PREGNANCY AND GLOMERULAR DISEASE

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Director, Divisions of Nephrology & Obstetric Medicine
Sunnybrook Health Sciences Centre
Clinical Director of Research, Toronto GN Registry
Disclosers

• Developed a web page with the support of Baxter for the management of pregnant women on HD
Pregnancy and Kidney Disease (PreKID) Clinic
• Collaborative approach – MFM & nephrologist at 2 sites
• Patients Counseled – >1500
• Number of Pregnancies  65%
• 75 new patients consulted at clinic undergo pregnancy annually
Pregnancy and Glomerular Disease

• For most women, a child is a life goal and women with CKD are not an exception

• Aggressive counseling against pregnancy results in feelings of traumatization

Tong et al NDT 2015
Pregnancy and Glomerular Disease

“You know, you can’t always live in the anxiety of the future.”

“So I’m just a little bit worried now, my Cr what if it does go higher. And I’m not pregnant now, and now I’m old. Who knows if its sets me back another 2 years or 3 years I can’t even afford it any more.”

“If I wait, what if I am not be able to have a healthy pregnancy… I was actually quite scared, I was really going crazy, I was thinking one of the goals in to have a child, to have a family, to raise this child.”

Beanlands, Cattran and Hladunewich KFOC
Pregnancy and Glomerular Disease

• CKD is an often progressive journey
• Nephrologist’s role to assist with family planning at all stages of CKD
  • Identify “safest window of opportunity”
  • Discussing and even encouraging pregnancy in earlier stage CKD
  • Providing options in ESRD including on dialysis and after transplantation
Pregnancy and Kidney Disease

Pre-pregnancy women with kidney disease (n = 71)
- 18% not at all comfortable
- 23% somewhat comfortable
- 60% very comfortable

Pregnant women with kidney disease (n = 71)
- 10% not at all comfortable
- 24% somewhat comfortable
- 60% very comfortable

Not at all comfortable
Somewhat comfortable
Very comfortable
Overall Objectives

- Principles of Pregnancy Risk Assessment and Counseling
  - Risk of Loss of Kidney Function
  - Risk of Adverse Pregnancy Outcomes: Preeclampsia, Poor fetal growth, Pre-term Delivery
  - Risk of Flare or Worsening Proteinuria

- Disease Specific Outcomes
- Optimization/Management Strategies
RISK OF DETERIORATION IN KIDNEY FUNCTION
## Risk of Deterioration in Kidney Function

<table>
<thead>
<tr>
<th>Mild Renal Insufficiency</th>
<th>&lt;125 umol/L (1.4 mg/dl)</th>
<th>&gt;70 ml/min</th>
<th>Stage 1 &amp; 2</th>
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<td>Moderate Renal Insufficiency</td>
<td>125-220 umol/L (1.4-2.4 mg/dl)</td>
<td>40-70 ml/min</td>
<td>Stage 2 &amp; 3</td>
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<tr>
<td>Severe Renal Insufficiency</td>
<td>&gt;220 umol/L (2.4 mg/dl)</td>
<td>&lt;40 ml/min</td>
<td>Stage 3 &amp; 4</td>
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</tbody>
</table>
Risk of Deterioration in Kidney Function

- Comparison of 504 pregnancies in women with CKD shifted stage or progressed to ESRD (Turin and Cagliari)

<table>
<thead>
<tr>
<th></th>
<th>Stage 1</th>
<th>Stage 2</th>
<th>Stage 3</th>
<th>Stage 4-5</th>
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<tr>
<td>N</td>
<td>28/370</td>
<td>1/87</td>
<td>2/37</td>
<td>2/10</td>
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<tr>
<td>%</td>
<td>7.6</td>
<td>12.6</td>
<td>16.2</td>
<td>20</td>
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</tbody>
</table>
Risk of Deterioration in Kidney Function

- Retrospective Study

- Moderate to Severe Renal Insufficiency
  - Moderate – 59 pregnancies (125-220 umol/L)
  - Severe – 15 pregnancies (>220 umol/L)

- Pregnancy Related Loss of Kidney Function (during or within 6 weeks postpartum)
  - 43% of all pregnancies
  - 23% progressed to ESRD within 6 months

Jones et al NEJM 335(4): 226, 1996
RISK OF DETERIORATION IN KIDNEY FUNCTION

Dashed lines - pregnancy related decline in GFR

Top: Cr <168
Middle: 199-212
Bottom: Cr >220

1/6 progression to ESRD - moderate renal insufficiency
1/3 progression to ESRD - severe renal insufficiency

Jones et al NEJM 1996
Risk of Deterioration in Kidney Function

- “mostly” prospective cohort (1977-2004)

- 49 women with GFR < 60 ml/min/1.73m²

- No diabetes or systemic illness

Primary Outcome  

- Rate of GFR loss prior to and after pregnancy

<table>
<thead>
<tr>
<th>GFR Proteinuria</th>
<th>&gt; 40 ml/min &lt; 1 gm</th>
<th>&gt; 40 ml/min &gt; 1 gm</th>
<th>&lt; 40 ml/min &lt; 1 gm</th>
<th>&lt; 40 ml/min &gt; 1 gm</th>
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<tbody>
<tr>
<td>n=</td>
<td>16</td>
<td>6</td>
<td>12</td>
<td>15</td>
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<tr>
<td>Pre-pregnancy</td>
<td>0.47±0.35</td>
<td>0.35±0.31</td>
<td>0.55±0.38</td>
<td>0.21±0.20</td>
</tr>
<tr>
<td>Post-delivery</td>
<td>0.30±0.48</td>
<td>0.33±0.31</td>
<td>0.55±0.39</td>
<td>1.17±1.23</td>
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</tbody>
</table>
Risk of Deterioration in Kidney Function

Mostly Retrospective
Small & Single Centre
Use serum creatinine to determine baseline renal insufficiency and often lack pre-pregnancy Cr
Combine all renal diseases together
Fail to sort out the impact of pre-pregnancy proteinuria/glomerular-based disease (not all proteinuria is created equally)
Difficult to determine independent impact of hypertension, proteinuria and renal insufficiency
Highest Risk for Progression

• Renal Dysfunction
• Proteinuria
• Hypertension

ADDITIVE

Three Strikes, YOU’RE OUT!
Extrapolation of $1/Cr$ to Time of Dialysis (Serum Cr = 8 mg/dl)
RISK OF ADVERSE PREGNANCY OUTCOMES
Risk of Adverse Pregnancy Outcomes

- Systematic Review and Meta-Analysis
  - 23 studies of 14 included patients with CKD
  - 933 pregnancies
- Preeclampsia OR 10.36 (95% CI 6.27-17.09)
- Preterm Delivery OR 5.72 (95% CI 3.26-10.03)
- SGA OR 4.85 (95% CI 3.03-7.76)
- C Section OR 2.67 (95% CI 2.01-3.54)

- Heterogeneity was significant
- Effect modifiers included proteinuria & type of disease

Zhang et al CJASN 2015
Is CKD an Independent Risk Factor for Poor Pregnancy Outcomes?

