18 QUANTITATIVE FETAL FIBRONECTIN SCREENING AT 24 WEEKS SUBSTANTIALLY DISCRIMINATES THE RISK OF RECURRENT PRETERM DELIVERY IN ASYMPTOMATIC PATIENTS WITH PRIOR PRETERM BIRTH

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OBJECTIVE: To determine the degree to which a single quantitative vaginal fetal fibronectin (fFN) screen at 24 weeks gestational age (wks GA) discriminates the risk of recurrent preterm delivery (PTD) in an asymptomatic high risk population.

STUDY DESIGN: We performed a secondary analysis of a prospectively collected data set (PREMET study, Shennan et al, BJOG, 2005) in which 900 high risk asymptomatic patients (pts) with singletons underwent vaginal fFN screening at 24 wks. 53 pts randomized to antibiotic intervention were excluded as were pts whose delivery information was incomplete. As > 80% of the remaining pts had a previous PTD, the analysis was focused on this high risk group, and those pts without prior PTD were also excluded. The remaining 572 patients who underwent fFN screening at 24 wks were analyzed, and all outcomes were included. Patients with indicated PTDs were excluded from the spontaneous PTD rate for that GA. All fFN tests were quantified (results not previously reported).

RESULTS: The overall spontaneous PTD rate <34 wks was 7.0% (40/571), and the spontaneous PTD rate < 37 wks was 21% (120/571). Rates of PTD at 32-37 wks generated 4 distinct stratified cluster groups (fFN 0, 1-49, 50-199, > 200). As fFN values increased, PTD rates also increased progressively. For example, the rates of PTD < 34 wks in the 4 groups were 5.1%, 15.0%, 22.2%, and 50%, respectively. Compared to the fFN 0 group, the relative risk for PTD < 34 wks was significantly and progressively increased in each group: 2.9 (1.3-6.7, p=.017), 4.3 (1.7-11.1, p=.013), and 9.7 (4.4-21.3, p=.0003). Using delivery probability analysis, similar trends were seen between groups at different GAs between 32-37 wks.

CONCLUSION: In asymptomatic pts with a prior PTD, a single quantitative fFN at 24 wks enables substantial discrimination of recurrent PTD risk which progressively increases for each increase in fFN level. A quantitative fFN provides more precise information regarding the risk of subsequent PTD compared to a standard qualitative fFN test (using a single 50 ng/mL cutoff).

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19 THE IMPACT OF CERVICAL LENGTH ON RISK OF PRETERM BIRTH IN TWIN GESTATIONS

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OBJECTIVE: To compare rates of preterm birth(PTB) <35 weeks(wks) in women with twin gestations identified to have a short cervix defined as cervical length(CL) <25thpercentile(%ile) at 16-20 wks who received 17 alpha hydroxyprogesterone caproate(17OHPC) versus placebo.

STUDY DESIGN: A secondary analysis of a randomized,double-blind,placebo-controlled trial of twin gestations exposed to 17OHPC versus placebo. Baseline transvaginal ultrasound of CL was performed prior to treatment assignment at 16-20 wks. The measurement cut off for 25th%ile was identified. Those with CL<25th and ≥25th%ile were compared regarding PTB <35 wks. The impact of 17OHPC in women with short cervix was evaluated.

RESULTS: Of 661 twin gestations studied,221(33.4%) women underwent CL measurement. Of these,101 were randomized to 17OHPC; 120 received placebo.The 25th%ile CL at 16-20 wks was 36 mm(range 16-72 mm). Clinical characteristics such as race,gravidity,parity,pregravid BMI,prior PTB,chorionicity,assisted reproductive technology,gestational age at randomization were similar between groups. Women with CL ≥25th%ile were older than those with cervix <25th%ile(31±6.8 vs 29±6.5 years,p=0.046).The risk for PTB <35 wks was increased for women with short cervix after controlling for treatment(RR 1.5,95%CI 1.12, 2.14,see Table,*one lost to follow up). 17OHPC did not reduce PTB <35 wks among those with short or long cervix.

CONCLUSION: In twin gestations, short CL at 16-20 wks is a marker for PTB. In the subgroup of women with twin gestation and CL <25th%ile, 17OHPC did not prevent PTB <35 wks.

