Hypertensive Disorders in Pregnancy

Treatment of Severe Persistent Hypertension in Pregnancy

**Hydralazine Hydrochloride:**
A direct arterial smooth muscle relaxant
- Indicated for severe (systolic \( \geq 160 \text{ mmHg} \) or diastolic \( \geq 110 \text{ mmHg} \)), persistent (lasting 15 minutes or more) blood pressure
- Side effects include maternal hypotension, tachycardia, flushing, and headache
- Contraindicated in patients with coronary artery disease, mitral valvular rheumatic heart disease and known hypersensitivity
- Dosage with initial first-line management with hydralazine:
  1. Administer hydralazine 5 or 10 mg IV over 2 minutes
  2. Repeat BP in 20 minutes
  3. If BP is above either threshold, administer hydralazine 10 mg IV over 2 minutes
  4. Repeat BP in 20 minutes
  5. If BP is above either threshold, administer labetalol 20 mg IV over 2 minutes
  6. Repeat BP in 10 minutes
  7. If BP is above either threshold, administer labetalol 40 mg IV over 2 minutes and obtain MFM consult.
  8. Repeat BP in 10 minutes

**References:**
1. ACOG Committee Opinion 692, April 2017.

**Labetalol:**
A combined alpha- and beta-adrenoreceptor antagonist decreases systemic vascular resistance.
- Indicated for severe (systolic \( \geq 160 \text{ mmHg} \) or diastolic \( \geq 110 \text{ mmHg} \)), persistent (lasting 15 minutes or more) blood pressure
- Side effects include posture-related dizziness, scalp tingling, tiredness, headache, skin rash, fever and upper GI disturbances
- Contraindicated in patients with bronchial asthma, overt cardiac failure, greater than first degree heart block, cardiogenic shock, severe bradycardia and known hypersensitivity.
- May cause neonatal bradycardia.
- Dosage with initial first-line management with labetalol:
  1. Administer labetalol 20 mg IV over 2 minutes
2. Repeat BP in 10 minutes
3. If BP is above either threshold, administer labetalol 40 mg IV over 2 minutes
4. Repeat BP in 10 minutes
5. If BP is above either threshold, administer labetalol 80 mg IV over 2 minutes
6. Repeat BP in 10 minutes
7. If BP is above either threshold, administer hydralazine 10 mg IV over 2 minutes and obtain MFM consult.
8. Repeat BP in 20 minutes

References:
2. ACOG Committee Opinion 692, April 2017.

Nifedipine:
A calcium channel blocker that relaxes arterial smooth muscle
- Indicated for severe (systolic ≥ 160 mmHg or diastolic ≥ 110 mmHg), persistent (lasting 15 minutes or more) blood pressure
- Side effects include headache, flushing, tachycardia, and overshoot hypotension.
- Contraindicated in patients with known hypersensitivity
- Caution should be used in patients being treated concomitantly with MgSO4. An exaggerated hypotensive response, smooth muscle blockage and respiratory depression have been reported.
- Oral nifedipine may be given with special attention to heart rate and BP in normal range. Only PO (not IV or SL)
- Dosages
  1. Administer nifedipine 10 mg PO
  2. Repeat BP in 20 minutes
  3. If BP is above either threshold, administer nifedipine 20 mg PO
  4. Repeat BP in 20 minutes
  5. If BP is above either threshold, administer nifedipine 20 mg PO
  6. Repeat BP in 20 minutes
  7. If BP is above either threshold, administer labetalol 40 mg IV over 2 minutes and obtain MFM consult.
  8. Repeat BP in 10 minutes

References:
Hypertension in Pregnancy

Definition (from Executive Summary)

Hypertension in pregnancy can be classified into four categories:

1. **Preeclampsia/eclampsia:** Hypertension in association with thrombocytopenia, elevated liver function, new development of renal insufficiency, pulmonary edema or new-onset cerebral or visual disturbances. This may be further classified as preeclampsia with severe features or preeclampsia without severe features. Eclampsia refers to the occurrence of one or more generalized convulsions in the setting of preeclampsia and in the absence of other neurologic conditions. HELLP syndrome is a subset of preeclampsia.

