Pregnancy Can Kill (or Maim) You!

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PGY12
Learning Objectives

• Discuss key modifications to preeclampsia terminology
• Discuss management of varying clinical presentations of preeclampsia
• Discuss important issues affecting preeclamptic women that should be addressed in the postpartum period
• Name 3-4 mechanisms that are associated with the underlying pathophysiology of preeclampsia
PGY2

- Paged that a Somali patient who was pregnant was being brought in by EMS
  - Sister discovered patient unconscious at home
  - SaO₂ reportedly low 90s
  - BPs 180s/100s
  - Patient conscious on non-rebreather (level of lucidity difficult to ascertain due to language barrier)
  - Transferred to Triage bed
  - CV collapse
Don’t Panic
PGY2

- Code Blue
  - Attending and Chief Resident to triage
  - BLS initiated
  - Intubation attempted
- What have we not assessed at this point?
- Sono performed and agonal heart tones observed
- Femur measurement suggested EGA ~32 weeks
PGY2

- Attending performed peri-mortem CD in triage
- NICU staff present
- Delivery of newborn
- Then........
- Delivery of a second baby!
Maternal Outcome

- Resuscitated
- Transferred to the ICU
- Uncal herniation $\rightarrow$ Death
Neonatal Outcomes

• Both twins
  • HIE
  • Seizures

• Discharged home with the patient’s mother
• Long term outcomes unknown
• 27 y/o Somali Female with dichorionic twin gestation
  • Admitted for preeclampsia
  • Not thrilled with Western Medicine
  • Left AMA
  • Instructed to follow up twice weekly
Impact of Preeclampsia

- 10 million women will develop preeclampsia worldwide
  - 76,000 die/year from preeclampsia
  - Number of perinatal and newborn deaths ~500,000
  - Numbers higher in developing countries
- Accounts for 10% of maternal obstetric related deaths in the U.S.
## CMACE 2006–2008

### Causes – direct

<table>
<thead>
<tr>
<th>Direct causes of maternal deaths</th>
<th>Rates per 100 000 maternities</th>
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</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>1.13</td>
</tr>
<tr>
<td>Pre-eclampsia and eclampsia</td>
<td>0.83</td>
</tr>
<tr>
<td>Thrombosis and thromboembolism</td>
<td>0.79</td>
</tr>
<tr>
<td>Amniotic fluid embolism</td>
<td>0.57</td>
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<tr>
<td>Early pregnancy deaths</td>
<td>0.39</td>
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<tr>
<td>Anesthetic</td>
<td>0.31</td>
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<tr>
<td>Other direct deaths</td>
<td>0.17</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>4.67</strong></td>
</tr>
</tbody>
</table>
CDC 2006-2008

- Cardiovascular diseases: 14.6%
- Cardiomyopathy: 12.4%
- Hemorrhage: 11.9%
- Infection/sepsis: 11.5%
- Hypertensive disorders of pregnancy: 11.1%
- Thrombotic pulmonary embolism: 10.5%
- Amniotic fluid embolism: 10.3%
- Cerebrovascular accidents: 5.9%
- Anesthesia complications: 5.7%
- Other: 0.6%
<table>
<thead>
<tr>
<th><strong>Preeclampsia Characteristics</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Proteinuria</td>
</tr>
<tr>
<td>Renal vasoconstriction</td>
</tr>
<tr>
<td>$\uparrow \text{TPR} \downarrow \text{CO}$</td>
</tr>
<tr>
<td>Endothelial dysfunction</td>
</tr>
<tr>
<td>Intrauterine growth restriction</td>
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</tbody>
</table>
What is the link between placental ischemia and hypertension?

Endothelial activation/dysfunction

- ET-1
- TBX
- NO
- PG_2
- ANG II Sensitivity

pressure natriuresis

peripheral resistance

Hypertension

What is the link between placental ischemia and endothelial dysfunction?

