Hypertensive Disorders in Pregnancy

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Objectives

• To differentiate various hypertensive disorders during pregnancy
• To familiarize with antenatal management of such disorders
• To review neonatal outcomes in pregnancies complicated with hypertensive disorders
Task Force on Hypertension in Pregnancy, 2013

• Pre-eclampsia–eclampsia
• Chronic hypertension (of any cause)
• Chronic hypertension with superimposed preeclampsia
• Gestational hypertension
Pre-eclampsia

• Hypertension after 20 weeks
  • a systolic BP $\geq 140$ mm Hg or a diastolic BP $\geq 90$ mm Hg, or both
  • at least two determinations, 4 hours apart
  • a shorter interval (even minutes) when faced with severe hypertension
Pre-eclampsia

• New-onset proteinuria
  • 24-hour excretion ≥300 mg in 24 hours
  • the ratio of measured protein to creatinine in a single voided urine ≥3.0 mg/dL
  • qualitative dipstick ≥1+ ; should be reserved for use when quantitative methods are not available or rapid decisions are required
Pre-eclampsia

- Pre-eclampsia-eclampsia
  - in the absence of proteinuria
    - thrombocytopenia (platelet count <100,000/μL)
    - transaminases to twice the normal concentration
    - renal insufficiency (elevated serum creatinine greater than 1.1 mg/dL or a doubling of serum creatinine in the absence of other renal disease)
    - pulmonary edema
    - new-onset cerebral or visual disturbances
Pre-eclampsia with severe features

- Systolic blood pressure $\geq 160$ mm Hg, or diastolic blood pressure $\geq 110$ mm Hg
- Thrombocytopenia
- Elevated transaminases, severe persistent right upper quadrant or epigastric pain unresponsive to medication
- Progressive renal insufficiency
- Pulmonary edema
- New-onset cerebral or visual disturbances
  - *Growth restriction or proteinuria* $>5g/24$ h excluded
HELLP

• H = hemolysis
• EL = elevated liver function tests
• LP = low platelets
Chronic hypertension with superimposed pre-eclampsia

- women with hypertension only in early gestation who
  - develop proteinuria after 20 weeks of gestation
- women with hypertension and proteinuria before 20 weeks of gestation who
  - experience a sudden exacerbation of hypertension, or a need to escalate the antihypertensive drug dose
  - suddenly manifest other signs and symptoms
  - sudden, substantial, and sustained increases in protein excretion
Definition: Gestational Hypertension

• Systolic >140mm Hg, diastolic >90 mm Hg
  and
• First detected >20 weeks
  and
• No proteinuria
Physiologic blood pressure change during pregnancy

Systolic BP, mm Hg

Gestational age, wks
Gestational hypertension includes the following mix of patients

- Women who go on to develop preeclampsia - 15 to 25%
- Women with 'transient hypertension of pregnancy'
- Women with previously unrecognized 'chronic hypertension'
Increased Trophoblastic Apoptosis

Trophoblastic invasion of a maternal vessel

Failed trophoblastic invasion
Altered Global Gene Expression in First Trimester Placentas of Women Destined to Develop Preeclampsia

Sandra A. Founds\textsuperscript{1}, Yvette P. Conley\textsuperscript{1,2}, James F. Lyons-Weiler\textsuperscript{3}, Arun Jeyabalan\textsuperscript{4}, W. Allen Hogge\textsuperscript{4}, and Kirk P. Conrad\textsuperscript{5}

What causes systemic endothelial damage?

Proangiogenic factors:
- Vascular endothelial growth factor (VEGF)
- Placental growth factor (PIGF)

Anti-angiogenic factors:
- Soluble fms-like tyrosine kinase-1 (sFlt-1)
- Endoglin

Levine, 2004
Impaired trophoblast invasion
Impaired trophoblast differentiation
Medical conditions that predispose to vascular insufficiency
Obstetrical conditions that increase placental mass with a relative decrease in placental blood flow

- Placental hypoperfusion/ischemia
  - Fetal growth restriction
  - Oligohydramnios

- Increased secretion of sFlt-1, decreased availability of VEGF, PI GF, and other mediators of endothelial function

- Systemic endothelial dysfunction
  - Platelet activation
  - Edema
  - Hemolysis

- Hypertension
- CNS changes leading to headache, seizures and visual disturbances
- Glomerular endotheliosis, proteinuria, and renal insufficiency
- Hepatic ischemia and necrosis
GOALS OF THE INITIAL EVALUATION

• Exclude other disorders characterized by hypertension and proteinuria

• Assess the severity of disease

• Assess fetal well-being
Fetal Assessment

- Fetal heart rate monitoring
- Fetal growth
- Amniotic fluid volume
- Umbilical artery Doppler studies

[Images showing different Doppler wave patterns: Diminished, Diminished, Absent, Reversed]
Key Points in Management

• Definitive treatment is delivery
• There is no advantage for the mother to remain pregnant after pre-eclampsia is diagnosed
• Expectant management is for the baby’s sake
Maternal Mortality and Morbidity due to Hypertension in Pregnancy

Causes of significant maternal mortality and morbidity

- Stroke
- Posterior reversible encephalopathy syndrome
- Placental abruption
- DIC
- Renal failure
- Hepatic rupture
- Pulmonary edema
Why do we need to control severe hypertension?