- Comparison of 504 pregnancies in women with CKD to 836 low-risk pregnancies (Turin and Cagliari)

Table 4. Comparisons across CKD stages

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>CKD Stage</th>
<th>P Value across Stages</th>
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<tbody>
<tr>
<td></td>
<td>1 (n=370)</td>
<td>2 (n=87)</td>
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<tr>
<td>Maternal-fetal outcomes</td>
<td></td>
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<tr>
<td>Cesarean sections</td>
<td>46.4</td>
<td>70.1</td>
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<tr>
<td>Gestational week</td>
<td>37.6±2.6</td>
<td>35.7±3.2</td>
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<tr>
<td>Preterm delivery (&lt;37 wk)</td>
<td>23.5</td>
<td>50.6</td>
</tr>
<tr>
<td>Early preterm (&lt;34 wk)</td>
<td>7.3</td>
<td>20.7</td>
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<tr>
<td>Birth weight (g)</td>
<td>2966.5±659</td>
<td>2484±707</td>
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<tr>
<td>SGA score (Parazzini)</td>
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<tr>
<td>&lt;10%</td>
<td>13.3</td>
<td>17.9</td>
</tr>
<tr>
<td>&lt;5%</td>
<td>5.1</td>
<td>6.0</td>
</tr>
<tr>
<td>Need for NICU</td>
<td>10.3</td>
<td>27.6</td>
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<tr>
<td>General combined outcome</td>
<td>34.1</td>
<td>63.2</td>
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<tr>
<td>Severe combined outcome</td>
<td>21.4</td>
<td>44.8</td>
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<tr>
<td>New-onset hypertension (%)</td>
<td>7.9 (23/290)</td>
<td>17.6 (9/51)</td>
</tr>
<tr>
<td>New-onset or doubling of proteinuria</td>
<td>20.5 (76/370)</td>
<td>37.9 (33/87)</td>
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<tr>
<td>CKD stage shift or RRT start</td>
<td>7.6 (28/370)</td>
<td>12.6 (1/87)</td>
</tr>
</tbody>
</table>
Risk of Poor Pregnancy Outcome

- Renal Dysfunction
- Proteinuria
- Hypertension

ADDITIVE

Three Strikes, YOU’RE OUT!
RISK OF FLARE OR WORSENING PROTEINURIA
Risk of a Flare or Worsening of Proteinuria

- Pregnancy Exacerbated Glomerular Diseases
  - ? MCD, FSGS, MN, IgA
    - Deserves further study
- Lupus
- ANCA
Pregnancy Outcomes of Primary GN

• **Systematic Review**
  
  • After 1980
    • Difficult to ascertain pathological diagnosis prior
    • Advances in neonatal care
  
  • Minimum of 10 women
  
  • Report live birth weight

• **18 studies, 887 women, 1414 pregnancies**
  
  • Baseline characteristics – not reported or inadequately described
  
  • Significant heterogeneity
  
  • Study quality poor

**CJASN in press**
## Pregnancy Outcomes of Primary GN

### Table 1. Pregnancy outcomes by primary glomerular disease type

<table>
<thead>
<tr>
<th>Study, yr</th>
<th>Women (No. of Preg)</th>
<th>Average Age at Pregnancy, yr</th>
<th>Prepregnancy Hypertension (%)</th>
<th>Prepregnancy Creatinine (%)</th>
<th>Pregnancy with Preeclampsia (%)</th>
<th>Preg BP Postpregnancy</th>
<th>Creatinine Postpregnancy</th>
<th>No. of Infants</th>
<th>BW, g</th>
<th>GA, wk</th>
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<td>Surian et al. (3)</td>
<td>21 (29)</td>
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<td>NA</td>
<td>NA</td>
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<td>29 [26 (80)]</td>
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<td>FSGS</td>
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<td>GN, disease type not specified</td>
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<td>50 [43 (86)]</td>
<td>NA</td>
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</tbody>
</table>
Pregnancy Outcomes in Primary GN

- IgA Nephropathy
  - Live birth rate: 70-100%
    - Worse before 2000
  - Birth weight: 2911-3200 g (n=5)
  - Preeclampsia: 0-25% (n=5)
  - Histology (n=1)
    - Fibrosis and sclerosis associated with worse outcomes
Pregnancy Outcomes in Primary GN

- Largest study of 229 pregnancies
  - Cr < 1.2 mg/dl

<table>
<thead>
<tr>
<th>Table 3. Progressive Models of Kidney Function Decrease Over Time</th>
</tr>
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<tbody>
<tr>
<td><strong>Covariates</strong></td>
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<tr>
<td>Model 1&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Baseline mean Cr (intercept)</td>
</tr>
<tr>
<td>Overall change (slope)</td>
</tr>
<tr>
<td>Model 2&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Mean Cr, nonpregnancy group</td>
</tr>
<tr>
<td>Mean Cr, pregnancy group</td>
</tr>
<tr>
<td>Slope, nonpregnancy group</td>
</tr>
<tr>
<td>Slope, pregnancy group</td>
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<tr>
<td>Model 3&lt;sup&gt;b&lt;/sup&gt;</td>
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<td>Mean Cr, nonpregnancy group</td>
</tr>
<tr>
<td>Mean Cr, pregnancy group</td>
</tr>
<tr>
<td>Slope, nonpregnancy group</td>
</tr>
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<td>Slope, pregnancy group</td>
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<tr>
<td>Model 4&lt;sup&gt;b&lt;/sup&gt;</td>
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<td>Mean Cr, nonpregnancy group</td>
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<td>Slope, nonpregnancy group</td>
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<tr>
<td>Slope, pregnancy group</td>
</tr>
</tbody>
</table>

