) | 0.8 |
| Neonatal | | | |
| Proportion with glucose <40 mg/dL within 2 hours of birth | 9 (24) | 9 (24) | 1.0 |
| Proportion with glucose <50 mg/dL within 2 hours of birth | 17 (45) | 15 (40) | 0.8 |
| Number of glucose evaluations in 1st 24 hours | 5 (3-19) | 4 (4-11) | 0.11 |
| Hours until blood glucose normalized | 7 [11] | 2 [4] | 0.14 |
| *Receiving any intervention (PO and/or IV) | 17 (45) | 12 (32) | 0.35 |
| Receiving IV intervention | 4 (11) | 0 (0) | 0.12 |

Data are median (range), number (%) or mean [SD]
*Threshold for intervention was neonatal blood glucose < 40 mg/dL at any time within the first 24 hours of life

## 45 Microstructural thalamic injury in a rat model of chorioamnionitis: potential avenues for neurorepair

**Vivek R. Katukuri[1], Jenny E. Camacho[1], Jessie R. Maxwell[1], Tracylyn R. Yellowhair[1], Jessie Newville[1], Shenandoah Robinson[2], Conrad Chao[1], Lauren L. Jantzie[3]**
[1]University of New Mexico, Albuquerque, NM, [2]Johns Hopkins Medicine, Baltimore, MD, [3]University of New Mexico, Albuqerque, NM

**OBJECTIVE:** The thalamus has an essential role in cognition and pain processing in former preterm children with cerebral palsy. Using our well-established model of chorioamnionitis (CHORIO) with mature CNS deficits that mimic those of preterm survivors, we tested the hypothesis that CHORIO would yield microstructural injury in the thalamus. We also tested whether postnatal treatment with a combination of erythropoietin (EPO) and melatonin (MLT) would reverse thalamic injury.

**STUDY DESIGN:** To induce CHORIO, a laparotomy was performed on embryonic day 18 (E18) in pregnant Sprague-Dawley rats. Uterine arteries were transiently occluded for 60 minutes followed by intra-amniotic injection of lipopolysaccharide (LPS, 4$\mu$g/sac). The laparotomy was closed and dams recovered. Shams had laparotomy but no other intervention. On postnatal day 1 (P1), pups were randomized to receive EPO (2000mg/kg/day from P1-P5) and MLT (20mg/kg/day from P1-P10). On P90, brain tissue was collected and processed for *ex vivo* diffusion tensor imaging (DTI) on a 7T