Pregnancy and Long-Term Outcomes

Project ECHO
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Pregnancy:
A Window from the Past –
A Window to the Future

Family History

Pregnancy

Future Health
Hypothesis

Pregnancy complications identify families (women and children) at increased risk for long-term adverse health outcomes.
Lecture Outline

• Background

• Maternal Complications:
  – Gestational Diabetes
  – Preeclampsia
  – Others

• Barker Hypothesis
Physiologic Changes in Pregnancy

• Cardiovascular:
  – 30-50% increase in cardiac output, blood volume, and renal blood flow
  – 20-30 fold increase in uterine blood flow

• Endocrine:
  – 50-80% increase in insulin resistance

• Decreased cellular immunity
Feig et al. CMAJ 2008;179:229-34
Consequences of GDM

• Maternal:
  – Type 2 Diabetes
    • 5 years → RR = 4.79; 10 years → RR = 9.34
  – Metabolic Syndrome
    • 20 years → RR 7.0
    • Further increase (2.4x) if >1 GDM pregnancy

• Child
  – Abnormal Glucose Metabolism
  – Obesity
  – Metabolic Syndrome
How to Follow Women with GDM?

• **Follow-Up:**
  - ACOG, ADA, WHO – 75 gm 2-hour OGTT.
  - 42 – 67% of US women with GDM have no follow-up glucose testing.

• **What will increase follow-up rates in your practice?**

• **Breastfeeding:**
  - >12 months of breastfeeding reduces T2DM risk by 14 – 27%.
Deaths from Heart Disease, USA

Heart Disease Mortality in Women and Men in Absolute Numbers, 1979 – 2004 (American Heart Association, 2007)
Cause-Specific Mortality Following Hypertensive Diseases of Pregnancy – Utah, 1939-2012*

- 60,580 women with ≥ 1 HDP in UPDB
  - 2 controls (age, year of birth, parity)
- All-cause mortality HR = 1.65 (95% CI 1.57-1.73)
- Greatest excess mortality risks:
  - Ischemic heart disease; HR = 2.23 (95% CI 1.90-2.63)
  - Diabetes; HR = 2.80 (95% CI 2.20 – 3.55)
  - Stroke; HR = 1.88 (95% CI 1.53 – 2.32)
  - Alzheimer’s Disease; HR = 3.44 (95% CI 1.00 – 11.82)

*Thielen et al; 2016 Society for Maternal-Fetal Medicine
<table>
<thead>
<tr>
<th>AGE</th>
<th>35-44</th>
<th>45-54</th>
<th>55-64</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>30,893</td>
<td>69,859</td>
<td>112,414</td>
</tr>
<tr>
<td>RANK</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Cancer – 25.7%</td>
<td>Cancer – 35.8%</td>
<td>Cancer – 41.0%</td>
</tr>
<tr>
<td>2</td>
<td>Injuries – 16.5%</td>
<td>Heart Disease – 15.3%</td>
<td>Heart Disease – 18.1%</td>
</tr>
<tr>
<td>3</td>
<td>Heart Disease – 12.0%</td>
<td>Injuries – 8.4%</td>
<td>COPD – 5.3%</td>
</tr>
<tr>
<td>4</td>
<td>Suicide – 4.9%</td>
<td>Stroke – 4.1%</td>
<td>Diabetes – 4.2%</td>
</tr>
<tr>
<td>5</td>
<td>HIV – 3.8%</td>
<td>Liver Disease – 3.1%</td>
<td>Stroke – 4.1%</td>
</tr>
<tr>
<td>6</td>
<td>Stroke – 3.4%</td>
<td>Diabetes – 3.1%</td>
<td>Injuries – 3.2%</td>
</tr>
<tr>
<td>7</td>
<td>Liver Disease – 2.9%</td>
<td>COPD – 2.8%</td>
<td>Liver Disease – 1.9%</td>
</tr>
<tr>
<td>8</td>
<td>Diabetes – 2.3%</td>
<td>Suicide – 2.6%</td>
<td>Kidney Disease – 1.7%</td>
</tr>
<tr>
<td>9</td>
<td>Homicide – 2.4%</td>
<td>HIV – 1.6%</td>
<td>Septicemia – 1.7%</td>
</tr>
<tr>
<td>10</td>
<td>COPD – 1.4%</td>
<td>Septicemia – 1.5%</td>
<td>Influenza/pneumonia – 1.1%</td>
</tr>
</tbody>
</table>
How do these statistics correlate with obstetric complications?
### PRIMIGRAVID WOMEN EXPERIENCING PREGNANCY COMPLICATIONS AND THE RISK OF SUBSEQUENT DEATH FROM ANY CAUSE