2. **Chronic hypertension:** Hypertension that predates pregnancy.

3. **Chronic hypertension with superimposed preeclampsia:** Chronic hypertension in association with preeclampsia or eclampsia. This may be further classified as chronic hypertension with superimposed preeclampsia with severe features or chronic hypertension with superimposed preeclampsia without severe features.

4. **Gestational hypertension:** Blood pressure elevation after 20 weeks in the absence of proteinuria or the aforementioned systemic findings.

Hypertension in pregnancy is a multisystemic, dynamic process that requires timely recognition, accurate diagnosis and close surveillance.

Preeclampsia

Definition

Blood pressure:

- Greater than or equal to 140 mmHg systolic or greater than or equal to 90 mmHg diastolic on 2 occasions at least 4 hours apart after 20 weeks’ gestation in a woman with a previously normal blood pressure,

- Greater than or equal to 160 mmHg systolic or greater than or equal to 110 mmHg diastolic, hypertension can be confirmed within a short interval (minutes) to facilitate timely antihypertensive therapy.

AND

Proteinuria:

- Greater than or equal to 300 mg per 24 hour urine collection (or this amount extrapolated from a time collection),

- Or protein/creatinine ratio greater than or equal to 0.3 (each measured mg/dL),

- Or dipstick reading of 1+ (used only if other quantitative methods are not available).

OR IN THE ABSENCE OF PROTEINURIA, NEW ONSET HYPERTENSION WITH THE NEW-ONSET OF ANY OF THE FOLLOWING:

- Thrombocytopenia (platelet count less than 100,000/microliter)
• Renal insufficiency (serum creatinine concentration greater than 1.1 mg/dL or a doubling of the serum creatinine concentration in the absence of other renal disease)
• Impaired liver function (elevated blood concentrations of liver transaminases to twice normal concentration)
• Pulmonary edema
• Cerebral or visual disturbances

Preeclampsia with severe features

Definition
Any single finding below is diagnostic of preeclampsia with severe features.
• Systolic blood pressure 160 mmHg or higher, or diastolic blood pressure of 110 mmHg or higher on two occasions at least 4 hours apart while the patient is on bed rest (unless antihypertensive therapy is initiated before this time)
• Thrombocytopenia (platelet count less than 100,000/microliter)
• Impaired liver function as indicated by abnormally elevated blood concentrations of liver enzyme (to twice laboratory normal concentration), severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by alternative diagnosis
• Progressive renal insufficiency (serum creatinine greater than 1.1 mg/dL or doubling of serum creatinine concentration in the absence of other renal disease)
• Pulmonary edema
• New-onset cerebral or visual disturbances

Preeclampsia without severe features

Definition
Blood pressure:
• Greater than or equal to 140 mmHg systolic or greater than or equal to 90 mmHg diastolic on 2 occasions at least 4 hours apart after 20 weeks’ gestation in a woman with a previously normal blood pressure

AND

Proteinuria:
• Greater than or equal to 300 mg per 24 hour urine collection (or this amount extrapolated from a time collection)
• Or protein/creatinine ratio greater than or equal to 0.3 (each measured mg/dL)
• Or dipstick reading of 1+ (used only if other quantitative methods are not available)

AND WITHOUT AFOREMENTIONED SYSTEMIC FINDINGS
HELLP Syndrome

**Definition:**
A subset of preeclampsia that includes hemolysis, elevated liver enzymes and low platelets.

The clinical course of with HELLP syndrome is typically characterized by progressive and often sudden deterioration in the maternal and fetal status.

Chronic Hypertension

**Definition:**
Hypertension is defined as elevated blood pressure that is present prior to pregnancy or before 20 weeks of gestation. Hypertension is defined as a systolic blood pressure of 140 mmHg or greater or a diastolic blood pressure of 90 mmHg or greater, or both.