Limardo et al AJKD 2010
Pregnancy Outcomes in Primary GN

- Excluded Pregnancies
  - Cr > 1.2 mg/dl
  - 8 live births and “other outcomes in keeping with studies of women with more advanced CKD”

```latex
\begin{tabular}{l|c|c}
\hline
Baseline characteristics & Became Pregnant & Did Not Become Pregnant \\
\hline
No. of patients & 10 & 12 \\
Age (y) & 28.6 ± 4.7 & 28.3 ± 5.2 \\
SCr (mg/dL) & 1.65 ± 0.39 & 1.60 ± 0.19 \\
CCr (mL/min) & 47.2 ± 14.7 & 49.2 ± 8.4 \\
Proteinuria (g/d) & 1.75 (0.48, 2.60) & 1.9 (1.43, 3.47) \\
Hypertension & 4 & 7 \\
Follow-up (y) & 5.3 (3-12) & 5.0 (4-10) \\
Outcomes (end of follow-up) & & \\
SCr (mg/dL) & 4.68 ± 3.47 & 4.72 ± 3.40 \\
CCr (mL/min) & 24.7 ± 18.6 & 28.5 ± 22.4 \\
ΔCCr (mL/min/y) & −4.25 ± 4.1 & −3.64 ± 4.1 \\
CKD stage 5 & 4 & 5 \\
Proteinuria (g/d) & 1 (0.2, 2.05) & 0.85 (0.28, 2.53) \\
Hypertension & 7 & 12 \\
\hline
\end{tabular}
```

Limardo et al AJKD 2010
Pregnancy Outcomes in Primary GN

- Pregnancy Outcomes
  - Live Birth Rate: 90%
  - Premature Delivery: 10%
  - Low Birth Weight: 11%
  - Exacerbation of HTN: 21%
  - Preeclampsia: 8.5%
    - Risk Factors proteinuria > 1 g and/or HTN
    - BUT median proteinuria 1 g and only 20% had HTN – WELL COHORT

Limardo et al AJKD 2010
Pregnancy Outcomes in Primary GN

A Pre-conception GFR vs. obstetrical outcome

- **Normal deliveries**
  - GFR ≥ 70 ml/min ($N = 146$): 67%
  - GFR < 70 ml/min ($N = 22$): 59%

- **Live births**
  - GFR ≥ 70 ml/min ($N = 146$): 87%
  - GFR < 70 ml/min ($N = 22$): 82%

- **Perinatal deaths**
  - GFR ≥ 70 ml/min ($N = 146$): 3%
  - GFR < 70 ml/min ($N = 22$): 14%

- **Spontaneous abortions**
  - GFR ≥ 70 ml/min ($N = 146$): 10%
  - GFR < 70 ml/min ($N = 22$): 5%

B Pre-conception BP vs. obstetrical outcome

- **Normotensive**
  - ($< 140/90$ mm Hg, $N = 153$): 71%
  - Hypertensive ($≥ 140/90$ mm Hg, $N = 15$): 20%

- **Live births**
  - Normotensive: 90%
  - Hypertensive: 60%

- **Perinatal deaths**
  - Normotensive: 1%
  - Hypertensive: 33%

- **Spontaneous abortions**
  - Normotensive: 9%
  - Hypertensive: 7%

Abe KI 1991
Pregnancy Outcomes in Primary GN

- 62 pregnancies
  - Preserved GFR 102 ± 22 ml/min
  - 57% > 1 g of proteinuria

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live birth</td>
<td>59 (86)</td>
</tr>
<tr>
<td>Preterm delivery</td>
<td>7 (10)</td>
</tr>
<tr>
<td>Delivery by cesarean section</td>
<td>42 (61)</td>
</tr>
<tr>
<td>Vaginal delivery</td>
<td>17 (25)</td>
</tr>
<tr>
<td>Fetal death</td>
<td>10 (15)</td>
</tr>
<tr>
<td>Intrauterine death</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Embryo damage</td>
<td>3 (4)</td>
</tr>
<tr>
<td>Fetal malformation</td>
<td>3 (4)</td>
</tr>
<tr>
<td>Spontaneous abortion</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Induced abortion</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Maternal severe pre-eclampsia</td>
<td>6 (9)</td>
</tr>
<tr>
<td>Low birth weight&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>8 (14)</td>
</tr>
<tr>
<td>Mean birth weight (g)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2,972 ± 654</td>
</tr>
</tbody>
</table>

Liu et al AJKD 2010
Pregnancy Outcomes in Primary GN

- Small and all published before 1990
  - FSGS (n=4)
    - Live Birth Rate: 54-94%
    - Preterm: 24%
  - MCD (n=2)
    - Live Birth Rate: 71-76%
  - Membranous Nephropathy (n=2)
    - Live Birth Rate: 67-76%
- Emerging Themes:
  - Low GFR, HTN & proteinuria = worse outcomes
## Pregnancy Outcomes in Primary GN

