Preeclampsia Delivered
Now What?

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Objectives

• Update on current diagnosis and management of preeclampsia with emphasis following delivery
• Understand risk of later cardiovascular disease (CVD) with history of preeclampsia
• Identify cardiovascular risk factors and know recommended interventions
• Be able to provide long-term health plan for patients with history of preeclampsia

Hypertension in Pregnancy
ACOG Task Force Report 2013

• Update in Definitions
  – Gestational hypertension
    • Elevated BP [140/90] on 2 occasions 4 hr. apart after 20 weeks
  – Chronic hypertension
    • Elevated BP [140/90] predates pregnancy (before 20 weeks)
  – Preeclampsia/Eclampsia
    • Elevated BP [140/90] with proteinuria (300mg./24 hr or PCR 0.3) OR severe feature
  – Preeclampsia with severe features (HELP syndrome)
    • BP 160/110 2 occasions 4 hr apart
    • 5 gm proteinuria in 24 hr
    • <3,000,000 plt, AST/ALT 2x normal, Cr >1.1,
    • pulmonary edema, cerebral or visual disturbances
  – Eclampsia
    • Seizure in pregnancy, not epilepsy
  – Chronic hypertension with superimposed preeclampsia
    • Preeclampsia in women with CHI HTN

• DISCONTINUE USE OF PIH- Pregnancy Induced Hypertension
• Discourage use of “mild” preeclampsia

Disclosures

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  – NIH
  – Stanford Children’s Health Research Institute
  – Stanford Cardiovascular Institute
  – Stanford Department of Obstetrics and Gynecology
• Spouse employee of Merck
Management

- **Gestational HTN or Preeclampsia without Severe features**
  - Daily symptoms and fetal movement
  - BP twice weekly
  - Labs weekly
  - NST/AFI (1-2x week) and growth scan (q2-3 weeks)
  - Delivery at 37 weeks

- **Preeclampsia with Severe features**
  - BMI (<34 weeks)
  - Delivery by 34 weeks, sooner for certain maternal or fetal status
  - Expectant following BMZ if BP well controlled and none of the below (occur at hospital with adequate maternal and fetal resources)
    - Don’t delay following BMZ (uncontrolled BP, eclampsia, pulmonary edema, abruption DIC, non-reassuring fetal status, IUD)
    - Can delay 48 hr if stable but then deliver (PPROM, labor, low plt, elevated AST/ALT, oligo, abnl Dopplers, increasing renal dysfunction) for HELLP 24-48 hr delay
  - Treat BP 160/110 *
  - MgSO4 (maintain through delivery even if C/S)

Case

- 35 yo AA G1P0 at 36 weeks by LMP and first trimester U/S.
  - BMI 30 and Fx of HTN
  - BP 145/92, UPC 0.32,
  - Labs normal,
  - SVE Closed/long/firm
  - Ultrasound, EFW 65%, normal fluid

ARQ #1 What is your Diagnosis?

A. Gestational HTN
B. Preeclampsia without severe features
C. Preeclampsia with severe features
D. Chronic Hypertension
E. Superimposed Preeclampsia

ARQ #2 What is your management?

A. Plan Induction at 37 weeks
B. Plan Induction at 38 weeks
C. Plan Induction at 39 weeks
D. Expectant Management ‘til spontaneous labor but induce by 40 weeks
In labor her BP rise to 164/110

ARQ#3 Now what is the Diagnosis?

A. Severe Gestational HTN
B. Preeclampsia with Severe Features
C. Preeclampsia without Severe Features
D. Chronic Hypertension

ARQ#4: What is your management?

A. Start IV MgSO4
B. Treat with IV labetalol
C. Prep for LTCS
D. A and B
E. A, B and C

Management Postpartum: What has changed?

• Monitor BPs for at least 72 hrs and again at 7-10 days PP
  – Extend inpatient or arrange for outpatient monitoring
• Avoid NSAIDs particularly in
  – Severe preeclampsia
  – Chronic hypertension
  – BP remains elevated after first 24hr
• Educate all patients regarding warning symptoms for preeclampsia that can develop after delivery

Management at 6 week Postpartum Visit

• Measure BP and adjust Dx if still elevated
  – Chronic hypertension +/- preeclampsia
• Educate about risk of subsequent preeclampsia
  – Educate women to start baby ASA at 12 weeks in subsequent pregnancy
• Lose weight if elevated BMI
• Screen BP and assess CVD risks starting at 6-12 months and then annually particularly for preterm or recurrent preeclampsia
  – BP, lipids, fasting glucose, BMI
Background: ASCVD in Women

