

- 146 ANTENATAL VARIABLES AND INFANT NEURODEVELOPMENTAL DAMAGE (ND) AMONG BABIES WITH BIRTH WEIGHT <1500 GRAMS** ANNA LOCATELLI<sup>1</sup>, MARIANNA ANDREANI<sup>1</sup>, AGNESE PIZZARDI<sup>1</sup>, ALESSANDRO GHIDINI<sup>1</sup>, SILVIA MALGUZZI<sup>1</sup>, JOHN PEZZULLO<sup>2</sup>, PATRIZIA VERGANI<sup>1</sup>, <sup>1</sup>University of Milano-Bicocca, Monza, Italy, Italy, <sup>2</sup>Georgetown University, Washington, District of Columbia

**OBJECTIVE:** To determine the association between antenatal factors and neurodevelopmental damage in preterm infants.

**STUDY DESIGN:** A cohort of babies born at <34.0 week gestation over a 8 year period with a weight <1500 grams underwent neurodevelopmental follow up. Obstetric and perinatal predictors, including clinical and histological signs of infection were analyzed using logistic regression analysis and related to neurodevelopmental delay (ND) including cerebral palsy.

**RESULTS:** 86.5% (n=225) of babies who survived underwent follow up for a median of 24 months (range 12-96) and 39 (17.3%) had ND. Only birth weight <1000 g (3.7 95%CI 1.7-7.7) and SGA (OR=0.3, 95% CI 0.2-0.7) were independently related to ND. Of interest, neither clinical or placental evidence of intrauterine infection was independently predictive of ND; however, infection was significantly correlated with lower gestational age at delivery (p=0.004, r=-0.36).

**CONCLUSION:** Lower birth weight is a risk factor and SGA a protective factor for development of ND. Intrauterine infection is not directly related to ND, but its effect may be mediated by lower gestational age at delivery.

#### Univariate analysis

	ND yes	ND no	p
	n=39	n=186	
GA at delivery	28.3±2	29.5±2	0.009
Birth-weight	982±264	1105±265	0.002
SGA	13%	31%	0.02
Histologic chorioamnionitis	20%	29%	0.3
Clinical chorioamnionitis	5%	7%	1
PROM	28%	19%	0.2

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- 147 CERVICO-VAGINAL CYTOKINE PROFILE THROUGH GESTATION AS A TOOL TO PREDICT PRETERM BIRTH IN WOMAN AT INCREASED RISK OF PREMATURITY** MARIYA SHYNOVA<sup>1</sup>, WENDY WHITTLE<sup>1</sup>, CAROLE WATSON<sup>1</sup>, KELLY SUMMERS<sup>2</sup>, ALAN BOCKING<sup>1</sup>, <sup>1</sup>Mount Sinai Hospital, Toronto, Ontario, Canada, <sup>2</sup>University of Western Ontario, London, Ontario

**OBJECTIVE:** To determine if pro and anti-inflammatory cytokine concentrations in the cervico-vaginal secretions through gestation are predictive of spontaneous preterm birth (SPTB) in women at increased risk of SPTB.

**STUDY DESIGN:** A prospective observational cohort study was conducted at Mount Sinai Hospital (Toronto, CA); women at increased risk of prematurity due to obstetrical history (n=56) underwent vaginal swabs at <16w, 18-22w, 28-32w and >32w gestational ages. Concomitantly, TVUS assessment of cervical length was recorded. Obstetrical outcome data was collected. Cytokine concentrations were measured by multiplex ELISA. Significance was set at p<0.05.

**RESULTS:** The mean gestation age at delivery for this cohort was 36.9 + 5.0w (21-41w); the rate of SPTB <37w was 27%. There was no significant change in the concentrations of IL-1beta; GM-CSF, TNFalpha and IL-10 through gestation for all patients. There was a significant increase in IL-6 and IL-8 concentration from the initial (<16w) to the final assessment prior to delivery in patients who delivered both at term and preterm; for patients delivering at term the concentration of IL-6 and IL-8 did not increase until after 32w gestation. There was a significant decrease in IL-4 concentration prior to delivery patients who delivered at term but a significant increase prior to delivery in patients delivering preterm. There was no correlation between cervical length and the concentration of any cytokine measured.

**CONCLUSION:** The cervico-vaginal concentration of pro-inflammatory cytokines IL-8 and IL-6 increased prior to delivery at term and preterm and thus may be a useful tool to predict SPTB in asymptomatic women at increased risk of prematurity.

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- 148 JOINT HYPERMOBILITY IS ASSOCIATED WITH IMPROVED LABOR OUTCOMES IN THE SECOND STAGE** KIMBERLY MAXON<sup>1</sup>, ELIZABETH SHAW<sup>1</sup>, SURAJ ACHAR<sup>1</sup>, DOUGLAS WOELKERS<sup>1</sup>, <sup>1</sup>University of California, San Diego, Departments of Internal, Family, and Reproductive Medicine, San Diego, California

**OBJECTIVE:** Connective tissue laxity affects athletic and orthopedic performance. Our objective was to determine if joint hypermobility, as measured by the thumb-to-forearm flex-test (Flex) was associated with labor outcomes and cesarean section.