- **UNC Contribution Am J Neph 2017**

<table>
<thead>
<tr>
<th></th>
<th>All (n = 48)</th>
<th>FSGS (n = 17)</th>
<th>IgAN (n = 18)</th>
<th>MN (n = 6)</th>
<th>MCD (n = 7)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fetal outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fetal loss, n</td>
<td>6 (12.5)</td>
<td>2 (11.7)</td>
<td>2 (11.1)</td>
<td>1 (16.7)</td>
<td>1 (14.3)</td>
<td>1.00</td>
</tr>
<tr>
<td>Stillbirth at &gt;20 weeks</td>
<td>4 (8.3)</td>
<td>2 (11.7)</td>
<td>0</td>
<td>1 (16.7)</td>
<td>1 (14.3)</td>
<td>0.29</td>
</tr>
<tr>
<td>Neonatal death</td>
<td>2 (4.2)</td>
<td>0</td>
<td>2 (11.1)</td>
<td>0</td>
<td>0</td>
<td>0.73</td>
</tr>
<tr>
<td>Gestational age, weeks, median (IQR)</td>
<td>37 (31.5–38.5)</td>
<td>36 (29–36)</td>
<td>37.5 (36–39)</td>
<td>38 (28–39)</td>
<td>32 (32–37)</td>
<td>0.39</td>
</tr>
<tr>
<td>Premature delivery</td>
<td>23 (47.9)</td>
<td>10 (58.8)</td>
<td>6 (33.3)</td>
<td>2 (33.3)</td>
<td>5 (71.4)</td>
<td>0.24</td>
</tr>
<tr>
<td>32–37 weeks gestation</td>
<td>11 (22.9)</td>
<td>5 (29.4)</td>
<td>2 (11.1)</td>
<td>0</td>
<td>4 (57.1)</td>
<td>0.04</td>
</tr>
<tr>
<td>Before 32 weeks gestation</td>
<td>12 (25.0)</td>
<td>5 (29.4)</td>
<td>4 (22.2)</td>
<td>2 (33.3)</td>
<td>1 (14.3)</td>
<td>0.83</td>
</tr>
<tr>
<td>Reason for premature delivery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.15</td>
</tr>
<tr>
<td>Not premature</td>
<td>25 (52.1)</td>
<td>7 (41.2)</td>
<td>12 (66.7)</td>
<td>4 (66.7)</td>
<td>2 (28.6)</td>
<td></td>
</tr>
<tr>
<td>Spontaneous premature delivery</td>
<td>5 (10.4)</td>
<td>2 (11.8)</td>
<td>1 (5.6)</td>
<td>0</td>
<td>2 (28.6)</td>
<td></td>
</tr>
<tr>
<td>Induced delivery or C-section</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal indication</td>
<td>13 (27.1)</td>
<td>6 (35.3)</td>
<td>5 (27.8)</td>
<td>0</td>
<td>2 (28.6)</td>
<td></td>
</tr>
<tr>
<td>Fetal indication</td>
<td>1 (2.1)</td>
<td>0</td>
<td>0</td>
<td>1 (16.7)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Intrauterine fetal demise</td>
<td>4 (8.3)</td>
<td>2 (11.8)</td>
<td>0</td>
<td>1 (16.7)</td>
<td>1 (14.3)</td>
<td></td>
</tr>
<tr>
<td>Birth weight, g, median (IQR)</td>
<td>2,529 (1,496–3,273)</td>
<td>2,360 (1,118–3,240)</td>
<td>2,627 (2,136–3,315)</td>
<td>2,940 (815–3,317)</td>
<td>1,960 (1,470–2,796)</td>
<td>0.80</td>
</tr>
<tr>
<td>IUGR below 10th percentile</td>
<td>6 (12.5)</td>
<td>4 (23.5)</td>
<td>2 (11.1)</td>
<td>0</td>
<td>0</td>
<td>0.50</td>
</tr>
<tr>
<td>IUGR below 3rd percentile</td>
<td>2 (4.2)</td>
<td>2 (11.8)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.59</td>
</tr>
<tr>
<td>Apgar scores, median (IQR), min</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>8 (6–8.5)</td>
<td>7 (5–8)</td>
<td>8 (7–9)</td>
<td>7.5 (7–8)</td>
<td>8 (6–9)</td>
<td>0.60</td>
</tr>
<tr>
<td>5</td>
<td>9 (7–9)</td>
<td>9 (7–9)</td>
<td>9 (9–9)</td>
<td>8.5 (8–9)</td>
<td>9 (7–9)</td>
<td>0.51</td>
</tr>
</tbody>
</table>

## Maternal outcomes

<table>
<thead>
<tr>
<th></th>
<th>All (n = 48)</th>
<th>FSGS (n = 17)</th>
<th>IgAN (n = 18)</th>
<th>MN (n = 6)</th>
<th>MCD (n = 7)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preeclampsia</td>
<td>16 (33.3)</td>
<td>8 (47.1)</td>
<td>6 (33.3)</td>
<td>0</td>
<td>2 (28.6)</td>
<td>0.23</td>
</tr>
<tr>
<td>Active GN during pregnancy</td>
<td>35 (72.9)</td>
<td>15 (88.2)</td>
<td>12 (66.7)</td>
<td>4 (66.7)</td>
<td>4 (57.1)</td>
<td>0.29</td>
</tr>
<tr>
<td>≥200% increase in proteinuria*</td>
<td>7/18 (38.9)</td>
<td>3/8 (37.5)</td>
<td>2/6 (33.3)</td>
<td>1/2 (50.0)</td>
<td>1/2 (50.0)</td>
<td>1.0</td>
</tr>
<tr>
<td>≥150% increase in serum creatinine*</td>
<td>6/22 (27.3)</td>
<td>5/10 (50.0)</td>
<td>1/8 (12.5)</td>
<td>0/2</td>
<td>0/2</td>
<td>0.23</td>
</tr>
<tr>
<td>Dialysis during pregnancy</td>
<td>1 (2.1)</td>
<td>1 (5.9)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1.0</td>
</tr>
<tr>
<td>ESRD 12 months post-partum</td>
<td>3 (6.3)</td>
<td>1 (5.9)</td>
<td>2 (11.1)</td>
<td>0</td>
<td>0</td>
<td>1.0</td>
</tr>
</tbody>
</table>

ASA 9% 13% 6% 0% 14%
# Pregnancy Outcomes in Primary GN

- **Hope on the Horizon – Cure GN**

<table>
<thead>
<tr>
<th></th>
<th>Before Diagnosis</th>
<th>After Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of Pregnancies</strong></td>
<td>612</td>
<td>33</td>
</tr>
<tr>
<td><strong>Elective Terminations</strong></td>
<td>4.4% (27/612)</td>
<td>9.1% (3/33)</td>
</tr>
<tr>
<td><strong>Kidney Disease Impacted Elective Termination</strong></td>
<td>NA</td>
<td>66.7% (2/3)</td>
</tr>
<tr>
<td><strong>Number of Pregnancies excl. Elective Terminations</strong></td>
<td>585</td>
<td>30</td>
</tr>
</tbody>
</table>

## Cohort

- **MCD (inc. IgM Nephropathy)**
  - Before: 10.6% (61/576)
  - After: 13.3% (4/30)
- **FSGS**
  - Before: 28.1% (162/576)
  - After: 40.0% (12/30)
- **MN**
  - Before: 25.0% (144/576)
  - After: 13.3% (4/30)
- **IgAN (incl. HSP)**
  - Before: 35.8% (206/576)
  - After: 33.3% (10/30)

## Increasing Proteinuria

- Before: 12.5% (67/534)
- After: 48.1% (13/27)