• 2/3 maternal deaths in the UK between 2003-2005 resulted from cerebral hemorrhage or infarction

• 27/28 who had severe preeclampsia and stroke had BP ≥ 160 mmHg just before a hemorrhagic stroke
- Observe in labor and delivery for first 24-48 hours
- Corticosteroids, magnesium sulfate prophylaxis, and antihypertensive medications
- Ultrasonography, monitoring of fetal heart rate, symptoms, and laboratory tests

**Contraindications to continued expectant management**
- Eclampsia
- Pulmonary edema
- Disseminated intravascular coagulation
- Uncontrollable severe hypertension
- Nonviable fetus
- Abnormal fetal test results
- Abruptio placentae
- Intrapartum fetal demise

**Are there additional expectant complications?**
- Greater than or equal to 33 5/7 weeks of gestation
- Persistent symptoms
- HELLP or partial HELLP syndrome
- Fetal growth restriction (less than fifth percentile)
- Severe oligohydramnios
- Reversed end-diastolic flow (umbilical artery Doppler studies)
- Labor or premature rupture of membranes
- Significant renal dysfunction

**Expectant management**
- Facilities with adequate maternal and neonatal intensive care resources
- Fetal viability—33 6/7 weeks of gestation
- Inpatient only and stop magnesium sulfate
- Daily maternal-fetal tests
- Vital signs, symptoms, and blood tests
- Oral antihypertensive drugs

**Delivery**
- Yes

- Achievement of 34 0/7 weeks of gestation
- New-onset contraindications to expectant management
- Abnormal maternal-fetal test results
- Labor or premature rupture of membranes
Expectant Management of Severe Preeclampsia at 27\%7 to 33\%7 Weeks’ Gestation: Maternal and Perinatal Outcomes According to Gestational Age by Weeks at Onset of Expectant Management

Annette E. Bombrys, D.O.,¹ John R. Barton, M.D.,² Mounira Habli, M.D.,¹ and Baha M. Sibai, M.D.¹

AMERICAN JOURNAL OF PERINATOLOGY/VOLUME 26, NUMBER 6 2009
### Table 1 Neonatal and Pregnancy Outcomes Stratified by Gestational Age at Onset of Expectant Management

<table>
<thead>
<tr>
<th>GA at Admission (wk)</th>
<th>Number of Fetuses</th>
<th>Median Days Gained (Range)</th>
<th>Median Delivery GA (wk)</th>
<th>Mild RDS, n (%)</th>
<th>BPD, n (%)</th>
<th>NEC, n (%)</th>
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<tbody>
<tr>
<td>28–28²/₇ₙ</td>
<td>8</td>
<td>9 (3–35)</td>
<td>31.1</td>
<td>6 (76)</td>
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<tr>
<td>29–29²/₇ₙ</td>
<td>14</td>
<td>6 (3–26)</td>
<td>30.4</td>
<td>8 (57)</td>
<td>0 (0)</td>
<td>1 (7)</td>
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<tr>
<td>30–30²/₇ₙ</td>
<td>13</td>
<td>4 (3–15)</td>
<td>30.9</td>
<td>6 (47)</td>
<td>0 (0)</td>
<td>1 (8)</td>
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<tr>
<td>31–31²/₇ₙ</td>
<td>16</td>
<td>5 (3–12)</td>
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<td>32–32²/₇ₙ</td>
<td>5</td>
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<tr>
<td>33–33²/₇ₙ</td>
<td>6</td>
<td>4 (3–10)</td>
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<tr>
<td>Total</td>
<td>71</td>
<td>5 (3–35)</td>
<td>31.4</td>
<td>31/70 (44)</td>
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<td>5 (7)</td>
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</table>

GA, gestational age; RDS, respiratory distress syndrome; BPD, bronchopulmonary dysplasia; NEC, necrotizing enterocolitis.

### Table 2 Maternal Outcome Stratified by Gestational Age at Onset of Expectant Management

<table>
<thead>
<tr>
<th>GA at Admission (wk)</th>
<th>Number of Patients</th>
<th>HELLP, n (%)</th>
<th>Abruptio Placentae, n (%)</th>
<th>Pulmonary Edema, n (%)</th>
<th>Renal Insufficiency, n (%)</th>
<th>Composite Outcome, n (%)</th>
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<tr>
<td>27–27²/₇ₙ</td>
<td>9</td>
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<td>0 (0)</td>
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<td>1 (8)</td>
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<td>1 (8)</td>
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<tr>
<td>30–30²/₇ₙ</td>
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<td>1 (8)</td>
<td>1 (8)</td>
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<tr>
<td>Total</td>
<td>66</td>
<td>5 (8)</td>
<td>7 (11)</td>
<td>6 (9)</td>
<td>2 (3)</td>
<td>18 (27)</td>
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</table>

These complications developed during expectant management and were the maternal indications for delivery. GA, Gestational age; HELLP, hemolytic anemia, elevated liver enzymes, and low platelet count.
Neonatal outcomes in severe preeclampsia between 24-36 weeks: does HELLP syndrome matter?

