DIABETES

Abstracts 62 – 70

Moderators: Mark Landon, MD; Kim Boggess, MD

62 Hyperglycemia impairs cytotrophoblast function via stress signaling

Chase Cawyer[1], Darijana Horvat[2], Dean Leonard[3], Richard Jones[1], Steven Allen[1], Thomas Kuehl[1], Mohammad Uddin[1]
[1]Scott & White Healthcare/Texas A&M Health Science Center College of Medicine, Obstetrics and Gynecology, Temple, TX, [2]Scott & White Healthcare/Texas A&M Health Science Center College of Medicine, Medical Physiology, Temple, TX, [3]Baylor University, Waco, TX

OBJECTIVE: Diabetes mellitus is a risk factor for preeclampsia (preE). The normal extent of cytotrophoblast (CTB) invasion of the decidua, which is facilitated by plasmin, may be inhibited in preE. Inactive plasminogen is converted to plasmin by urokinase plasminogen activator (uPA), and uPA is regulated by plasminogen activator inhibitor 1 (PAI-1). Peroxisome proliferator-activated receptor gamma (PPARγ) also is implicated in the dysfunction of CTBs in hyperglycemic conditions. This study assesses the signaling mechanisms of hyperglycemia-induced CTB dysfunction.

STUDY DESIGN: Human CTBs (Sw. 71) were treated with 45, 135, 225, 495 or 945 mg/dL glucose for 48h. Some cells were pretreated with a p38 inhibitor (SB203580) or a PPARγ ligand (rosiglitazone). Thereafter, cell lysates were utilized to measure uPA, PAI-1 and PPARγ expression and p38 Mitogen Activated Protein Kinase (MAPK) phosphorylation by western blot. The mRNA expression of uPA and PAI-1 in CTB lysates was measured by qPCR. Levels of angiogenic (soluble fms-like tyrosine kinase-1 (sFLT-1), soluble endoglin (sENG)) and anti-angiogenic factors (VEGF, PlGF) and IL-6 were measured in the culture media by ELISA.

RESULTS: Both uPA and PAI-1 protein and mRNA expression were downregulated ($p<0.05$) in CTBs treated with >135 mg/dL glucose compared to basal (45 mg/dL). Anti-angiogenic factors (sENG, sFLT-1) and IL-6 were up-regulated, while the angiogenic factors (VEGF, PlGF) were down-regulated in the presence of >135 mg/dL glucose. The p38 MAPK phosphorylation and PPARγ expression were up-regulated ($p<0.05$) in hyperglycemia-exposed CTBs. SB203580 and rosiglitazone pretreatment attenuated glucose-induced down-regulation of uPA and up-regulation of p38 MAPK.

CONCLUSION: Exposure of CTBs to excess glucose inhibits the invasive profile of CTBs by decreasing the expression of uPA and PAI-1; by downregulating of VEGF and PlGF; and upregulating of sENG, sFLT-1, and IL-6. Attenuation of CTB dysfunction by SB203580 or rosiglitazone pretreatment suggests the involvement of stress signaling.

63 Macrosomia has roots in early placental development

Nadav Schwartz[1], Hayley Quant[1], Samuel Parry[1]
[1]University of Pennsylvania Perelman School of Medicine, Maternal and Child Health Research Program, Dept. Obstetrics and Gynecology, Philadelphia, PA

OBJECTIVE: Macrosomia (MACRO: ≥4000g) is associated with adverse neonatal outcomes and has been associated with modifiable risk factors such as weight gain and glycemic control. An early predictor of MACRO may identify patients for whom effective interventions can reduce their risk of macrosomia. We sought to determine if early placental size may be associated with the development of macrosomia.

STUDY DESIGN: 3D ultrasound volume sets were obtained at 11-14 weeks (N=578) and at 20-22 weeks (N=373) in a prospective cohort of singleton pregnancies. VOCAL (4DVIEW, GE) was used to calculate placental volume (PV). PV was normalized to gestational age to yield placental quotient (PQ). In addition, mean placental diameter (MPD) was the mean of 4 traced measurements of the maternal surface of the placenta taken every 45° degrees around the placental circumference. Potential confounders were included in multivariable regression models for the prediction of MACRO.

RESULTS: 7.6% (44/587) of our cohort had a MACRO infant. MACRO was associated with a higher median maternal age (33 vs 32y; P=0.09) and BMI (26.4. vs 24.6; P=0.01), a lower rate of nulliparity (4.6% vs 19.9%, P=0.01) and a higher rate of diabetes (6.8% vs 2.1%, P=0.08). Race was not significantly associated with MACRO (P=0.37). Both 1st and 2nd trimester placental measures were significantly associated with the development of MACRO (Table). These associations remained significant after adjusting for potential confounders. ROC analysis showed no significant difference in the predictive ability of the various adjusted models ($P>0.05$). Thus, 1st trimester placental measurements were similarly predictive of MACRO as 2nd trimester measures.

CONCLUSION: Early placental size is associated with the development of macrosomia even after adjusting for potential confounders. A non-invasive, point-of-care test that can identify those at greatest risk of MACRO may be useful in allowing for targeted counseling and interventions regarding diet, weight gain and diabetes screening that may impact pregnancy outcomes.

Placental Measure	Normal*	MACRO*	P-value	AUC alone	Adjusted AUC**
PV1 (cc)	65.8 (52.3-80.0)	74.5 (65.2-85.7)	0.006	0.6247	0.7235
PQ1	0.74 (0.60-0.90)	0.87 (0.75-0.98)	0.002	0.6395	0.7308
MPD1 (cm)	11.3 (11.1-11.4)	11.7 (11.3-12.2)	0.06	--	--
PV2 (cc)	237.9 (200.0-274.2)	265.8 (231.9-321.9)	0.005	0.662	0.7383
Volume/week (cc)	21.4 (16.8-26.0)	23.6 (20.1-30.8)	0.04	0.6438	0.7212
PQ2	1.7 (1.4-1.9)	1.9 (1.7-2.2)	0.002	0.6718	0.7462
MPD2 (cc)	15.5 (15.3-15.7)	16.7 (16.0-17.4)	0.0007	0.687	0.7719

*Descriptive data expressed as median (interquartile range); **1st trimester models adjusted for nulliparity, BMI, and DM; 2nd trimester models adjusted for nulliparity and DM.

64 In utero exposure to a maternal high fat diet Alters the epigenetic histone code in a murine model

Melissa Suter[1], Jun Ma[1], Patricia Vuguin[2], Kirsten Hartil[2], Ariana Fiallo[2], Maureen Charron[2], Kjersti Aagaard[1]
[1]Baylor College of Medicine, Obstetrics and Gynecology, Houston, TX, [2]Albert Einstein College of Medicine, Biochemistry, New York, NY

OBJECTIVE: Data from animal models show that in utero exposure to a maternal high fat diet (HFD) is deleterious to the health of the offspring, increasing the susceptibility to the adult onset of metabolic