Hypertensive Disorders in Pregnancy
Which May Lead to Transfer of Care
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Overview:
- Normal changes in pregnancy
- Diagnosis and Epidemiology of underlying hypertension
- Work Up of Chronic Hypertension
- Gestational Hypertension
- Preeclampsia
- Superimposed Preeclampsia
- Treatment and Management Strategies
- Transfer?

Normal changes of BP and Pulse
- BP normally drops in the second trimester
  - Nadir at 16 to 18 weeks
  - DBP of 80 or higher in second trimester suggests underlying hypertension
- Booking BP (in first trimester) is a good screen for underlying hypertension.
- Labile BP (high when they first come in or when they are “excited”) is not really normal

Normal changes of BP and Pulse
- One should use an appropriate-sized cuff (length 1.5 times the upper arm circumference or a cuff with a bladder that encircles 80% or more of the arm) to ensure accurate readings.
- Blood pressure should be measured only after the patient has rested (preferably 10 minutes or more) and is seated with the cuff positioned at the level of her heart. Range...

Normal changes of BP and Pulse
- Pulse rises at rest about 10 – 15 bpm
- Why would pulse be higher than 100 bpm?
  - Anemia
  - Multiple Gestation
  - Hyperthyroidism
  - Exogenous (recreational) drugs
  - Fever

Disclosures
- I make my living as a consultant
- I am hoping to help you identify which patients can stay in your practice and stay out of mine
**Why do we worry about Hypertension? What is the big deal?**

Risks to the mother-
influenced by co-morbidities like high BMI, diabetes, thyroid disease, meds
Short term: Stroke, MI
Long term: Cardiovascular Disease
Abruption (1% of chronic HTN, 8% of severe)
Cesarean Section (OR, 2.7; 95% CI, 2.4–3.0)
Postpartum hemorrhage (OR, 2.2; 95% CI, 1.4–3.7)

**Risks to the baby and the placenta**
- Small for gestational age increased x2-5
- 16% of women with uncomplicated nonproteinuric hypertension
- Oligohydramnios
- Placental insufficiency
- Preterm Birth
- Increased perinatal morbidity and mortality (RR 2-2.5)

**Chronic Hypertension in Pregnancy about 5% of pregnant women**

**Diagnosis:**
- Use of antihypertensive medications before pregnancy
- Onset of hypertension before 20th week of gestation
- Persistence of hypertension for greater than 12 weeks postpartum

**Chronic Hypertension**

Compared to normotensive pregnant women:
- Maternal mortality was nearly fivefold higher (odds ratio [OR], 4.8; [CI], 3.1–7.6)
- Cerebrovascular accidents (OR, 5.3; 95% CI, 3.7–7.5)
- Pulmonary edema (OR, 5.2; 95% CI, 3.9–6.7)
- Renal failure (OR, 6.0; 95% CI, 4.4–8.1)

**Severity of HTN-highest risk group includes end-organ damage, or severely high BP**

- Higher rates of superimposed preeclampsia (50% in severe, 20% in mild)
- SGA infants (25–40%),
- Preterm delivery (up to 67%),
- Placental abruption (10–20%),
- Higher rate of perinatal death of 11.4%

Work up of hypertensive woman at initial presentation

- Assess Renal function:
  - serum creatinine, blood urea nitrogen, 24-hour urinary protein excretion or spot urine for protein/creatinine ratio and creatinine clearance
  - EKG, Echocardiography
  - Dilated Retinal Exam

Suggested Evaluation for Secondary Causes of Hypertension (up to 10% of young women)

- Pheochromocytoma
  - Plasma metanephrines
  - 24-hour urine assessment for metanephrines, unconjugated catecholamines
  - Magnetic resonance imaging or computed tomography of adrenal gland
- Primary aldosteronism
  - Serum potassium level assessment
  - Plasma renin activity, 24-hour urine aldosterone excretion assessment
- Cushing syndrome
- Sleep apnea
- Methamphetamine or cocaine use
- Renal artery stenosis
  - Renal ultrasonography
  - Doppler flow or magnetic resonance angiography

Late transfer of care with HTN

- Nulliparous - think preeclampsia
- Labs:
  - Uric acid (> 5.5 suspicious)
  - Urinary PR:Cr, 24h urine for protein, CrCL
  - LFTs
  - CBC - platelets for HELLP, hemoconcentration?
  - Serum creatinine
- Underlying renal disease or SLE?

