Background

- In May 2009, after considering short and long-term maternal/child outcomes, the Institute of Medicine (IOM) revised recommendations for gestational weight gain (GWG); however preeclampsia was dismissed due to insufficient evidence.
- Since change in recommendations, epidemiologic studies have been published that support an association between GWG adherence and hypertensive disease of pregnancy.

AJOG 2009; 200(2):167.e1-7

Objective

To evaluate preeclampsia risk by angiogenic-biomarker profile by both BMI and GWG-adherence.

Hypothesis

We hypothesized that overweight/obese (OW-OB) women and over-gainers (OG) would have altered angiogenic profiles as compared to underweight/normal-weight (U-N) women and under-/appropriate-gainers (U-AG), respectively.

Materials & Methods

Pregnant subjects <24 weeks gestation enrolled from outpatient prenatal clinics at UMass Memorial Health Care between May 2004 and January 2006.

Each subject had ≥1 of the following risk factors for preeclampsia:

**Inclusion Criteria**

- Chronic HTN
- Renal Disease/COD
- Gestational DM
- History of Preeclampsia
- Teen Pregnancy ≤18
- Multi-fetal gestation
- Obesity (BMI > 30)
- APL Ab Syndrome
- SLE

**Exclusions**

- missing outcomes
- gestational HTN
- preeclampsia diagnosis

Subjects included in analyses 82 (342 specimens)

Excluded due to association with altered angiogenic profile:

- Hypertensive diseases of pregnancy (gestational HTN & preeclampsia) Moore Simas et al, AJOG, 2007;197:244.e1-244.e8

- sFlt1, PlGF and sEng levels were measured by ELISA

- BMI & GWG-adherence categories by 1990 IOM recommendations

- Pre-pregnancy BMI Category
  - Pre-pregnancy BMI* (kg/m2)
  - Total GWG at 40 weeks

- Underweight (U) <19.8 28-40 lbs
- Normal weight (N) 19.8-26.0 25-35 lbs
- Overweight (OW) 26.1-29.0 15-25 lbs
- Obese (OB) ≥30 At least 15 lbs

Adherence defined by GWG and GA @ last prenatal visit subtracted from pre-pregnancy weight; thus preterm and term deliveries included

Analytic sample included 82 subjects (342 specimens). See Table 1 for Demographic Comparisons.

BMI Categories

1. **Underweight**
   - Underweight - Normal
     - Normal weight - Overweight
     - Overweight - Obese

2. **GWG-adherence categories**
   - Under/appropriate gainer
     - Over gainer

**Demographic Characteristics**

<table>
<thead>
<tr>
<th>Demographic Characteristics</th>
<th>Underweight</th>
<th>Normal</th>
<th>Overweight</th>
<th>Obese</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>25.9±6.5</td>
<td>31.1±6.6</td>
<td>29.6±7.9</td>
<td>29.5±7.4 NS</td>
</tr>
<tr>
<td>Gravity</td>
<td>2.4±1.7</td>
<td>2.9±1.8</td>
<td>2.9±2.1</td>
<td>2.7±1.5 NS</td>
</tr>
<tr>
<td>Living Children</td>
<td>0.8±1.1</td>
<td>1.0±1.0</td>
<td>0.9±1.1</td>
<td>0.9±1.0 NS</td>
</tr>
<tr>
<td>GA at 1st PNV (wk)</td>
<td>11.8±4.4</td>
<td>12.0±6.0</td>
<td>11.8±4.8</td>
<td>12.0±6.3 NS</td>
</tr>
<tr>
<td>SBP at 1st PNV (mmHg)</td>
<td>114.0±12.5</td>
<td>119.5±13.7</td>
<td>117.1±14.2</td>
<td>119.1±13.1 NS</td>
</tr>
<tr>
<td>GA at first delivery (wks)</td>
<td>38.6±2.2</td>
<td>38.0±2.7</td>
<td>38.6±2.7</td>
<td>37.9±2.8 NS</td>
</tr>
<tr>
<td>Placenta weight (g)</td>
<td>443.8±90.1</td>
<td>443.6±206.9</td>
<td>526.4±155.7</td>
<td>371.3±176.2 NS</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td>White</td>
<td>Hispanic</td>
<td>Black</td>
<td>Other</td>
</tr>
<tr>
<td></td>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>White</td>
<td>13 (54.2)</td>
<td>35 (60.3)</td>
<td>19 (55.9)</td>
<td>29 (60.4) NS</td>
</tr>
<tr>
<td>Hispanic</td>
<td>10 (41.7)</td>
<td>13 (22.4)</td>
<td>10 (29.4)</td>
<td>13 (27.1) NS</td>
</tr>
<tr>
<td>Black</td>
<td>0 (0)</td>
<td>9 (15.5)</td>
<td>4 (11.8)</td>
<td>5 (10.4) NS</td>
</tr>
<tr>
<td>Other</td>
<td>1 (4.2)</td>
<td>1 (1.7)</td>
<td>1 (2.8)</td>
<td>1 (2.0) NS</td>
</tr>
<tr>
<td>Smoking Status</td>
<td>Current</td>
<td>Never</td>
<td>Current</td>
<td>Never</td>
</tr>
<tr>
<td></td>
<td>1 (4.2)</td>
<td>17 (70.3)</td>
<td>4 (11.8)</td>
<td>25 (73.5) NS</td>
</tr>
<tr>
<td>Prior Pregnancy</td>
<td>6 (25.0)</td>
<td>4 (14.7)</td>
<td>5 (14.7)</td>
<td>20 (58.8) NS</td>
</tr>
<tr>
<td>History of Preeclampsia</td>
<td>3 (12.5)</td>
<td>25 (73.5)</td>
<td>7 (20.6)</td>
<td>35 (72.9) NS</td>
</tr>
<tr>
<td>History of Renal Disease</td>
<td>4 (16.7)</td>
<td>9 (15.5)</td>
<td>7 (20.6)</td>
<td>6 (12.5) NS</td>
</tr>
<tr>
<td>Lupus</td>
<td>4 (16.7)</td>
<td>9 (15.5)</td>
<td>4 (11.8)</td>
<td>2 (4.2) NS</td>
</tr>
<tr>
<td>Antiphospholipid Syndrome</td>
<td>0 (0)</td>
<td>1 (2.8)</td>
<td>0 (0)</td>
<td>2 (4.2) NS</td>
</tr>
</tbody>
</table>