- Cytokines (TNF / IL-6)
- Autoantibodies
- Oxidative Stress
- sFLT1
- Circulating Trophoblast

Endothelial Dysfunction

HYPERTENSION
Placental Ischemia

TNF-α

AT1-AA

Vascular Sensitivity

Blood Pressure
Agonistic Angiotensin II type 1 Receptor Autoantibodies
Fellowship

- 32 y/o G2P1001 with IUP at 28W
- Presented as a transfer due to diagnosis of severe preeclampsia (elevated liver enzymes)
- RUQ pain
- Shortly after arrival discovered that patient was in DIC
- Liver bleed
Outcome

- Liver capsule stayed intact
- Likely saved the patient’s life
- Blood product replacement
- CD

- Both mother and newborn were discharged alive and well...eventually
HTN In Pregnancy Guidelines
Classifications of Hypertensive Disorders of Pregnancy

- Preeclampsia/Eclampsia
- Chronic Hypertension
- Chronic Hypertension with Superimposed Preeclampsia
- Gestational Hypertension
Preeclampsia: Important Modifications

- Proteinuria
  - No longer required for the diagnosis of preeclampsia
  - Intervention has been delayed in women with multiorgan dysfunction due to the absence of proteinuria
- New onset systemic findings
  - Thrombocytopenia (Platelets <100K)
  - Doubling of LFTs
  - Doubling of creatinine or creatinine >1.1mg/dL
  - Cerebral/visual disturbances
  - Pulmonary Edema
Preeclampsia
Important Modifications

• Preeclampsia with or without severe features
• Removed from severe features:
  • Proteinuria >5g
    • Minimal relationship, if any, between quantity of protein and pregnancy outcome
• Fetal growth restriction
  • Because it is managed similarly even in patients without preeclampsia
Can We Predict Preeclampsia

- Poorly
- Improvements to come
Preeclampsia Prevention

- **Calcium**
  - Not in the U.S.
- **Salt restriction**
- **Bed Rest**
- **Vitamins C and E**
- **Aspirin (80mg)**
  - Studied in >30,000 women (modest effect)
  - Recently backed by new USPTF statement
- **Prior history of PTD <34W associated with preeclampsia**
- **>1 previously affected pregnancy**
Management Recommendations

• Inpatient vs. Outpatient
  • Cohort studies show equivalent outcomes between these management styles
    • Selection bias is an issue
  • No randomized trials to date
Management Recommendations

• Preeclampsia without Severe Features
  • Twice weekly office visits
    • BP evaluations, Physical Exam
  • Twice weekly fetal surveillance
  • Once weekly assessment of LFTs and platelets
  • Serial Fetal Growth Assessment
  • Umbilical Artery Velocimetry (if growth restriction documented) performed with fetal surveillance
Management Recommendations

• Gestational HTN
  • Office visits once to twice weekly
    • BP evaluations, proteinuria assessment
  • Serial Fetal Growth Assessment
Management Recommendations

- Anti-hypertensives
- Persistent SBPs >160 or DBPs >110
HYPITAT

- Open label randomized controlled trial
  - 38 centers in the Netherlands
  - Gestational HTN and "Mild" Preeclampsia
- Deliver at 37 weeks vs expectant management up to 41 weeks

HYPITAT

• Primary outcome: Composite measure of poor maternal outcome—maternal mortality, maternal morbidity
  • Eclampsia, HELLP syndrome, pulmonary edema, thromboembolic disease, and placental abruption), progression to severe hypertension or proteinuria, and major post-partum haemorrhage (>1000 mL blood loss).
HYPITAT

• 117 (31%) allocated to induction of labor developed poor maternal outcome compared with 166 (44%) allocated to expectant monitoring (relative risk 0.71, 95% CI 0.59–0.86, p<0.0001)

• No strokes, no episodes of eclampsia

• No maternal or neonatal deaths
HYPITAT Criticisms

- Two thirds of the patients had a diagnosis of GHTN
- Common for BPs to rise in the third trimester
- Physiology of a well, hypertensive woman is drastically different than the physiology of a preeclamptic mother
- Birth weights 8% lower in the 37 week delivery group
- Adverse neonatal effects not powered for
Deliver or Deliberate

- Preeclamptic patients diagnosed after 34 weeks randomly assigned to deliver vs being monitored until 37 weeks
  - Monitored group: twice weekly office visits with antenatal surveillance and once weekly lab evaluation
    - 41% of those expectantly managed developed severe features of preeclampsia within 72 hours versus 3% in the immediately delivered group (p < 0.001).
    - Immediate delivery did not significantly increase cesarean delivery or neonatal morbidity.