Cestational Hypertension replaces the term “pregnancy-induced hypertension”

- Women with elevated BP without proteinuria after 20 weeks with return to normal BP postpartum
- SBP of ≥140 or DBP of ≥90 after 20 weeks in a woman with previously normal BP
- As many as one quarter of women will develop preeclampsia

When (and why) do we treat Hypertension?

- 50% decreased risk of developing severe hypertension (relative ratio [RR], 0.5%; 95% CI, 0.41–0.61) but no reduction in the risk of superimposed preeclampsia, perinatal mortality, preterm birth, or SGA infants
- BP > 160/110 have Incr. Risk STROKE, heart/renal
- All tend to agree that BP > 150 / 100 need Rx,
- Most locally would treat > 140/90
- Some treat 130-140/80-90 especially if fast PR

Drug  Dosage  Maternal Adverse Effects
A. Oral antihypertensives used commonly in pregnancy
- Labetalol  200-2,400 mg per day in 2-3 divided doses  Headache
- Nifedipine  30–120 mg per day of a slow-release preparation  Headache
- Methyldopa  0.5–3.0 g per day in 2–3 divided doses  Maternal sedation, elevated LFTs, depression
  Adjunctive agents
- Hydralazine  50–300 mg per day in 2–4 divided doses  Use with methyldopa or labetalol to prevent reflex tachycardia; risk of neonatal thrombocytopenia
- Hydrochlorothiazide  12.5-50 mg per day  Can
Atenolol, a pure beta antagonist, was shown to be associated with growth restriction in infants and is not currently recommended for the treatment of chronic hypertension in pregnancy. -- ACOG

UW data supports use of Atenolol if hyperdynamic heart with high Cardiac Output and rapid pulse – clearly controversial

B. Drugs for urgent control of severe acute hypertension in pregnancy

Hydralazine 5 mg IV or IM, then 5–10 mg every 20–40 minutes; or constant infusion of 0.5–10 mg per hour

- Long experience of safety and efficacy — Risk of delayed maternal hypotension, fetal bradycardia

Labetalol 20 mg IV, then 20–80 mg every 5–15 minutes, up to a maximum of 300 mg; or constant infusion of 1–2 mg per minute — Probably less risk of tachycardia and arrhythmia than with other vasodilators; increasingly preferred as first-line agent

Nifedipine 10–30 mg PO, repeat in 45 minutes if needed — Possible interference with labor

Bed rest is not beneficial but, no large randomized trials

- Cochrane review analyzed four small trials
  - Two trials (145 women) strict bed rest vs some rest in hospital (Proteinuric HTN) NS in outcomes
  - Two trials (304 women) bed rest in hospital vs routine activity at home (nonproteinuric HTN)

- Rest group had reduced risk of severe HTN (218 women; RR 0.58; CI 0.38–0.89)
- Rest group borderline reduction in risk of PTB (RR 0.53 CI 0.29–0.99)

BP treatment is to prevent stroke

- Lowering blood pressure does not affect the course of preeclampsia because the primary pathogenetic process is an abnormality of the placental vasculature that results in placental under perfusion, which, in turn, leads to release of factors that cause widespread maternal endothelial dysfunction with multi organ dysfunction.

Factors increasing risk for preeclampsia

- Nulliparity
- Preeclampsia in a previous pregnancy
- Age >40 years or <18 years
- Family history of preeclampsia
- Chronic hypertension
- Chronic renal disease
- Antiphospholipid antibody syndrome or inherited thrombophilia
- Vascular or connective tissue disease
- Diabetes mellitus (gestational and gestational)
- Multifetal gestation
- High body mass index
- Black race

Diagnosis of Preeclampsia

- SBP of 140 or greater OR
- DBP of 90 or greater AND
- 24h urine protein 0.3gm or greater

- 30-15 rule abandoned, but pay attention
Factors increasing risk for preeclampsia:
- Male partner whose mother or previous partner had preeclampsia
- Hydrops fetalis
- Unexplained fetal growth restriction
- Woman herself was small for gestational age
- Fetal growth restriction, abruptio placentae, or fetal demise in a previous pregnancy
- Prolonged interpregnancy interval
- Partner related factors (new partner, limited sperm exposure [e.g., previous use of barrier contraception])
- Hydatidiform mole
- Susceptibility genes

Hypothesis for the role of sFlt1 in preeclampsia:
- Remodeling of maternal spiral arteries does not occur
- (1) Macrophage hypofunction
- (2) Placental ischemia
- sFlt1 increases
- Free VEGF and PlGF decrease
- Systemic maternal endothelial dysfunction
- Thrombosis of arteries
- Hypertension
- Dysfunction of multiple organs, especially kidney, liver, and brain