**STUDY DESIGN:** Nulliparous women with singleton gestations were prospectively enrolled in this IRB-approved observational study. The Flex Test was assessed in clinic by trained providers. A positive test achieves contact between the dominant ipsilateral thumb and forearm without pain. Clinicians were blinded to the results. Primary outcomes were duration of active phase and second stage, and mode of delivery. Secondary outcomes included prematurity, hemorrhage, and lacerations. Univariate comparisons were made with Pearson Chi square, and Mann-Whitney U test. Significance was set at p<0.05.

**RESULTS:** Of 195 subjects, delivery data was available and complete for 163. The mean age was 23.3 yrs (SD 6.4) and the mean gestational age was 39.6 weeks (SD 1.6). 38 required cesarean section (23%). 60 subjects (37%) were Flex +. Among subjects who delivered vaginally, the median duration of the second stage of labor was shorter for Flex + than for Flex - subjects (31 vs 66 minutes, p=0.007). There was no difference in the duration of the total labor (6.2 vs. 6.3 hours, p=0.81) or in the overall rate of cesarean section between Flex+ and Flex- subjects (20 vs 25%, p=0.44). The rate of cesarean for dystocia, however, was lower in Flex + than in Flex - women (33% vs. 77%, p=0.01). There were no significant differences between groups in the risk for preterm labor, hemorrhage, or lacerations. After controlling for gestational age, birth weight and regional anesthesia, FlexTest + was still associated with a shorter second stage of labor (- 15 minutes, +/- 6, p=0.01).

**CONCLUSION:** Connective tissue laxity, as measured by the thumb-to-forearm Flex Test, is a modest predictor of obstetrical labor outcomes, and may identify women at lower risk of cesarean for dystocia in the second stage. Mechanisms for this association deserve further investigation.

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- 149 CYTOKINE GENE POLYMORPHISMS, BACTERIAL VAGINOSIS, AND SUSCEPTIBILITY TO SPONTANEOUS PRETERM BIRTH** JOSEPH BIGGIO<sup>1</sup>, ALICE GOEPFERT<sup>1</sup>, JAMES TANG<sup>2</sup>, SUZANNE OLIVER<sup>1</sup>, RICHARD KASLOW<sup>2</sup>, ELENA LOBASHEVSKAYA<sup>1</sup>, WILLIAM ANDREWS<sup>1</sup>, <sup>1</sup>University of Alabama at Birmingham, Obstetrics and Gynecology, Birmingham, Alabama, <sup>2</sup>University of Alabama at Birmingham, Epidemiology, Birmingham, Alabama

**OBJECTIVE:** The magnitude of inflammatory response to an environmental stimulus can vary as a result of genotypic differences in cytokine and receptor genes. Since spontaneous preterm birth (SPTB) is a complex disorder induced by gene-environment interaction, we examined whether polymorphisms in cytokine genes play a role in SPTB either independently or in combination with bacterial vaginosis (BV).

**STUDY DESIGN:** From a prospective cohort of 3,160 asymptomatic gravidas, we conducted a nested case-control study of 119 women with SPTB at <37 weeks and 135 randomly selected controls with birth ≥37 weeks. DNA was extracted from cervicovaginal swabs. PCR with sequence-specific primers was applied to define 14 SNPs in genes encoding *TNF*, *IL-2*, *IL-4*, *IL-6*, *IL-10*, *IL-12*, and the *IL-4* receptor (*IL4R*). BV was diagnosed on vaginal Gram stain obtained at 21-25 weeks' if the Nugent score was ≥7. SNP alleles and genotypes were compared before and after stratification by race, BV, and type of PTB.

**RESULTS:** In the overall cohort the only SNPs associated with SPTB were rs2070874 in the promoter region of *IL4* (T allele: OR 0.69; CI 0.48, 0.98) and rs1801275 in the coding region of *IL4R* (G allele: OR 0.54; 0.3, 0.98). Allele frequencies differed between African Americans (AA) (82% of patients) and Caucasians (P<0.0001). In AA, rs2070874 in was associated with SPTB at both the allele and genotype levels (T allele: OR 0.49; 0.27, 0.88). The T allele was associated with even lower likelihood of SPTB in AA with BV (OR 0.19; 0.06, 0.66). rs4251960 in *IL4* was also associated with SPTB in AA women with BV (T allele: OR 0.10; 0.04, 0.86). 68 cases were due to SPTL and 51 due to PROM. The *IL4* rs2070874 was associated with SPTL (OR 0.49; 0.27, 0.89), but not PROM (OR 0.84; 0.44, 1.62). Similarly, *IL2* rs2069762 was associated with SPTL (OR 0.3; 0.1, 0.9), but not PROM.

**CONCLUSION:** Several SNPs related to the *IL-4* pathway are associated with the risk of spontaneous preterm birth, especially in the presence of BV, and may play more of a role in SPTL than PROM.

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