## Worsening Kidney Function

- Before: 5.8% (31/538)
- After: 35.7% (10/28)

## Preeclampsia

- Before: 7.0% (39/559)
- After: 25.9% (7/27)

## Eclampsia (Seizures)

- Before: 0.7% (4/559)
- After: 0% (0/27)

## HELLP

- Before: 0.9% (5/547)
- After: 3.8% (1/26)

## Worsening Blood Pressure

- Before: 11.7% (65/556)
- After: 25.9% (7/27)

## Spontaneous Fetal Loss or Still Birth

- Before: 10.4% (61/585)
- After: 14.8% (4/27)

## Live Birth

- Before: 89.1% (521/585)
- After: 88.5% (23/26)

## Gestational Age of Live Births

- **Extremely Preterm (≤27 weeks)**
  - Before: 0.4% (2/477)
  - After: 4.7% (1/21)
- **Preterm (>27 to <34 weeks)**
  - Before: 3.4% (16/477)
  - After: 9.5% (2/21)
- **Late Preterm (≥34 to <37 weeks)**
  - Before: 7.8% (37/477)
  - After: 28.6% (6/21)
- **Full term (37+ weeks)**
  - Before: 88.5% (422/477)
  - After: 57.1% (12/21)
Pregnancy Outcomes in Primary GN

- Hope on the Horizon – Cure GN
- Pregnancies with complications in the before diagnosis group were much sooner to be diagnosed suggesting a mild GN may have already been in place, but not yet diagnosed

<table>
<thead>
<tr>
<th></th>
<th>Without Complication</th>
<th>With Complication</th>
<th>GEE p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Median (IQR)</td>
<td>N</td>
</tr>
<tr>
<td>Increasing Proteinuria</td>
<td>467</td>
<td>22.9 (12.5-33.2)</td>
<td>67</td>
</tr>
<tr>
<td>Worsening Kidney Function</td>
<td>507</td>
<td>22.2 (11.4-32.2)</td>
<td>31</td>
</tr>
<tr>
<td>Worsening Blood Pressure</td>
<td>491</td>
<td>22.1 (11.2-32.7)</td>
<td>65</td>
</tr>
</tbody>
</table>

*GEE model of square root-transformed pregnancy timing on complication status, unadjusted, accounting for clustering by individual using exchangeable correlation structure
Systemic Lupus Erythematosus & Pregnancy

• Fertility is normal in SLE
• Clinical course in pregnancy is unpredictable; it may improve, exacerbate, or remain unchanged
• Lupus flares can occur during all three trimesters with approximately equal frequency and often in the postpartum period
• Severe morbidity and mortality reported
**SYSTEMIC LUPUS ERYTHEMATOUS & PREGNANCY**

- Systematic Review & Meta-Analysis
- Pregnancy outcomes in SLE & lupus nephritis
- Studies between 1980-2009
- Purpose:
  - Examine the association of maternal and fetal complications and SLE

1842 patients
2751 pregnancies

## Systemic Lupus Erythematosus & Pregnancy

<table>
<thead>
<tr>
<th>Maternal Complications</th>
<th>Rate [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Unsuccessful pregnancies</td>
<td>23.4% [19.5% to 27.3%]</td>
</tr>
<tr>
<td>Lupus flare</td>
<td>25.6% [17.4% to 33.8%]</td>
</tr>
<tr>
<td>Hypertension</td>
<td>16.3% [10.3% to 22.3%]</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>7.6% [3.6% to 11.6%]</td>
</tr>
<tr>
<td>Severe complications (eclampsia, stroke, maternal death)</td>
<td>1%</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>2 patients</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Fetal Complications</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Prematurity</td>
<td>39.4% [32.4% to 46.4%]</td>
</tr>
<tr>
<td>Spontaneous abortions</td>
<td>16.0% [12.1% to 19.9%]</td>
</tr>
<tr>
<td>IUGR</td>
<td>12.7% [8.8% to 16.7%]</td>
</tr>
<tr>
<td>Stillbirth</td>
<td>3.6% [2.0% to 5.2%]</td>
</tr>
<tr>
<td>Neonatal Death</td>
<td>2.5% [1.2% to 3.8%]</td>
</tr>
</tbody>
</table>

Systemic Lupus Erythematosus & Pregnancy Multivariate Analysis

<table>
<thead>
<tr>
<th>Maternal Variable</th>
<th>Outcome</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active Nephritis</td>
<td>Maternal Hypertension</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Premature Birth</td>
<td>&lt;0.020</td>
</tr>
<tr>
<td>History of Nephritis</td>
<td>Maternal Hypertension</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Pre-eclampsia</td>
<td>0.017</td>
</tr>
<tr>
<td>Positive Anti-phospholipid antibodies</td>
<td>Maternal Hypertension</td>
<td>0.029</td>
</tr>
<tr>
<td></td>
<td>Premature Birth</td>
<td>0.004</td>
</tr>
<tr>
<td></td>
<td>Induced abortion</td>
<td>0.016</td>
</tr>
</tbody>
</table>

Systemic Lupus Erythematosus & Pregnancy

Buyon et al Ann Intern Med 2015

• PROMISSE included 385 women with SLE
  • Excluded
    • U PCR >1000 mg/g
    • Cr>1.2 mg/dL
    • BP > 140/90 mmHg

Adverse Pregnancy Outcomes 19%
Lupus anticoagulant
Antihypertensive Agents
Increased PGA
Platelet count <100
Black or Hispanic

Adverse Pregnancy Outcomes 7.8%
Without Risk Factors
Systemic Lupus Erythematosus & Pregnancy