Preeclampsia in 5 to 8% risk factors:
- Multiple gestation
- Preeclampsia in prior pregnancy
- Chronic HTN
- Pregestational diabetes
- Vascular/Connective tissue disease (SLE)
- Obesity
- APAS
- African-American Race
- Age 35 or older
- Nephropathy
- Preeclampsia in prior pregnancy
- Hypertension
- Diabetes
- Obesity
- SLE
- APS
- African-American Race
- Vascular/Connective tissue disease

Frequency and severity of laboratory findings among indicators of preeclampsia:

<table>
<thead>
<tr>
<th>Laboratory finding</th>
<th>HELLP syndrome</th>
<th>p-value</th>
<th>TIP</th>
<th>IUGR percent</th>
<th>Extent of SLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>SALT</td>
<td>56%</td>
<td>0.001</td>
<td>Yes</td>
<td>53%</td>
<td>56%</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>50%</td>
<td>0.25</td>
<td>No</td>
<td>50%</td>
<td>49%</td>
</tr>
<tr>
<td>Hemolytic anemia</td>
<td>55%</td>
<td>0.02</td>
<td>Yes</td>
<td>50%</td>
<td>54%</td>
</tr>
<tr>
<td>Elevation of liver enzymes</td>
<td>54%</td>
<td>0.03</td>
<td>Yes</td>
<td>52%</td>
<td>59%</td>
</tr>
<tr>
<td>Elevation of creatinine</td>
<td>53%</td>
<td>0.04</td>
<td>Yes</td>
<td>51%</td>
<td>59%</td>
</tr>
</tbody>
</table>

Frequency of various signs and symptoms among indicators of preeclampsia:

<table>
<thead>
<tr>
<th>Signs and symptoms</th>
<th>HELLP syndrome, percent</th>
<th>TIP, percent</th>
<th>IUGR, percent</th>
<th>Extent of SLE, percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>65%</td>
<td>00%</td>
<td>00%</td>
<td>00%</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>65%</td>
<td>00%</td>
<td>00%</td>
<td>00%</td>
</tr>
<tr>
<td>Anemia</td>
<td>65%</td>
<td>00%</td>
<td>00%</td>
<td>00%</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>65%</td>
<td>00%</td>
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<td>Hypertensive</td>
<td>65%</td>
<td>00%</td>
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<tr>
<td>Proteinuria</td>
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11/18/12
She presents to office complaining of a headache and “I just don’t feel well.”

She has gained 3 pounds in a week.
BP is 130/80. (All prior BPs were 120/70 or lower)
U/A is negative for protein

Persistent and/or severe headache
Visual abnormalities (scotomata, photophobia, blurred vision, or temporary blindness)
Upper abdominal or epigastric pain
Nausea, vomiting
Oliguria
Dyspnea
Altered mental status

ALL NEGATIVE IN THIS PATIENT

What is your differential diagnosis?
GESTATIONAL HYPERTENSION VS MILD PREECLAMPSIA

What difference does it make?

What labs should be done?
What is your differential diagnosis?
- Gestational hypertension vs Mild Preeclampsia

What difference does it make?

What labs should be done?
- CBC, BUN, Creatinine, Uric Acid, AST/ALT
- Coagulation studies do not need to be done unless suspicious for severe preeclampsia

Her labs are NORMAL.

What are likely / possible scenarios?
- Await spontaneous labor and delivery
- Promote induction at 39 weeks, not before
#1 continued
- What are likely / possible scenarios?
- Await spontaneous labor and delivery
- Promote induction at 39 weeks, not before
- She comes in at 40 weeks with 2+ proteinuria, epigastric pain, and decreased fetal movement
  - She needs to be admitted for magnesium sulfate, fetal evaluation, and delivery

Indications for delivery in preeclampsia

<table>
<thead>
<tr>
<th>Maternal indications</th>
<th>Fetal indications</th>
</tr>
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<tbody>
<tr>
<td>Gestational age greater than or equal to 37 weeks of gestation</td>
<td>Severe fetal growth restriction</td>
</tr>
<tr>
<td>Platelet count less than 100,000 cells per cubic millimeter</td>
<td>Nonmeasuring results from fetal testing</td>
</tr>
<tr>
<td>Deteriorating liver function</td>
<td>Oligohydramnios</td>
</tr>
<tr>
<td>Progressive deterioration in renal function (e.g., creatinine &gt;2 mg/dL, oliguria)</td>
<td>Persistent severe headache or visual changes</td>
</tr>
<tr>
<td>Abruptio placentae</td>
<td>Persistent severe epigastric pain, nausea, or vomiting</td>
</tr>
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756 patients were allocated to receive induction of labour (n=377 patients) or expectant monitoring (n=379). 397 patients refused randomisation.

