

0.36 ±0.22-fold, respectively;  $p=0.0003$ ). VE obtained from normal pregnant women also showed a down-regulation of sFlt1 expression in response to cAMP (0.56 ±0.2 fold). However, the VE from PE placenta showed an upregulation of sFlt1 (1.82 ±0.8 fold,  $p=0.0001$ ).

**CONCLUSION:** While cAMP-mediated regulation of sFlt1 is similar in the decidua of normal vs PE placentas, there are marked differences in this regulation in the villous cells from these 2 groups of patients. The increased expression of sFlt1 induced by cAMP in VE from PE patients suggests that placentas of women with PE may have alterations in cAMP-mediated regulation of this gene, leading to an overexpression and secretion of sFlt1.

### 328 The impact of sperm exposure on the risk of pregnancy complications



Michal Fishel Bartal<sup>1</sup>, Baha Sibai<sup>2</sup>, Yossi Bart<sup>1</sup>, Shali Mazaki-Tovi<sup>1</sup>, Irit Eisen<sup>1</sup>, Micha Baum<sup>1</sup>, Israel Hendler<sup>1</sup>, Eyal Schiff<sup>1</sup>

<sup>1</sup>Sheba Medical Center, Ramat Gan, Israel, <sup>2</sup>University of Texas Health Science Center at Houston, Houston, TX

**OBJECTIVE:** Short duration of exposure to sperm before conception has been immunologically related to pregnancy complications. The aim of this study was to explore obstetric outcomes in relation to the extent of donor sperm exposure before pregnancy.

**STUDY DESIGN:** This was a retrospective cohort study in a single tertiary care center. All women with a singleton pregnancy who conceived following sperm donation (SD) between 08/2004-01/2016 were included. Obstetrics and neonatal outcomes for pregnancies following single SD were compared to pregnancies following repeat SD from the same donor. In a secondary analysis, we compared pregnancy outcomes among 3 modes of assisted reproductive technology (intrauterine insemination [IUI-SD], in vitro fertilization [IVF-SD] and IVF-sperm+ egg donation [IVF-SD+ED]). Logistic regression models adjusted for: maternal age, medical history, nulliparity and number of sperm donations from the same donor were performed to assess the association between the mode of assisted reproductive technology and pregnancy complications.

**RESULTS:** 706 pregnant women met inclusion criteria, 243 (34.4%) following the first SD and 463 (65.6%) following repeat donations from the same donor. Compared to repeat sperm donations, single donation was not associated with higher rates of preterm delivery (12.8% vs 12.7% respectively,  $P=0.99$ ), preeclampsia (7.0% vs 6.9%, respectively,  $P=0.999$ ) and intrauterine growth restriction (4.1% vs 3.9%, respectively,  $P=0.88$ ). In a secondary analysis of the study group we found that pregnancies following IVF-SD+ED had increased risk for preeclampsia (Adjusted Odds ratio [OR], 3.1; 95% confidence interval [CI], 1.5-6.6) preterm labor (Adjusted OR, 2.4; 95% CI, 1.1-5.4) and cesarean section (Adjusted OR, 2.1; 95% CI, 1.0-4.3) compared to IUI-SD and IVF-SD.

**CONCLUSION:** The extent of donor sperm exposure did not correlate with pregnancy complications, however double gamete donation was associated with increased risk for preeclampsia, preterm labor and cesarean section independent to maternal age, gravidity and previous exposure to the donor sperm.