- 71 pregnancies with lupus nephritis

<table>
<thead>
<tr>
<th>Maternal adverse events</th>
<th>Number (%)</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal flares</td>
<td>14 (19.7)</td>
<td></td>
</tr>
<tr>
<td>Extra renal flares</td>
<td>3 (4.2)</td>
<td></td>
</tr>
<tr>
<td>Pre-edampsia</td>
<td>6 (8.4)</td>
<td></td>
</tr>
<tr>
<td>HELLP syndrome</td>
<td>2 (2.8)</td>
<td></td>
</tr>
<tr>
<td>Gestational diabetes</td>
<td>6 (8.4)</td>
<td></td>
</tr>
<tr>
<td>Severe infections</td>
<td>4 (5.6)</td>
<td></td>
</tr>
<tr>
<td>Pregnancies ended in fetal loss</td>
<td>6 (8.4)</td>
<td></td>
</tr>
<tr>
<td>Delivery at term</td>
<td>45 (63.4)</td>
<td></td>
</tr>
<tr>
<td>Pre-term delivery</td>
<td>20 (28.2)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLEDAI</td>
<td>1.184763</td>
</tr>
<tr>
<td>Active nephritis</td>
<td>17.73333</td>
</tr>
<tr>
<td>Proteinuria g/day</td>
<td>2.746724</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>18.85714</td>
</tr>
<tr>
<td>Previous renal flares</td>
<td>5.25</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>During pregnancy</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quarterly change of a single unit in SLEDAI</td>
<td>1.580907</td>
</tr>
<tr>
<td>Quarterly increase of proteinuria &gt; 1 g/ day</td>
<td>14.86718</td>
</tr>
</tbody>
</table>

Fetal adverse events

- Fetal Loss: 6 (8.2)
- Miscarriages: 3 (4.1)
- Stillbirths: 3 (4.1)
- Neonatal deaths: 0 (0)
- Full term birth: 45 (61.6)
- Pre-term births: 22a (30.1)
- Small for gestational age: 12 (16.4)
- Low birth weight <2500 g: 12 (16.4)
- Very low birth weight <1500 g: 20a (27.4)
- Birth weight g (M±SD): 2753 ± 682

Moroni et al J Autoimmun 2016
What is Quiescent disease?

- Absence of clinical symptoms
- Laboratory investigations:
  - Normal WBC, PLTs, Hgb
  - Normal or stable C3, C4
  - Stable anti-dsDNA
  - Stable renal function
  - Bland urinary sediment
  - Proteinuria <1g/day OFF RAS
  - On Hydroxychloroquine

CONSIDER BIOPSY
ANCA Associated Vasculitis

Survey from the Vasculitis Clinical Research Consortium Patient Contact Registry

18 % exacerbated

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pregnancies delivered prior to diagnosis of</td>
</tr>
<tr>
<td></td>
<td>vasculitis</td>
</tr>
<tr>
<td></td>
<td>Pregnancies delivered after diagnosis</td>
</tr>
<tr>
<td></td>
<td>of vasculitis</td>
</tr>
<tr>
<td>No. of pregnancies</td>
<td>496</td>
</tr>
<tr>
<td>Elective terminations, no.</td>
<td>58</td>
</tr>
<tr>
<td>Pregnancy loss, no. (%)</td>
<td>98 (22.4)</td>
</tr>
<tr>
<td>Miscarriages, no. (%)</td>
<td>93 (94.9)</td>
</tr>
<tr>
<td>Stillbirths, no. (%)</td>
<td>5 (5.1)</td>
</tr>
<tr>
<td>Preterm births, no. (%)†</td>
<td>36 (11.1)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pregnancies delivered after diagnosis of</td>
</tr>
<tr>
<td></td>
<td>vasculitis</td>
</tr>
<tr>
<td></td>
<td>Pregnancies delivered after diagnosis</td>
</tr>
<tr>
<td></td>
<td>of vasculitis</td>
</tr>
<tr>
<td>No. of pregnancies</td>
<td>74</td>
</tr>
<tr>
<td>Elective terminations, no.</td>
<td>9</td>
</tr>
<tr>
<td>Pregnancy loss, no. (%)</td>
<td>22 (33.8)*</td>
</tr>
<tr>
<td>Miscarriages, no. (%)</td>
<td>21 (95.5)</td>
</tr>
<tr>
<td>Stillbirths, no. (%)</td>
<td>1 (4.5)</td>
</tr>
<tr>
<td>Preterm births, no. (%)†</td>
<td>10 (23.3)*</td>
</tr>
</tbody>
</table>

Clowse et al Arthritis Care and Research 2013
Optimization and Management Strategies

**Prepregnancy**
- Discuss timing of conception
- Contraception advice if needed
- Fertility assessment if needed
- Assess disease activity with repeat biopsy confirmation if necessary
- Optimize blood pressure control
- Change to non-teratogenic medications and provide reassurance about continuation of safe medications in pregnancy
- Explain risk of pregnancy complications and need for heightened surveillance

**Antenatal**
- Target BP <140/90 mmHg
- Start low dose aspirin
- Consider Vitamin D and Calcium supplements
- Baseline and serial renal function, proteinuria (albumin to creatinine or protein to creatinine ratios or 24 hour collections) and markers of disease activity
- Monitoring of calcineurin levels if required

**Delivery**
- Delivery if presence of fetal or maternal decompensation
- NOT at pre-specified gestation
- Corticosteroid administration for fetal lung maturation at least 24 hours and up to 7 days prior to anticipated delivery if <34 weeks' gestation
- Aim for vaginal delivery if possible
- Hydrocortisone stress dosing if required

**Postnatal**
- Encourage breast feeding
- Careful surveillance for active GN
- Calcineurin inhibitor level if dose changed in pregnancy
- Continue VTE prophylaxis for at least 6 weeks if necessary
- Emotional support

CJASN in Press
## Treat Proteinuria

**Pregnancy Safe Immunosuppression**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Grade</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prednisone</td>
<td>B</td>
<td>Increased risk of cleft Palate (3/1000 vs 1/1000 in general population)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mood/sleep disturbance</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cushingoid appearance</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hypertension</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hyperglycemia/Diabetes Mellitus/Gestational Diabetes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Osteoporosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Avascular necrosis (rare)</td>
</tr>
<tr>
<td>Calcineurin Inhibitors: Monitoring of drug levels recommended during pregnancy</td>
<td>C</td>
<td>Use associated with smaller babies</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hypertension</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nephrotoxicity/elevated creatinine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TTP (rare)</td>
</tr>
<tr>
<td>Cyclosporine (Neoral, Sandimmune)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tacrolimus (Prograf)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azathioprine (Imuran)</td>
<td>D</td>
<td></td>
</tr>
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<td></td>
<td></td>
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</tr>
</tbody>
</table>

Rituximab (Dose early in pregnancy)

Pulse Methylprednisone

PLEX
**Calcineurin Inhibitors**

Drug Dosing
- CsA levels go down
- Increased GFR and metabolism
- Tacrolimus levels may go up or down
- Pregnancy may inhibit cytochrome P450 enzymes