HYPITAT II

- Randomized Open Label Trial
- Deliver at 34 weeks or expectant until 37 weeks
- 51 Hospitals in the Netherlands
- Primary outcomes:
  - Composite of adverse maternal outcomes (thromboembolic disease, pulmonary oedema, eclampsia, HELLP syndrome, placental abruption, or maternal death)
  - Neonatal respiratory distress syndrome,
HYPITAT II

- 351 patients randomly assigned to immediate delivery
- 352 patients randomly assigned to expectant management until 37 weeks
  - Composite Maternal Adverse Outcomes
    - 1.1% vs. 3.1% (RR 0.36, 95% CI 0.12-1.11)
  - Respiratory Distress Syndrome
    - 5.7% vs. 1.7% (RR 3.3, 95% CI 1.4-8.2)
- Immediate delivery does not seem justified and a strategy of expectant monitoring until the clinical situation deteriorates can be considered.
Timing of Delivery

• 37 Weeks
  • Gestational HTN
  • Preeclampsia without severe features
• Preeclampsia with severe features
  • No later than 34 weeks
  • Pre-viable ➔ deliver
Stroke and Severe Preeclampsia and Eclampsia: A Paradigm Shift Focusing on Systolic Blood Pressure

- Characteristics of patients being treated immediately before stroke:
  - Systolic pressure ≥ 160 mmHg in 95.8% of patients
  - >155 mm Hg in 100%.
  - 12.5% exhibited pre-stroke diastolic pressures ≥ 110 mmHg
  - 17% =105 mm Hg
  - 25% exceeded a mean arterial pressure of 130 mm Hg before stroke.

Martin et al. Obstet Gynecol Feb 2005
Management Recommendations

- Defer delivery for steroid benefit x 48 hours:
  - Labor
  - Platelets <100K
  - Elevated LFTs
  - HELLP Syndrome*
  - Fetal growth restriction
  - Oligohydramnios
  - Critically abnormal umbilical artery Doppler indices
  - New-onset renal dysfunction or deteriorating renal function
Management Recommendations

• Do not delay delivery x 48 hours:
  • Uncontrolled severe range BPs
  • Eclampsia
  • Pulmonary Edema

• No Sh*$ Indications
  • Abruptio placentae
  • DIC
  • Non-reassuring fetal status
  • Intrapartum Demise
Magnesium Sulfate to prevent Eclampsia

- Not UNIVERSALLY recommended:
  - SBPs <160 and/or DBPs <110
  - No maternal symptoms
Magnesium Sulfate to Prevent Eclampsia

- **Recommended:**
  - Preeclampsia with severe features
  - Eclampsia
- Intrapartum/Intraoperative/Postpartum
Postpartum Management

- Magnesium Sulfate x 24 hour postpartum (if initiated during the intrapartum/intraoperative period)
- Pain management
  - NSAIDs (Avoid if HTN persists >24 hours)
- Remain inpatient for BP monitoring x 72 (can arrange for outpatient BP monitoring)
- Follow up 7-10 days after delivery for BP assessment
Postpartum Management

- Strict preeclampsia precautions at discharge
- Postpartum findings of maternal neurologic symptoms with HTN and/or preeclampsia with severe HTN
  - Magnesium Sulfate x 24 hours
- Initiate anti-hypertensive medication
  - SBPs $\geq 150$ or DBPs $\geq 100$ (at least 2 occasions occurring 4-6 hours apart)
  - Immediate treatment if SBPs are $\geq 160$ or DBP $\geq 110$
Pre-conceptual Counseling

- Weight loss
- Increased physical activity
- Optimize medical management of pre-existing medical conditions
- USPTF
  - Aspirin (80mg)
    - Previous delivery <34 weeks due to preeclampsia
    - More than one previous pregnancy affected by preeclampsia
Pre-existing Hypertension

- CHTN and pregnancy with well controlled BPs
  - Moderate exercise can be continued
- SBPs <160mmHg and DBPs <105mmHg and no evidence of end organ damage:
  - No anti-hypertensive therapy
- Women taking anti-hypertensives
  - Maintain SBPs 120-160mmHg and DBPs 80-105mmHg
Control of Hypertension in Pregnancy (CHIPS) Study