<table>
<thead>
<tr>
<th>PREGNANCY OUTCOME</th>
<th>ALL WOMEN</th>
<th>WOMEN WITH COMPLICATION</th>
<th>RATE/10,000 WOMAN-YEARS</th>
<th>HR</th>
<th>95% CI</th>
<th>P-VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm Delivery</td>
<td>41,659</td>
<td>675</td>
<td>11.7</td>
<td>1.66</td>
<td>1.53, 1.79</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SGA</td>
<td>43,109</td>
<td>1,002</td>
<td>14.2</td>
<td>1.91</td>
<td>1.79, 2.04</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gestational Hypertension</td>
<td>7,449</td>
<td>115</td>
<td>10.3</td>
<td>1.23</td>
<td>1.03, 1.48</td>
<td></td>
</tr>
<tr>
<td>Mild pre-eclampsia</td>
<td>26,810</td>
<td>364</td>
<td>8.7</td>
<td>1.11</td>
<td>1.00, 1.23</td>
<td>0.001</td>
</tr>
<tr>
<td>Severe pre-eclampsia</td>
<td>7,016</td>
<td>84</td>
<td>9.2</td>
<td>1.38</td>
<td>1.11, 1.71</td>
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</tr>
<tr>
<td>Abruption</td>
<td>7,684</td>
<td>147</td>
<td>11.4</td>
<td>1.41</td>
<td>1.20, 1.67</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stillbirth</td>
<td>4,039</td>
<td>98</td>
<td>15.6</td>
<td>1.83</td>
<td>1.50, 2.23</td>
<td>&lt;0.001</td>
</tr>
</tbody>
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## Primigravid Women Experiencing Pregnancy Complications and the Risk of Subsequent Death from Non-Cardiovascular Causes

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<tr>
<th>Pregnancy Outcome</th>
<th>All Women</th>
<th>Women with Complication</th>
<th>Rate/10,000 Woman-Years</th>
<th>HR</th>
<th>95% CI</th>
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<td>SGA</td>
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<td>578</td>
<td>8.2</td>
<td>1.66</td>
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</tr>
<tr>
<td>Gestational Hypertension</td>
<td>7,449</td>
<td>50</td>
<td>4.5</td>
<td>0.82</td>
<td>0.62, 1.08</td>
<td>0.11</td>
</tr>
<tr>
<td>Mild pre-eclampsia</td>
<td>26,810</td>
<td>187</td>
<td>4.4</td>
<td>0.86</td>
<td>0.74, 1.00</td>
<td></td>
</tr>
<tr>
<td>Severe pre-eclampsia</td>
<td>7,016</td>
<td>41</td>
<td>4.5</td>
<td>1.00</td>
<td>0.76, 1.36</td>
<td></td>
</tr>
<tr>
<td>Abruption</td>
<td>7,684</td>
<td>105</td>
<td>8.1</td>
<td>1.56</td>
<td>1.29, 1.89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stillbirth</td>
<td>4,039</td>
<td>62</td>
<td>9.9</td>
<td>1.79</td>
<td>1.39, 2.30</td>
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What About Nulliparity?

• Nulliparity is consistently associated with an increased risk of ovarian cancer, including in BRCA1 and BRCA2 carriers\(^1\).

• Same observation for endometrial and breast cancer\(^2\).

• Mixed results for colon and rectal cancer\(^3\).

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Pregnancy and Subsequent Breast Cancer

• Long-recognized associations:
  – Reduced risk with young age of first birth
  – Reduced risk with increasing parity

• Most studies demonstrate decreased risks of breast and ovarian cancer in women with a history of preeclampsia (and their daughters).
Gender Differences in Mental Illness

More common in women (all > 2x):
- Eating disorders,
- major depressive disorders,
- obsessive compulsive disorder,
- posttraumatic stress disorders,
- anxiety and panic disorders,
- seasonal affective disorder,
- Alzheimer’s disease / dementia.

More common in men:
- Autism
- Schizophrenia.
Prevalence

- > 500,000 pregnancies / year (1 of every 8) complicated by psychiatric disorders (US).
- 13% of all psychiatric hospital admissions for women occur during the first postpartum year.
- Less than 20% of women who meet criteria for major depressive disorder seek treatment during pregnancy and the puerperium.
Graves’ Disease

• 10x more common in women.
• 30% of women who are diagnosed with Grave’s disease have been pregnant within the preceding 12 months.
FETAL AND INFANT ORIGINS OF ADULT DISEASE

Edited by DJP Barker

David Barker (1938 – 2013)
Death rates from coronary heart disease among 15,726 men and women

![Bar chart showing standardized mortality ratio by birthweight (lbs)]
Mean systolic pressure in men and women aged 60 - 71 years

Mean systolic pressure (mmHg)

birthweight (lbs)
Prevalence of insulin resistance syndrome in men aged 59 - 70
Conclusions - Mother

• Gestational Diabetes increases a woman’s risk for T2DM. This risk can be reduced with:
  – Lifestyle modifications (diet, exercise, weight loss)
  – Breastfeeding

• Preeclampsia increases a woman’s risk for subsequent vascular disease and may reduce her risk for cancer.
Conclusions - Baby

• The best strategy to avoid the negative effects of fetal programming is to improve the health of young women via:
  – Better nutrition
  – Reduced stress
  – More exercise

• The health of the baby depends on the health of the mother before and after conception.
Comments?  Questions?

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