- Leading cause of death among women in US
  - 1 in 4 deaths attributable to CAD
  - 1 in 2 deaths for all forms of CVD
- Heart disease:
  - Second-leading cause of death for women 45 to 64 years
  - Third-leading cause of death for women age 25 to 44 years
- CVD kills almost twice as many women as all forms of cancer combined

HDP increase risk diabetes and HTN

- Danish registry based cohort
- Median 16.4 years follow up
- 782,287 women ages 15-50 with first singleton pregnancy without previous CVD

<table>
<thead>
<tr>
<th></th>
<th>Diabetes</th>
<th>Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR(95% CI)</td>
<td>HR(95% CI)</td>
<td></td>
</tr>
<tr>
<td>No HDP</td>
<td>1 (ref)</td>
<td>1 (ref)</td>
</tr>
<tr>
<td>Gestational HTN</td>
<td>3.12 (2.63-3.70)</td>
<td>5.31 (4.9-5.75)</td>
</tr>
<tr>
<td>Mild preeclampsia</td>
<td>3.53 (3.23-3.85)</td>
<td>3.61 (3.43-3.80)</td>
</tr>
<tr>
<td>Severe preeclampsia</td>
<td>3.68 (3.04-4.46)</td>
<td>6.07 (5.45-6.77)</td>
</tr>
</tbody>
</table>

Lykke et al., Hypertension 2009

Preeclampsia: future risk CVD

Systematic Review and Meta-analysis

<table>
<thead>
<tr>
<th>CVD Outcome</th>
<th>RR</th>
<th>95% CI</th>
<th>RR</th>
<th>95% CI</th>
<th>Studies included</th>
<th>Mean follow-up</th>
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</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>3.70</td>
<td>2.70-5.05</td>
<td>14</td>
<td>14 years</td>
<td>14</td>
<td>14 years</td>
</tr>
<tr>
<td>CHD (fatal/nonfatal)</td>
<td>2.16</td>
<td>1.86-2.52</td>
<td>8</td>
<td>11.7 years</td>
<td>8</td>
<td>11.7 years</td>
</tr>
<tr>
<td>Stroke (fatal/nonfatal)</td>
<td>1.81</td>
<td>1.45-2.27</td>
<td>4</td>
<td>10.4 years</td>
<td>4</td>
<td>10.4 years</td>
</tr>
<tr>
<td>VTE</td>
<td>1.19</td>
<td>1.37-2.33</td>
<td>3</td>
<td>10.4 years</td>
<td>3</td>
<td>10.4 years</td>
</tr>
</tbody>
</table>

- Recurrent preeclampsia: 7-fold increased risk for HTN
- Preeclampsia before 37 wks
- 8-fold increased risk for CHD (2 studies)
- 5-fold increased risk for stroke


Brown et al. 2013; Wu et al. 2017

2011 CVD prevention

AHA Guideline

Effectiveness-Based Guidelines for the Prevention of Cardiovascular Disease in Women—2011 Update
A Guideline From the American Heart Association

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- Pregnancy provides a unique opportunity to estimate a woman’s lifetime risk
- Referral to primary care provider or cardiologist so risk factors can be carefully monitored and controlled.
- History of preeclampsia, GDM, Gestational HTN is considered major risk factor

Mosca et al., Circulation 2011
2014 stroke prevention

AHA/ASA Guideline

Guidelines for the Prevention of Stroke in Women
A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association

The American Academy of Neurology offers the value of this guideline as an educational tool for neurologists. Endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons.

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- Consider evaluating all women starting 6 months to 1 year post partum, as well as those who are past childbearing age, for a history of preeclampsia/eclampsia and document their history of preeclampsia/eclampsia as a risk factor.
- Clinicians are not aware of the association between adverse pregnancy outcomes and CVD and stroke.

ASCVD Risk Calculator from ACA
http://tools.acc.org/ascvd-risk-estimator/

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value 1</th>
</tr>
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<tr>
<td>Age</td>
<td>35 (40)</td>
</tr>
<tr>
<td>Sex</td>
<td>F</td>
</tr>
<tr>
<td>Race</td>
<td>AA</td>
</tr>
<tr>
<td>Total Cholesterol</td>
<td>200</td>
</tr>
<tr>
<td>HDL Cholesterol</td>
<td>45</td>
</tr>
<tr>
<td>SBP</td>
<td>120</td>
</tr>
<tr>
<td>Treatment for HTN</td>
<td>N</td>
</tr>
<tr>
<td>DM</td>
<td>N</td>
</tr>
<tr>
<td>Smoker</td>
<td>N</td>
</tr>
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- Several smart phone apps available