Of randomised:
- 117 (31%) allocated to induction of labour developed poor maternal outcome vs
- 166 (44%) allocated to expectant monitoring had poor maternal outcome (relative risk of IOL: 0.71, 95% CI 0.59-0.86, p<0.0001).

No maternal or neonatal death or eclampsia.

Induction of labor at 37 weeks is recommended rather than expectant management.

##2 33 yo G2P1 presents at 14 weeks
- History includes preeclampsia with her first pregnancy but she says that her BP is normal between pregnancies
- Should she be on preventive medicine?
  - Low dose aspirin 81mg optional
  - Calcium if calcium insufficient diet
  - Fish oil, Vitamin D not beneficial


#2 33 yo G2P1 presents at 14 weeks
- History includes preeclampsia with her first pregnancy but she says that her BP is normal between pregnancies
- Should she be on preventive medicine?
  - Low dose aspirin 81mg optional
  - Calcium if calcium insufficient diet
  - Fish oil, Vitamin D not beneficial
- BP is 134/80. Is this normal?

#2 continued
- You offer her LDA. U/S at 20 weeks reveals bilateral uterine artery notching which gives her a 50% chance of 3rd trim. BP/growth issue
- At 28 weeks, her BP is 144/90. Next steps?
  - Home BP cuff, baseline 24h urine protein, labs
  - Consultation with Ob/MFM
  - Consideration to medication
- Her risk of superimposed preeclampsia is at least 30%.

#3 28 yo G1 now P1 calls you 2 days postpartum
- c/o headache and edema
- She hasn’t slept for past 2 nights since BF is challenging
- BP is 140/90. 1+ proteinuria.

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#3 28 yo G1 now P1 calls you 2 days postpartum
- c/o headache and edema
- She hasn’t slept for past 2 nights since BF is challenging
- BP is 140/90. 1+ proteinuria.
- MUST obtain labs. If abnormal: needs admission and magnesium sulfate

Atypical preeclampsia
- Occurs prior to 20 weeks – think H. mole
- Occurs with either HTN or proteinuria but not both (about 15% of severe/HELLP)
- Delayed Postpartum Preeclampsia

Delayed Postpartum Preeclampsia
- In a retrospective cohort study including 152 patient:
  - 63.2 percent had no antecedent diagnosis of hypertensive disease in the current pregnancy,
  - 18.4 percent had preeclampsia,
  - 9.2 percent had chronic hypertension,
  - 4.6 percent had gestational hypertension, and
  - 4.6 percent had preeclampsia superimposed on chronic hypertension during the peripartum period
- Of these patients, 1.5% developed postpartum eclampsia.

#4 18 yo G1P0 presents at 33 weeks after calling that she had some bleeding
- She also has a headache that didn’t respond to tylenol and she has had some nausea and vomiting. She hasn’t been urinating very much. Her mother thinks she has the flu.
- The baby hasn’t been moving well all day

#4 18 yo G1P0 presents at 33 weeks after calling that she had some bleeding
- She also has a headache that didn’t respond to tylenol and she has had some nausea and vomiting. She hasn’t been urinating very much. Her mother thinks she has the flu.
- The baby hasn’t been moving well all day
- Her uterus is mildly tender and she says it keeps “balling up”
Does she have the flu?
BP is 160/110
She has gained 5 pounds in two weeks
U/A reveals 4+ proteinuria
She has severe preeclampsia and needs STAT admission for labs, fetal assessment, magnesium sulfate for eclampsia prophylaxis as well as neuroprophylaxis, and BMZ

Blood pressure $\geq 160$ mm Hg systolic or $\geq 110$ mm Hg diastolic on 2 occasions at least 6 h apart while patient is on bed rest
Proteinuria 5 g in 24-h urine specimen on 2 random urine samples collected at least 4 h apart
Oliguria < 500 mL in 24 h

Severe preeclampsia

- Cerebral or visual symptoms
- Pulmonary edema or cyanosis
- Epigastric or RUQ pain
- Impaired liver function
- Thrombocytopenia
- Fetal growth restriction