	Total	Cervix < 25th %ile	Cervix ≥ 25th %ile	P-value
PTB <35wks		29/52 (55.8%)	62/168 (36.9%)	0.016
17OHPC	43/101 (42.6%)	18/28 (64.3%)	25/73 (34.3%)	0.006
Placebo	48/119 (40.3%)	11/24 (45.8%)	37/95 (39%)*	0.53
P-value	0.74	0.18	0.53	

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20 POLYMORPHISMS IN THROMBOPHILIA AND RENIN-ANGIOTENSIN SYSTEM PATHWAYS IN RELATION TO PRETERM DELIVERY, PLACENTAL ABRUPTION AND HISTOLOGIC EVIDENCE OF DISRUPTED VASCULAR INTEGRITY

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OBJECTIVE: In light of discrepant evidence linking polymorphisms in the renin-angiotensin system and inherited thrombophilias to risk of placental abruption and/or preterm delivery (PTD), we sought to further elucidate the roles of four candidate genes in placental vascular disruption.

STUDY DESIGN: Pregnant women from five Michigan communities were recruited at midtrimester (N=3019). At enrollment, women reported episodes of vaginal bleeding and provided blood samples. A subcohort (N=1371) had medical records abstracted, placental histopathology exams, and the following maternal DNA polymorphisms measured: methylenetetrahydrofolate reductase (MTHFR)677C->T, MTHFR1298A->C, Factor V (FVL)1691G->A, and angiotensinogen (AGT)704C->T. Associations between genes and abruption, PTD, hypertension, and bleeding were assessed using race-specific logistic models. Race-adjusted polytomous logistic regression was used to estimate risk of PTD subtypes defined by (1) placental abruption, (2) subclinical microscopic hemorrhage, and (3) no evidence of hemorrhage.

RESULTS: Among 959 white or African-American women, allele frequencies differed by race. No polymorphisms were associated with significantly increased risk of PTD, first trimester bleeding, or hypertension. FVL was associated with abruption (OR=3.9, 95% CI [1.3, 12]) in whites. However, stratifying PTD by evidence of hemorrhage revealed increased risk of both PTD/abruption (OR=3.2 [0.9, 12]) and PTD/subclinical hemorrhage (OR=3.6 [1.1, 12]) among FVL carriers, and trends toward increased risk of PTD/abruption with AGT (OR=2.7, [1.0, 7.7], and PTD/subclinical hemorrhage for MTHFR 677 (OR=2.1 [0.9, 4.7]) and MTHFR1298 (OR=1.8 [0.9, 3.7]). These results were unchanged after including hypertension and bleeding in the models.

CONCLUSION: Although only FVL was associated with abruption risk overall, these results suggest that other polymorphisms may contribute to a subset of PTDs through pathways involving disrupted vascular integrity. We found no evidence that these relations were mediated by first trimester bleeding or hypertension.

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21 BEYOND WHITE MATTER DAMAGE: NEURONAL INJURY IN PRETERM BIRTH

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OBJECTIVE: Novel to our laboratory, we have demonstrated that inflammation-induced preterm birth (II-PTB) results in perturbations in neuronal morphology and function. The objective of our study was to elucidate the mechanisms of this neuronal injury and to investigate whether the neurological damage could be reversed by mediators produced by the normal glial or neuronal milieu.

STUDY DESIGN: A mouse model of intrauterine inflammation was utilized for these studies. At E15, LPS was injected in to uterine horn; controls received no intervention. From each treatment group, fetal brains (fb) were harvested and either cortical cultures (neurons) or co-culture (glial +neurons) were created: 1) control cortical culture (CN) (n=12fb); 2) LPS-treated cortical culture (LN) (n=12); 3) control co-culture (CCC) (n=12); 4) LPS-treated co-culture (LCC) (n=12). Co-cultures were characterized. At 24 hours, CN and LN were treated with media from LCC, LN, CCC and CN. Confocal microscopy (NF200, MAP, GFAP, NeuN, A4B5) was performed. Morphology and number of dendritic processes recorded at division day 3 (DD3) for different treatment groups.

RESULTS: At 48 hours after treatment (DD3), media from LN and LCC induced morphological changes in CN comparable to LN .The neurological damage caused by in vivo exposure to inflammation could not be reversed by media from CN or CCC. Culture characterization at DD7, showed no significant changes between controls and LPS treated co-cultures (74% astrocytes, 23% neurons and 2% microglia); however, LCC showed neuronal morphological changes comparable to that of LN, including decreased aggregation and abnormal growth of processes.

CONCLUSION: II-PTB may be responsible for irreversible neuronal damage which may lead to a long term adverse neurodevelopment in ex-preterm infants including motor, cognitive and behavioral abnormalities. This work suggests that traditional lesions such as PVL or WMD may not be required for adverse long-term outcome and strategies to prevent specific neuronal injury are now warranted.

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