<table>
<thead>
<tr>
<th>10-year ASCVD Risk</th>
<th>Lifetime ASCVD Risk</th>
</tr>
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<tbody>
<tr>
<td>Actual Risk</td>
<td>NA (0.8%)</td>
</tr>
<tr>
<td>Risk with Optimal Factors</td>
<td>NA (0.4%)</td>
</tr>
</tbody>
</table>

10-year ASCVD Risk: 27% (27%)
Lifetime ASCVD Risk: 8% (8%)

Definition of Heart Failure
AMERICAN COLLEGE OF CARDIOLOGY/AMERICAN HEART ASSOCIATION

- **Stage A**: At least one condition strongly associated with heart failure (HF)
  - No identified structural or functional
  - No signs or symptoms of HF
- **Stage B**:  
  - No known signs or symptoms
  - LV concentric remodeling, LV hypertrophy, mildly impaired systolic function (EF<55%) or valvular disease
- **Stage C**:  
  - Current or prior symptoms of HF
  - Underlying structural heart disease.
- **Stage D**:  
  - Advanced structural heart disease, marked symptoms of HF at rest despite maximal medical therapy.

Risk Reduction Options

- Quit smoking
- Work toward BMI<25
- DASH diet/ AHA diet
- Regular Exercise
- Breastfeeding (Schwarz et al 2009, Rajaei et al. 2016)
- Baby ASA
- Statins
Hx of Preeclampsia and Prehypertension Have Highest OR for HF Class B

Heart Failure Risk Reduction

- Exercise 20 to 45 minutes several times a week
- Ace inhibitors/ARB
- Beta blocker
- BNP to monitor HF

Is it the chicken or the egg?

- Is increased future CVD risk due to underlying biologic traits of the mother or exposures during pregnancy?
- Perhaps both

Risk factors that overlap for preeclampsia and CVD

- Chronic hypertension
- Diabetes
- Obesity
- Insulin resistance
- Dyslipidemia
- Systemic inflammation

Bushnell, C et al., Stroke Research and Treatment 2011
Powe et al., Circulation 2011
Model for pregnancy as a stress test for long-term CVD

Powe et al., Circulation 2011

Rationale Approach for PP Counseling and Health Planning

- BP check at 6 weeks, Educate about risk factor counseling and lifestyle recommendations
  - Recommendations for future pregnancies
- Follow-up at 6 or 12 months (PCP, Heart Clinic)
  - BP, weight, Cholesterol, HDL, LDL,
  - In future may consider CRP, HbA1c, maternal echo, Coronary Artery Calcification
- Annual screening and ASCVD risk assessment for women with preterm or recurrent preeclampsia
  - medications as warranted

Future Research and Personalized Medicine

- Incorporation of Hx of preeclampsia and specific details into risk calculators
- Determine which women with Preeclampsia at greatest risk
- Determine if risk reduction approaches are less, same or more effective in women his Hx Preeclampsia
- Understand underlying biology linking Preeclampsia and CVD to determine most important interventions

Resources

Preeclampsia Foundation
https://www.preeclampsia.org

American Heart Association
https://www.goredforwomen.org

ACOG http://www.acog.org/Womens-Health/Preeclampsia-and-Hypertension-in-Pregnancy
SecondsCount.org
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• Tekoa King

References:


Associated risks for disease later in life following preeclampsia

• Hypertension  
  – 4 fold in 10 years
• Stroke  
  – 2-fold
• Ischemic heart disease  
  – 2-fold
• Renal Disease  
  – 4 fold
• Heart Failure B (Breetvold et al 2016; Ghossein-Doha et al 2017)  
  – 4-fold increase (27% at 1 and 4 years PP)
CVD Risk Categories

- **High Risk:**
  - Established CVD/PVD/AAA
  - DM
  - Chronic Renal Insuff.
  - Framingham risk >20%
- **Low "optimal" Risk:**
  - No CVD risk factor AND
  - Healthy Lifestyle
- **At Risk:**
  - ≥1 Major CVD risk factor
  - Evidence of Subclinical Dz (CAC)
  - Family hx early CVD
  - Metabolic Syndrome
  - Poor exercise capacity
  - Hx preeclampsia, GDM, HDP

Mosca et al., Circulation 2011

Pregnancy complications are associated with premature CVD

- Gestational hypertension, pre-eclampsia, placental abruption, placental infarction
  - Doubles risk of developing premature CVD
  - Gradient effect
  - Causal or simply a reflection of pre-pregnancy risks that continue after delivery


Retrospective cohort study
- 1.03 million women
- No CVD prior to pregnancy
- Mean age 28
- Mean follow up 8.7 years

Mean age for first CV event was 38