### 329 Excess complement activation is associated with adverse outcomes in women with hypertensive disorders of pregnancy



Jesus Velasquez<sup>1,2,3</sup>, Richard Burwick<sup>3,4,5</sup>, Catalina M. Valencia<sup>3,6</sup>, Johanna Vargas<sup>7</sup>, Jaime L. Silva<sup>3,8</sup>, Francisco Edna-Estrada<sup>3,9</sup>, Jorge H. Gutiérrez-Marín<sup>3,10</sup>, Juliana Trujillo-Otálvaro<sup>11</sup>, Ana M. Gómez<sup>1</sup>, Mónica Rincón<sup>3,4</sup>, Carlos Cabas<sup>12</sup>, Alvaro Quintero<sup>11</sup>, Nataly González<sup>13</sup>, Viviana Lenis-Ballesteros<sup>1</sup>, Jorge E. Tolosa<sup>2,3,4</sup>

<sup>1</sup>Universidad de Antioquia, Hospital Universitario San Vicente Fundación, Medellín, Colombia, <sup>2</sup>Universidad de Antioquia, Departamento de Obstetricia y Ginecología; NACER Salud Sexual y Reproductiva, Medellín, Colombia, <sup>3</sup>FUNDARED-MATERNA, Bogotá, Colombia, <sup>4</sup>Oregon Health & Science University, Department of Obstetrics & Gynecology, Division of Maternal Fetal Medicine, Portland, OR, <sup>5</sup>Cedars-Sinai Medical Center, Los Angeles, CA, <sup>6</sup>Clínica Colsanitas S.A, Bogotá, Colombia, <sup>7</sup>Laboratorio Clínico Sanitas - Clínica Colsanitas S.A.- Grupo de Investigación INPAC, Bogotá, Colombia, <sup>8</sup>Hospital Universitario San Ignacio, Pontificia Universidad Javeriana, Bogotá, Colombia, <sup>9</sup>ESE Clínica de Maternidad Rafael Calvo, Grupo de Investigación Maternidad Segura, Cartagena, Colombia, <sup>10</sup>Clínica Universitaria Bolivariana, Universidad Pontificia Bolivariana, Medellín, Colombia, <sup>11</sup>Hospital General de Medellín, Luz Castro de Gutiérrez ESE, Medellín, Colombia, <sup>12</sup>Universidad del Sinú-ESE Clínica de Maternidad Rafael Calvo, Cartagena, Colombia, <sup>13</sup>Universidad de Cartagena-ESE Clínica de Maternidad Rafael Calvo, Cartagena, Colombia

**OBJECTIVE:** Complement activation occurs in normal pregnancy, but excess activation is associated with preeclampsia. Terminal complement activation generates C5b-9, the lytic membrane attack complex, which mediates organ damage. We hypothesize that activation of C5b-9 is increased in women with hypertensive disorders of pregnancy and adverse outcomes

**STUDY DESIGN:** We assessed urine and plasma C5b-9 levels in hypertensive subjects from project COPA (COmplement and Preeclampsia in the Americas), an IRB approved, multi-center observational study, which enrolled subjects from 6 centers and 3 cities in Colombia (Bogotá, Cartagena and Medellín; Nov 15-Jul 16). Hypertensive subjects enrolled in blocks by gestational age ( $\leq$  or  $\geq$  34 weeks) and diagnosis (ACOG criteria): 1. chronic hypertension (CHTN); 2. gestational hypertension (GHTN); 3. preeclampsia (PE) and; 4. PE with severe features (PE-SF). COPA was powered for PE-SF ( $n=100$ ). Clinical data, urine and plasma were collected by trained coordinators, with C5b-9 measured by enzyme linked immunosorbent assays (Human C5b-9 ELISA, BD Biosciences). Maternal and neonatal outcomes were assessed individually and as composite outcomes. Data were analyzed by Chi-square, t-test and logistic regression

**RESULTS:** 293 subjects were evaluated [CHTN ( $n=42$ ), GHTN ( $n=92$ ), PE ( $n=58$ ), PE-SF ( $n=101$ )]. Adverse maternal and neonatal outcomes, by plasma C5b-9 quartiles 1-4 (pC5b9, Q1-4), are shown in Table 1. Composite maternal outcomes were increased with low pC5b9 (Q1,  $\leq 1443$  ng/ml), particularly for those  $\geq 34$ wks (OR 2.93, 95% CI 1.0-8.6,  $p=0.05$ ). For neonates, preterm birth (PTB) was increased with lower pC5b9 levels (PTB,  $2870 \pm 1904$  vs. term,  $3572 \pm 2262$  ng/ml,  $p=0.006$ ). Adverse outcomes, by urine C5b-9 (uC5b9) quartiles, are shown in Table 2. They were more common with high uC5b9 levels (Q4,  $\geq 8.49$  ng/ml), predominantly due to increased kidney injury (OR 3.0, 95%CI 1.1-8.4,  $p=0.036$ ) and PTB (OR 2.0, 95% CI 1.2-3.5,  $p=0.01$ )