- Randomized Controlled Trial
- Control based on DBP
  - Tight control = DBP $\leq$ 85 mmHg
  - Less tight control = $\leq$ 100 mmHg
- Primary outcome (composite neonatal outcome)
  - 31.4% (Tight Control) vs. 30.7% (Less Tight) with an aOR 1.02 (0.7-1.4)

Control of Hypertension in Pregnancy (CHIPS) Study

• Secondary Outcome (composite adverse maternal outcomes)
  • 3.7% (Less Tight Control) vs. 2.0% (Tight Control) with an aOR of 1.74 (0.8-3.8)

• Other secondary observations
  • Severe Maternal HTN (≥160 mmHg SBP and/or ≥110 mmHg DBP)
    • Less Tight Control (40.7%) vs. Tight Control (27.5%) [p<0.001]
  • Small-for-gestational-age newborns in less tight controlled
    • OR 0.66 (95% CI, 0.44 to 1.00)
Pre-existing HTN

• Delivery
  • Uncomplicated; even if taking anti-hypertensives
    • ≥39 weeks
  • Superimposed preeclampsia without severe features
    • 37 weeks
  • With severe features
    • Can expectantly manage if both maternal and fetal conditions are stable
    • No later than 34 weeks
Pre-existing HTN

- Antenatal surveillance
  - Anti-hypertensives
  - Fetal growth restriction
  - Other co-existing medical conditions (e.g. Diabetes)
Later-Life CV Disease
Unclear How to Use this Information

• Suggestion from the Task Force:
  • Women with a PMH of PreE and PTB <37W
  • Women with a history of recurrent PreE
    • Earlier Intervention?
    • Annual:
      • BP, Lipids, FBG and BMI
  • Use of clinical judgment advised
PGY 9

• 35 y/o G4P4004 s/p uncomplicated SVD
• Presented 6 days postpartum with severe HA and elevated BPs
• Started on magnesium at an outside facility
• Began to lose function on the left side of her body
• Stroke was the working diagnosis
• Transferred to my facility for Neurosurgical ICU care
Clinical Course

• Reversible cerebral vasoconstriction
  • Call-Fleming syndrome
  • Postpartum angiopathy
• Found to have hemorrhagic and ischemic strokes present
• Stabilized and began showing improvement
• Worsening symptoms
• Taken to CT→coded→Resuscitated→another stroke!
Outcome

• Eventually discharged to an inpatient physical rehabilitation unit and was expected to regain some function
Scenario #1

- G3P2 with new onset HTN at 33 weeks.
- 24 hour protein <300mg.
- All other labs are WNL.
- Asymptomatic
- Management?
- Delivery?
Scenario #2

- 23 y/o G1P1 delivered term infant 24 hours ago
- Complains of a severe HA and blurred vision
- SBPs >160
- Pain control?
- Management?
Scenario # 3

- 32 y/o G3P2 with IUP at 22W presents with complaints of “really bad heartburn”
- BPs 130s/90s
- Work Up?
- Management?
Scenario #4

- 39 y/o G1 with IUP at 31W
- New onset HTN within the last week
- BPs 150s/100s
- Asymptomatic with normal blood work
- 24 hour protein=10g
- Fetal growth restriction <10%-ile
- Diagnosis?
- Management
Scenario #5

- 18 y/o G2P0 at 29 weeks
- New onset HTN (BPs persistently 160s/110s) and proteinuria
- HA and blurred vision initially but has since subsided
- Diagnosis?
- Management?
- Postpartum considerations?
Multi-Systemic Disorder
Deliver Me From Evil!
Cytokines
TNF / IL-6

Autoantibodies

Oxidative Stress

sFLT1

Endothelial Dysfunction

Multisystemic Disease
Preeclampsia Awareness Saves Lives

- Rising High Blood Pressure Above Normal
- Sudden Weight Gain
- Protein In Urine
- Blurred Vision, Headache & Irritability
- Pitting Edema
- Swollen Face, Hands & Feet
- Abdominal Pain
- Muscle Twitching
- Seizures & Coma

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