- HELLP syndrome, n=68
- Partial HELLP, n= 65
- Severe preeclampsia, n=139
- Comparisons stratified by gestational age: ≤28, 29-32, 33-36 weeks
- No difference
  - Neonatal death
  - RDS
  - IVH grade 3 and 4
  - NEC
  - BPD
  - Mechanical ventilation
  - Latency
  - Gestational age at delivery
  - Birth weight
  - IUGR rate

Abramovici et al, 1999
Neonatal outcomes following expectant management of severe pre-eclampsia presenting before 26 weeks

Paris, France, 2000-2008

<table>
<thead>
<tr>
<th>Admission GA, wks</th>
<th>n</th>
<th>Fetal death, n (%)</th>
<th>Neonatal death, n (%)</th>
<th>Discharged alive from ICU, n (%)</th>
<th>Severe IVH, n (%)</th>
<th>NEC, n (%)</th>
<th>CLD, n (%)</th>
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<td>1 (6)</td>
<td>9 (50)</td>
<td>1/10 (10)</td>
<td>3/10 (30)</td>
<td>4/9 (44)</td>
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<tr>
<td>25-25.6/7</td>
<td>23</td>
<td>8 (35)</td>
<td>2 (9)</td>
<td>13 (57)</td>
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<tr>
<td>Total</td>
<td>53</td>
<td>27 (51)</td>
<td>4 (7)</td>
<td>22 (42)</td>
<td>3/26 (12)</td>
<td>3/23 (13)</td>
<td>7/22 (32)</td>
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</table>

Belghiti et al, 2011
<table>
<thead>
<tr>
<th>Admission GA, wks</th>
<th>Authors</th>
<th>No. of fetuses</th>
<th>Perinatal mortality %</th>
<th>Severe FGR</th>
<th>Maternal morbidity %</th>
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<td>71</td>
<td>NR</td>
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<tr>
<td></td>
<td>Current study (2010)</td>
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<td>69&lt;sup&gt;a&lt;/sup&gt;</td>
<td>7</td>
<td>100</td>
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<td>23-23&lt;sup&gt;6/7&lt;/sup&gt;</td>
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<td>17&lt;sup&gt;a&lt;/sup&gt;</td>
<td>47&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3</td>
<td>100</td>
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</table>
Maternal outcomes stratified by gestational age at admission in patients managed expectantly for severe pre-eclampsia

<table>
<thead>
<tr>
<th>Admission GA, wks</th>
<th>n</th>
<th>Composite morbidity, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;23</td>
<td>4</td>
<td>1 (25)</td>
</tr>
<tr>
<td>23-23(^{6/7})</td>
<td>7</td>
<td>7 (71)</td>
</tr>
<tr>
<td>24-24(^{6/7})</td>
<td>18</td>
<td>6 (33)</td>
</tr>
<tr>
<td>25-25(^{6/7})</td>
<td>21</td>
<td>10 (46)</td>
</tr>
<tr>
<td>Total</td>
<td>51</td>
<td>22 (43)</td>
</tr>
</tbody>
</table>

Composite morbidity: death, HELLP syndrome, placental abruption, eclampsia, pulmonary, edema, renal insufficiency, isolated thrombocytopenia, or DIC.
Prediction and Prevention

• Early, severe pre-eclampsia: risk of recurrence, 25-65%
• Mild pre-eclampsia: risk of recurrence, 5-7%
• First pregnancy normal; risk of pre-eclampsia in subsequent pregnancy: 1%
• No reliable predictive tests
• No effective prophylaxis
Chronic hypertension

- Superimposed preeclampsia — 10 to 25 percent
- Abruptio placentae — 0.7 to 1.5 percent
- Preterm birth <37 weeks — 12 to 34 percent
- Fetal growth restriction — 8 to 16 percent
- These risks were even higher in women with severe chronic hypertension
Chronic hypertension

- Acceptable blood pressures: (systolic <160 /100 mmHg)
- Secondary or complicated hypertension: maintain BP within 120 to 140/80 to 90 mmHg
  - End-organ damage (e.g., ventricular dysfunction, retinopathy)
  - Dyslipidemia
  - Maternal age over 40 years old
  - Microvascular disease
  - History of stroke
  - Previous perinatal loss
  - Diabetes
  - Renal disease
Gestational hypertension

• Distinguish from preeclampsia
• Determine whether hypertension is mild or severe

• Mild
  • outcomes are generally favorable
  • frequent prenatal visits and fetal assessment and delivering at term

• Severe
  • Control blood pressure
  • severe gestational hypertension are at increased risk for maternal and perinatal morbidity, similar to the rates reported for women with severe preeclampsia
  • Consider treatment like severe pre-eclampsia