**CONCLUSION:** We describe a novel pattern of complement activation (low plasma / high urine C5b-9), which associates with adverse maternal and neonatal outcomes in women with hypertensive disorders of pregnancy. We postulate that excess complement activation

results in kidney injury and depletion of complement factors in plasma, with resultant pregnancy complications.

**Table 1.** Adverse maternal and neonatal outcomes, stratified by plasma C5b-9 quartiles in subjects with hypertensive disorders of pregnancy

Outcomes	Plasma C5b9 Quartile 1 (<1443)	Plasma C5b9 Quartile 2 (1444-2558)	Plasma C5b9 Quartile 3 (2559-4074)	Plasma C5b9 Quartile 4 (>4075)
Eclampsia (%)	0	1.5	0	1.4
Pulmonary edema (%)	0	0	0	1.4
Placental abruption (%)	1.8	1.5	1.3	1.4
Acute kidney injury, Cr ≥1.0 mg/dl (%)	14.9	5.3	2.7	6.1
Liver dysfunction AST/ALT ≥70 U/L (%)	9.1	6.8	5.2	4.0
<b>Composite Adverse Maternal Outcomes (Any of above, %)</b>	<b>18.3</b>	<b>12.9</b>	<b>3.4</b>	<b>10.0</b>
Preterm birth <37wks (%)	58.2	52.9	53.3	39.7
5 minute Apgar <7 (%)	4.1	8.1	0	6.0
NICU admission (%)	26.3	22.9	21.3	15.8
Respiratory distress syndrome (%)	20.0	19.4	18.0	14.5
<b>Composite Adverse Neonatal Outcomes (Any of above, %)</b>	<b>55.0</b>	<b>54.3</b>	<b>38.6</b>	<b>40.0</b>

**Table 2.** Adverse maternal and neonatal outcomes, stratified by urine C5b-9 quartiles in subjects with hypertensive disorders of pregnancy.

	Urine C5b9 Quartile 1 (<0.69)	Urine C5b9 Quartile 2 (0.70-2.34)	Urine C5b9 Quartile 3 (2.35-8.48)	Urine C5b9 Quartile 4 (>8.49)
Eclampsia (%)	0	0	1.5	1.4
Pulmonary edema (%)	0	0	0	1.4
Placental abruption (%)	0	0	6.0	0
Acute kidney injury, Cr ≥1.0 mg/dl (%)	7.1	1.7	4.8	12.3
Liver dysfunction AST/ALT ≥70 U/L (%)	5.4	7.0	4.6	6.3
<b>Composite Adverse Maternal Outcomes (Any of above, %)</b>	<b>8.7</b>	<b>7.9</b>	<b>13.9</b>	<b>17.1</b>
Preterm birth <37wks (%)	42.2	39.7	38.8	57.5
5minute Apgar <7 (%)	1.9	3.1	4.6	7.1
NICU admission (%)	16.4	19.4	17.1	31.1
Respiratory distress syndrome (%)	14.3	17.1	12.3	26.8
<b>Composite Adverse Neonatal Outcomes (Any of above, %)</b>	<b>43.5</b>	<b>42.1</b>	<b>41.7</b>	<b>56.6</b>

**330 Diet pattern is associated with an increased risk of hypertensive disorders of pregnancy**



Charlene Compher, Michal A. Elovitz, Samuel I. Parry, Jesse Chittams, Cody J. Griffith  
University of Pennsylvania, Philadelphia, PA

**OBJECTIVE:** Hypertensive disorders of pregnancy (HDP), including gestational hypertension and preeclampsia, remain significant contributors to maternal morbidity and preterm birth. Despite being a therapeutic target, the contribution of diet to these disorders is largely unstudied. The Diet Approach to Stop Hypertension (DASH) approach is rich in fruits, vegetables, and low fat dairy and limited in salt, saturated fat, total fat and cholesterol. DASH adherence was

linked to reduced cardiovascular risk factors and blood pressure in hypertensive, non-pregnant subjects. While the DASH approach is recommended to prevent and treat hypertension, it has not been studied in HDP. The objective of this study was to evaluate the impact of DASH diet adherence obtained before the 3<sup>rd</sup> trimester on the development of HDP.