SMFM supports guidance from the Task Force on Hypertension in Pregnancy that states:

- Mild-moderate chronic hypertension: systolic 140-159 mmHg and diastolic 90-105 mmHg.
- Pregnant women with mild-moderate chronic hypertension should not be treated with pharmacologic antihypertensive therapy.
- For women with chronic hypertension already on medication to control BP in mild-moderate range, the decision must be individualized. It is reasonable practice to discontinue medications during the first trimester and restart them if blood pressure approaches the severe range ≥ 160/110.

Chronic Hypertension with Superimposed Preeclampsia

**Definition:**
Superimposed preeclampsia refers to patients with chronic hypertension who developed preeclampsia. Distinguishing superimposed preeclampsia from benign gestational increases in blood pressure and proteinuria to be quite challenging.

Given the higher risk of adverse pregnancy outcome in patients with superimposed preeclampsia, vigilance in diagnosis is recommended to avoid catastrophic maternal and fetal outcomes.

Clinicians should be aware that there is considerable ambiguity in the diagnosis of superimposed preeclampsia.

For the purposes of classification there are two subsets of superimposed preeclampsia. These include a superimposed preeclampsia with severe features and superimposed preeclampsia without severe features. This is similar to the classification system for preeclampsia (i.e., preeclampsia with severe features or preeclampsia without severe features).
**Chronic Hypertension with Superimposed Preeclampsia with Severe Features**

**Definition:**
Superimposed preeclampsia with severe features is a subset of superimposed preeclampsia.

Superimposed preeclampsia with severe features is likely when any of the following exist:
- Severe range blood pressure despite escalation of antihypertensive medication
- Thrombocytopenia (platelet count less than 100,000/ microliter)
- Elevated liver transaminases (greater than or equal to 2 times the upper normal limits for the reference laboratory)
- New onset or worsening renal insufficiency
- Pulmonary edema
- Persistent cerebral or visual disturbances

**Chronic Hypertension with Superimposed Preeclampsia without Severe Features**

**Definition:**
Superimposed preeclampsia without severe features is a subset of superimposed preeclampsia.

Chronic hypertension with superimposed preeclampsia is likely when any of the following exist:
- A sudden increase in blood pressure that was previously well controlled or escalation of antihypertensive medication to control blood pressure
- New-onset proteinuria or sudden increase in proteinuria in a woman with known proteinuria before or early in pregnancy

**AND WITHOUT AFOREMENTIONED SYSTEMIC FINDINGS**

**Gestational hypertension**

**Definition:**
Gestational hypertension is defined as new onset of blood pressure elevation after 20 weeks’ gestation in the absence of accompanying proteinuria or aforementioned systemic findings.

An important distinction exists for patients with severe range elevations in blood pressures (≥ 160 mmHg systolic or ≥ 110 mmHg diastolic) with absent proteinuria. Patients with severe range elevated blood pressures with absent proteinuria carry the diagnosis of preeclampsia with severe features and not gestational hypertension.
Management of preeclampsia/gestational hypertension/chronic hypertension with superimposed preeclampsia

Delivery is the only cure for the disease. The decision for immediate delivery versus expectant management is dependent upon:

1. Rate and severity of disease progression
2. Gestational age
3. Maternal and fetal condition

**Maternal assessment:**
Frequent ongoing maternal assessments are required to assess for severity and progression of disease.

1. Laboratory assessment:
   - CBC
   - Creatinine
   - AST, ALT
   - 24-hour urine protein and creatinine clearance
   - Consider protein/creatinine ratio, urinalysis, uric acid, lactate dehydrogenase, total bilirubin, peripheral blood smear and coagulation profile to clarify diagnosis

2. Symptom assessment:
   - New-onset cerebral or visual disturbances
   - Shortness of breath
   - Right upper quadrant pain

3. Physical exam assessment:
   - Right upper quadrant tenderness
   - Pulmonary exam
   - Edema

4. Maternal assessments should be repeated as clinically indicated.

5. Outpatient expectant management should include twice-weekly maternal assessments.

6. Close maternal-fetal monitoring by a physician/nurse are advised during treatment of acute-onset severe hypertension.

7. No cardiac monitoring required.

Accurate blood pressure to optimally manage hypertension or pregnancy is necessary.