**GWG Adherence Categories**

<table>
<thead>
<tr>
<th>GWG Adherence Categories</th>
<th>Under/appropriate gain</th>
<th>Over gainer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>22/18</td>
<td>27/18</td>
</tr>
<tr>
<td>Normal weight</td>
<td>26/18</td>
<td>27/18</td>
</tr>
<tr>
<td>Overweight</td>
<td>29/18</td>
<td>31/18</td>
</tr>
</tbody>
</table>

**Inclusion Criteria**

- RR: Risk Ratio

**Exclusions**

- missing outcomes
- gestational HTN
- preeclampsia diagnosis

Subjects included in analyses 82 (342 specimens)

Excluded due to association with altered angiogenic profile:

- Multiple gestations (≥20) Maynard et al, AJOG, 2008;198:200
- Hypertensive diseases of pregnancy (gestational HTN & preeclampsia) Moore Simas et al, AJOG, 2007;197:244.e1-244.e8

- sFlt1, PlGF and sEng levels were measured by ELISA

- BMI & GWG-adherence categories by 1990 IOM recommendations

**BMI Categories**

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**Statistical Analysis**

- Demographic comparisons utilized Fisher exact test for categorical variables and Wilcoxon rank sum test for continuous variables (see Table 1)
- Within-women correlation and right-skewness handled by estimating linear mixed models for ln-transformed biomarkers and then exponentiating on ln scale (i.e., geometric means).
- Geometric mean and 95% confidence intervals displayed for sFlt1, PlGF and (sFlt1+sEng)/PlGF in each of 3 gestational-age windows for UW-N vs. OW-OB BMI and Under-Appropriate vs. Over-gainers (see figures 1-6)
- T-test compared means in 3 windows.

**Results**

- Analytic sample included 82 subjects (342 specimens). See Table 1 for Demographic Comparisons.

**BMI Comparisons** (see Figures 1–3)

- Mean sFlt1 lower in all windows in OW-OB compared to U-N (Figure 1)
- Mean PlGF lower in all windows in OW-OB compared to U-N (Figure 2)
- Mean ratio ([sFlt1+sEng]/PlGF) trended higher in OW-OB compared to U-N women at 27-30 and 31-36 wks (Figure 3)

**GWG Adherence Comparisons** (see Figures 4–6)

- Mean sFlt1 lower in all windows in OG compared to U-AG (Figure 4)
- Mean PlGF lower in all windows in OG compared to U-AG (Figure 5)
- Mean ratio ([sFlt1+sEng]/PlGF) trended higher in OG compared to U-AG at 31-36 wks (Figure 6)

**Limitations**

- Small sample size required collapsing of BMI and GWG-adherence categories; thus unable to look at adherence within each BMI category
- Secondary analysis not powered for this exploratory analysis
- Only had total GWG at end of pregnancy

Figure 1-3. Angiogenic biomarker profiles comparing under-/normal-weight to overweight/obese at 3 gestational age windows

Figure 4-6. Angiogenic biomarker profiles comparing under/appropriate-gainers to over-gainers at 3 gestational age windows