Close-up of Levels
Target lower Trough

Davison JM Renal Disease in Pregnancy 2008
Treat Proteinuria
  
  RAS Blockade
  
  • Second and Third Trimester Exposure
    • oligohydramnios
    • neonatal anuria and renal failure
    • limb contractures
    • craniofacial abnormalities
    • pulmonary hypoplasia
    • patent ductus arteriosus
Treat Proteinuria
RAS Blockade

• Systematic Review

Bullo et al Hypertension 2012
Treat Proteinuria
RAS Blockade

First Trimester Exposure

- 465 754 mother infant pairs
  - Kaiser Permanente Northern California
  - Adjusted maternal age, ethnicity, parity and obesity

- 0.9/1000 prevalence of use
- Congenital Heart Defects
  - ACEi vs Normal Control OR 1.54 (0.9-2.62)
  - Other BP Agents vs Normal Control OR 1.52 (1.04-2.21)
  - ACEi or Other BP Agents vs Hypertensive Controls NS

Li et al BMJ 2011
Treat Proteinuria
RAS Blockade

- First Trimester Exposure Direct Studies
  - All stopped by 8 weeks
  - No Teratogenicity

Porta et al
Diabetologica 2011
Treat Proteinuria
RAS Blockade

• 24 women with diabetic nephropathy

  • 6 months of pre-pregnancy treatment
    • Multiple insulin injections
    • Captopril (37.5-75 mg daily)

  • Pre-Treatment Proteinuria 1292 ± 656 mg/day
  • Post-Treatment Proteinuria 202 ± 141 mg/day
  • Beneficial effect was sustained throughout pregnancy
  • No deterioration in renal function at 2 years postpartum

• Recommendation:
  At least 6 months of ACEI, discontinued at conception

Hod et al. NDT 1995

TREAT PROTEINURIA
RAS BLOCKADE

Teratogenic

Extreme caution is required in women of child bearing age

Patients that reach ESRD have a decreased life expectancy

Stop at Conception:
Significant Proteinuria without Immunological Options (DM, scarring and IgA)
Regular Cycles Compliant
HYPERTENSION MANAGEMENT

Methyldopa  
Starting dose 250 BID  
Maximum of 500 QID

Labetolol  
Starting dose 100 BID  
Maximum 200 QID

Nifedipine XL  
Starting dose 30 OD  
Maximum 60 BID

Amlodipine  
2.5 to 10 mg OD

Hydralazine, thiazides and clonidine also safe
CHIPS Trial

- N= 987 (94 sites)
  - Pre-existing or gestational HTN
  - Excluded proteinuria
  - Randomized
    - Less tight control – DBP 100 mmHg
    - Tight Control – DBP 85 mmHg

- Primary (perinatal) outcome [31.4% vs. 30.7%; aOR 1.03, 95% CI 0.78, 1.36]
- Secondary (maternal) outcome [3.7% vs. 2.0%; aOR 1.74, 95% CI 0.79, 3.84]
- ‘less tight’ control more frequently developed BP ≥160/110mmHg) (40.4% vs. 27.5%; aOR 1.78, 95% CI 1.35, 2.36)

ALTHOUGH RENAL PATIENTS EXCLUDED BP CONTROL IS LOGICAL TARGET BP < 140/90 mmHg

Magee et al NEJM 2015
Secondary Analysis from the CHIPS Trial

• Methyldopa vs Labetalol was associated with less small babies (<10th centile) and preterm delivery (< 37 weeks)

Magee et al. BJOG 2015
Hypertension Management

- 1233 eligible women (300 on labetalol and 923 on methyldopa)
- Higher rates of RDS, sepsis and seizure in the infants of mothers prescribed labetalol OR 1.51, 95% CI 1.02-2.22

Manage Nephrotic Syndrome

- Management of edema
  - Diuretics
  - Albumin

Pilozzi-Edmonds et al FR-PO579
MANAGE NEPHROTIC SYNDROME

Risk of VTE in Pregnancy

- Population-based cohort study – CIHI data
  - N=3 852 569
  - DVT 12.1/10 000
  - PE 5.4/10 000
- Death rates were low

J OB Gyn of Can 2009

Barbour et al. KI 2012

Consider VTE prophylaxis

High Grade Proteinuria
Low Albumin
Membranous or Vasculitis
PREVENT PREECLAMPSIA

High-Risk CKD Population

• Renal Insufficiency
• Proteinuria
• Hypertension

Prescribe

• ASA 81 mg daily
• MVI with Folic Acid
• Calcium 1000 mg daily
• Vitamin D 600 IU

recommended to support maternal and fetal bone metabolism
prevent preeclampsia

• ASA prior to 16 weeks reduces only preterm, but not term preeclampsia

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>ASA events</th>
<th>ASA total</th>
<th>Control events</th>
<th>Control total</th>
<th>Weight %</th>
<th>Risk ratio M-H, random, 95% CI</th>
<th>Risk ratio M-H, random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>August, 1994</td>
<td>0</td>
<td>24</td>
<td>5</td>
<td>25</td>
<td>15.2</td>
<td>0.09 (0.01, 1.62)</td>
<td></td>
</tr>
<tr>
<td>Bakhti, 2011</td>
<td>1</td>
<td>82</td>
<td>9</td>
<td>82</td>
<td>29.4</td>
<td>0.11 (0.01, 0.86)</td>
<td></td>
</tr>
<tr>
<td>Ebrashy, 2005</td>
<td>0</td>
<td>73</td>
<td>23</td>
<td>63</td>
<td>15.9</td>
<td>0.02 (0.00, 0.30)</td>
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<tr>
<td>Vainio, 2002</td>
<td>0</td>
<td>43</td>
<td>1</td>
<td>43</td>
<td>12.2</td>
<td>0.33 (0.01, 7.96)</td>
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</tr>
<tr>
<td>Villa, 2010</td>
<td>1</td>
<td>61</td>
<td>5</td>
<td>60</td>
<td>27.4</td>
<td>0.20 (0.02, 1.63)</td>
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</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>283</strong></td>
<td><strong>273</strong></td>
<td></td>
<td></td>
<td>100.0</td>
<td><strong>0.11 (0.04, 0.33)</strong></td>
<td></td>
</tr>
</tbody>
</table>