The presence of one or more of the following criteria upstages preeclampsia from mild to severe

- Visual disturbances (proptosis, edema, central blindness, retinal vasospasm)
- Severe headache (i.e., incapacitating; the worst headache "I've ever had")
- Nausea, vomiting
- Heparin-induced thrombocytopenia
- Severe proteinuria: concentration $3$ times normal
- Severe blood pressure elevation:
  - Systolic blood pressure $\geq 160$ mm Hg
  - Diastolic blood pressure $\geq 110$ mm Hg
- Thrombocytopenia:
  - $< 100,000$ platelets/mm$^3$
- Proteinuria:
  - $\geq 5$ g in 24 h
- Oliguria < 500 mL in 24 h
- Fetal growth restriction
- Pulmonary edema or cyanosis

SEVERE PREECLAMPSIA
other considerations leading to delivery
- Noncompliance with medical treatment
- Persistent epigastric or RUQ pain
- Nausea or Vomiting
- PTL and/or PROM
- Note: labor induction more commonly fails at earlier gestational ages:
  - C/S rates 93-97% at < 28 weeks, 53-65% at 28-32 wks, and 31-38% at 32-34 weeks

SEVERE PREECLAMPSIA
- Degree of proteinuria (< 5gm, > 5gm, > 10gm/24h) is not predictive of pregnancy prolongation or perinatal complications
- Or rapidity of progression of preeclampsia
- Don’t use severity or degree of change to avoid or terminate expectant management

Evaluation and management of severe preeclampsia before 34 weeks’ gestation. SMFM Clinical Opinion. In Hospital assessment:
- R/O HELLP, nonreassuring fetal status
- Ultrasound for BPP and to r/o IUGR.
- Betamethasone Course
- Daily Assessment of:
  - fetal + maternal well-being, daily labs,
  - frequent Vital Signs, close urine output
- Respect the Contra-indications to Expectant Management
- Watch for recurrent severe HTN despite Rx

Contra-indications to Expectant Management of Severe Preeclampsia
- Persistent symptoms of severe preeclampsia
- Eclampsia
- Pulmonary Edema
- Persistent severe HTN despite initial Rx
- HELLP syndrome
- Significant renal dysfunction
- Abruptio
- DIC
- Non Reassuring Fetal Testing
- Preivable Gestation
- ONCE 34 WEEKS IS ACHIEVED - DELIVERY !!!!

HELLP
Sibai et al (each of following required)
- (1) Hemolysis on peripheral smear, lactate dehydrogenase ≥600 U/L, or total bilirubin ≥1.2 mg/dL
- (2) Aspartate aminotransferase > 70 IU/L
- (3) Platelet count <100,000 cells/mm3

HELLP - other definition by Martin, each of the following:
- (1) Lactate dehydrogenase >600 U/L
- (2) Aspartate aminotransferase or alanine aminotransferase >40 IU/L
- (3) Platelet count <150,000 cells/mm3
Superimposed preeclampsia
(> 1 of following criteria is required)

- New-onset proteinuria >0.3 g protein in woman with hypertension ≤ 20 wks gestation
- If both hypertension and proteinuria are present @ 20 wks gestation or sudden increase in proteinuria in woman whose HTN has previously been well controlled
- Sudden increase in HTN in woman whose HTN has previously been well controlled
- Thrombocytopenia (platelet count <100,000 cells/mm³)
- Increase in alanine aminotransferase or aspartate aminotransferase to abnormal levels
- Women with chronic HTN who develop persistent headache, scotoma, or epigastric pain also may have superimposed preeclampsia

Indications for Timed Delivery

- Chronic hypertension - no medications
  - 38-39 wk (grade B)
- Chronic hypertension - controlled on medication
  - 37-39 wk (grade B)
- Chronic hypertension - difficult to control (requiring frequent medication adjustments)
  - 36-37 wk (grade B)

Consultation

- Use your collegial relationships
- Consultation is education for the family and an opinion with recommendation by the physician
- Transfer of care involves an assumption of care by a provider
- SMOOTH TRANSITIONS

REFERENCES

   ACCOG Committee Opinion. 314B: Revised Therapy for Acute, Chronic, Severe Hypertension with Preeclampsia, Eclampsia, December 2011.
   Hypertension in preg
II. Meher S. Bed rest with or without hospitalisation for hypertension during pregnancy. Cochrane Database Syst Rev. 2005