**STUDY DESIGN:** A nested case-control study within a cohort of 303 nulliparous women was conducted. Mean intake from 3 dietary recalls obtained at weeks 21-26 was coded into a DASH adherence score (0-9), where higher score is a healthier dietary pattern. A diagnosis of HDP was obtained from chart review, using ACOG definitions for disorders, confirmed by a perinatologist. Cases with HDP (n= 81) were compared to controls (n=161) with no HDP or spontaneous preterm birth. Logistic regression models tested the association of DASH score or tertiles of DASH adherence score on outcomes of HDP. Models were uncontrolled or adjusted for age, BMI, insurance, and race.

**RESULTS:** Racial distribution and maternal age were not significantly different between the groups but mean BMI was slightly higher in cases, mean DASH score was lower, and high DASH diet adherence was less common in cases than controls (**Table 1**). Greater adherence to DASH diet was associated with reduced risk of HDP (OR -0.41, 95%CI -0.69 to -0.14) even when adjusted for race, type of insurance, BMI and age (OR -0.38, 95% CI -0.69 to -0.28) (**Table 2**). The lowest tertile of DASH diet adherence was associated with greatest likelihood of HDP (OR 2.52, 95%CI 1.23-5.19), even in the adjusted model (OR 2.29, 95% CI 1.03-5.19).

**CONCLUSION:** This study demonstrates that diet is associated with the development HDP. The provision of a healthy diet emphasizing fruits, vegetables, and low-fat dairy with limited salt and fat may hold promise as a therapeutic strategy towards prevention of HDP. (Penn March of Dimes Prematurity Research Center).

**Table 1. Demographic Characteristics of Study Participants**

	HDP (n=81)	Control (n=161)	P value
Age, y	29.8 (5.99)	29.1 (5.96)	0.371
Race, n(%)			0.088
• Black	48 (59.3%)	79 (49.1%)	
• Not Black	31 (38.3%)	82 (50.9%)	
Insurance, n(%)			0.375
• Private	45 (55.6%)	99 (61.5%)	
• Public	36 (44.4%)	62 (38.5%)	
Pre-pregnancy BMI, kg/m <sup>2</sup>	29.0±7.84	27.1±7.28	0.055
DASH Diet Score, mean(SD)	1.88 (1.10)	2.26 (1.23)	<b>0.029</b>
Tertiles of DASH score, n(%)			<b>0.0045</b>
• Low	28 (34.6%)	39 (24.2%)	
• Middle	29 (35.8%)	68 (42.2%)	
• High	10 (12.3%)	54 (33.5%)	

**Table 2. Models Predicting Hypertensive Disorders of Pregnancy**

	Unadjusted Models	P value	Adjusted Models+	P value
DASH Score				
HDP	-0.41 (95% CI -0.69 to -0.14)	<b>0.0029</b>	-0.38 (95% CI -0.69 to -0.28)	<b>0.013</b>
Control	Reference		Reference	
DASH tertile				
Low vs High	2.52 (95% CI 1.23-5.19)	<b>0.012</b>	2.29 (95% CI 1.03-5.09)	<b>0.042</b>
Low vs middle	1.74 (95% CI 0.92-3.29)	0.086	1.56 (95% CI 0.81-3.02)	0.188
Middle vs High	1.45 (95% CI 0.73-2.89)	0.294	1.47 (95% CI 0.70-3.10)	0.311

+ Model adjusted for age, BMI, race, insurance