Test for overall effect: Z = 3.92 (p < 0.0001)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>ASA events</th>
<th>ASA total</th>
<th>Control events</th>
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<th>Risk ratio M-H, random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>August, 1994</td>
<td>3</td>
<td>24</td>
<td>0</td>
<td>25</td>
<td>7.5</td>
<td>7.28 (0.40, 133.89)</td>
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<tr>
<td>Bakhti, 2011</td>
<td>0</td>
<td>82</td>
<td>0</td>
<td>82</td>
<td></td>
<td>not estimable</td>
<td></td>
</tr>
<tr>
<td>Ebrashy, 2005</td>
<td>25</td>
<td>73</td>
<td>17</td>
<td>63</td>
<td>42.8</td>
<td>1.27 (0.76, 2.13)</td>
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<tr>
<td>Vainio, 2002</td>
<td>2</td>
<td>43</td>
<td>9</td>
<td>43</td>
<td>20.4</td>
<td>0.22 (0.05, 0.97)</td>
<td></td>
</tr>
<tr>
<td>Villa, 2010</td>
<td>7</td>
<td>61</td>
<td>6</td>
<td>60</td>
<td>29.3</td>
<td>1.15 (0.41, 3.22)</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>283</strong></td>
<td><strong>273</strong></td>
<td></td>
<td></td>
<td>100.0</td>
<td><strong>0.98 (0.42, 2.33)</strong></td>
<td></td>
</tr>
</tbody>
</table>

Test for overall effect: Z = 0.04 (p = 0.97)
PREVENT PREECLAMPSIA

Calcium Supplementation

- **Overall Risk of Preeclampsia**
  - 13 trials (n=15 730)
  - RR 0.45 (0.31-0.65)

- **Low Calcium Intake**
  - 8 trials (n=10 676)
  - RR 0.36 (0.20-0.65)

- **High Risk Women**
  - 5 trials (n=587)
  - RR 0.22 (0.12-0.42)

Cochrane Review 2010
Diagnose Preeclampsia

• Urinalysis

• Serology

• Renal biopsy
  • <32 Weeks
    • Based on Expert Opinion
  • Systematic Review
    • 4/197 or 2% major complication rate
      • median of 25 weeks gestation
    • 5% minor complication rate
  • NOT HOW YOU WANT TO DIAGNOSE PREECLAMPSIA

Piccolli et al BJOG 2013
Diagnose Preeclampsia

Alternative splicing of Flt1 → sFlt1
serum levels of sFlt1 5x higher
unbound VEGF & PI GF are reduced
Antiangiogenic Factors

- **Prognosis Study**  
  - Developmental Cohort (n=500)  
  - Validation Cohort (n=550)  
  - Predictive Value of sFlt-1/PLGF ratio - < 24 in women suspected of having preeclampsia RULE OUT

- Low PLGF predictive of delivery within 14 days in women with HTN and CKD  
  Bramham KI 2016

- **Roche sFlt-1/PLGF Ratio Test (Elecsys®)**  
  - Electrochemiluminescence  
  - Available in the UK, Europe, Canada, Australia, Asia and parts of Latin America
Diagnose Preeclampsia
Clinical Indicators of Abnormal Placentation

<table>
<thead>
<tr>
<th>First Trimester Screen – 11 to 13 weeks gestation</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>PAPP-A</td>
<td>Activate inulin-like growth factors that facilitate placental growth</td>
</tr>
<tr>
<td></td>
<td>↓</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Maternal Serum Screen – 15 to 20 weeks gestation</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>AFP</td>
<td>Fetal liver is the source so its presence in a normal fetus suggests breach in the placental villi</td>
</tr>
<tr>
<td></td>
<td>↑</td>
</tr>
<tr>
<td>HGC</td>
<td>Excessive secretion by an abnormal syncytiotrophoblast (beware as cleared by kidneys)</td>
</tr>
<tr>
<td></td>
<td>↑</td>
</tr>
<tr>
<td>DIA</td>
<td>Excessive secretion by an abnormal trophoblast</td>
</tr>
<tr>
<td></td>
<td>↑</td>
</tr>
</tbody>
</table>

MSH Placenta Clinic – Dr. John Kingdom
http://www.mountsinai.on.ca/care/placenta-clinic
Abnormal placenta’s might include length<10cm, thickness>4cm, heterogeneous appearance, echogenic cystic areas or even appear “jelly-like”

Procter et al US Ob Gyn 34:274-282, 2009
Diagnose Preeclampsia
Clinical Indicators of Abnormal Placentation

Uterine Artery Doppler

Normal

Abnormal Presence of bilateral UA notching or Pulsatility index >1.45
Diagnose Preeclampsia
Clinical Indicators of Abnormal Placentation

Umbilical Artery Doppler

- Normal
- Absent EDF
- Reverse EDF
Diagnose Preeclampsia
Clinical Indicators of Abnormal Placentation

• Dropping fetal growth percentile
POST PARTUM CARE
DRUGS AND BREASTFEEDING

Immunosuppression

- Prednisone
- Imuran
- Cyclosporin
  - Up to 2% of the maternal weight adjusted dose
- Tacrolimus
  - 0.5% of the maternal weight adjusted dose
  - <0.2% of the paediatric dose – MOTHER RISK
  - 0.23% of the maternal weight adjusted dose

CJASN 2013

Anti-Hypertensives

Methyldopa

Lowest Milk/Plasma Ratios

- Labetalol
- Nifedipine
- Captopril
- Enalapril
- Quinalapril
Emotional Support

Uncertainties & unknowns

Adequacy of information

Societal expectations & responses

Lack of Control

Experiences with illness

Social roles

Self-image

Life goals

Beanlands, Catran and Hladunewich KFOC
Pre-Pregnancy Consultation Helps

- 179 women
  - 90% found the clinic informative
  - 92% stated it helped them decide to pursue a pregnancy

Counseling and preparation requires a significant investment of time and patience

Wiles et al BMC Nephrology 2015
You have to do better

http://www.npr.org/2017/05/12/527806002/focus-on-infants-during-childbirth-leaves-u-s-moms-in-danger
Summary Statements

Planning Pregnancy – Active Process

• Educate all young women with kidney disease as to the risks of unplanned pregnancy
• Treat the Disease Before Conception and during Pregnancy
• Identify “Windows of Opportunity” along the CKD Continuum as Early is Better than Late
• Multicenter efforts to refine our advice and management are desperately needed

Cure GN, Neptune, UKCAN Pregnancy Registry