- Standardized BP monitoring should be in place regardless arm size/shape
  - Gold standard: manual sphygmomanometer, however, validated calibrated equivalent automated equipment may be used.
  - Correct cuff size with directions to determine correct cuff size.
  - Sitting upright/semireclined with back support.
  - Do not put patient on side or in reclined supine position for lower readings.

**Fetal assessment:**
Frequent ongoing fetal assessments are required to assess for severity and progression of disease.

- Inpatient expectant management based upon gestational age diagnosis can be considered for patients with preeclampsia with severe features, proteinuria ≥ 1 gram over 24 hours, chronic hypertension with superimposed preeclampsia with
severe features. This should be accomplished at a tertiary care facility. Testing determined by severity 1-2x daily.

- **Outpatient expectant management** based upon gestational age at diagnosis can be considered for patients with preeclampsia without severe features, chronic hypertension with superimposed preeclampsia without severe features and gestational hypertension. At least 2x/week or as clinically indicated
- Assessment of fetal growth at the time of diagnosis and repeated as clinically indicated. Testing every 2 weeks.
- Fetal assessments should be repeated as clinically indicated.

**Magnesium Sulfate**

Intravenous magnesium sulfate to prevent eclampsia is recommended for all women with preeclampsia with severe features, HELLP syndrome and chronic hypertension with superimposed preeclampsia with severe features.

Intravenous magnesium sulfate to prevent eclampsia may be considered for women with preeclampsia without severe features, chronic hypertension with superimposed preeclampsia without severe features and gestational hypertension.

A loading dose of 4-6 over 20 minutes followed by maintenance therapy of 2 grams/hour is recommended.

Treatment is suggested for 24 hours post-delivery.

Frequent monitoring of respiratory rate, deep tendon reflexes, and state of consciousness must be carried out.

Intake and output should be strictly monitored. A Foley catheter with urometer may be required.

An ampule of calcium gluconate should be readily available.

**Labetalol**

Should there be no IV access and no nifedipine, may give labetalol 200 mg PO with repeat in 30 minutes, same 200 mg PO dose.

**Aspirin**

Consider aspirin if one or more criteria present:
- History of preeclampsia, especially if accompanied by an adverse outcome
- Multifetal gestation
- Chronic hypertension
- Type I or Type II diabetes mellitus
- Renal disease
- Rheumatologic disease (SLE, APA)
Goal for Timing of Delivery

Preeclampsia without severe features:
- At diagnosis goal of 37 0/7 weeks

Preeclampsia with severe features:
- At diagnosis goal of 34 0/7 weeks

HELLP syndrome
- At diagnosis goal of 34 0/7 weeks
- At diagnosis prior to gestational age of fetal viability
- At diagnosis in the presence of disseminated intravascular coagulation, liver infarction or hemorrhage, renal failure, placental abruption or nonreassuring fetal status.
- Consider delay of delivery for 24-48 hours if maternal and fetal conditions remain stable to complete a course of corticosteroids for fetal benefits from the gestational age of fetal viability to 33 6/7 weeks. Delivery after completion of corticosteroids

Chronic hypertension on no medication
- 38 0/7-39 6/7 weeks of gestation

Chronic hypertension on medication
- 37 0/7-39 and 6/7 weeks of gestation

Chronic hypertension with superimposed preeclampsia with severe features
- At diagnosis after 34 0/7 weeks

Chronic hypertension with superimposed preeclampsia without severe features
- At diagnosis after 37 0/7 weeks

Gestational hypertension:
- 37 0/7-38 6/7 weeks of gestation
- Strongly consider delivery after 37 0/7 weeks

References:
1. ACOG Committee Opinion 560 April 2013
Systolic BP ≥ 160 mmHg and/or
Diastolic BP ≥ 110 mmHg
2 times 15 minutes apart (notify provider after 1st)

- Inform OB Team
- IV Access
- Monitor FHR
- Send Labs

Hypertensive Medication

PO NIFEDIPINE
10 mg PO

Repeat BP in 20 min
if severe administer
Nifedipine 20 mg PO

Repeat BP in 20 min
if severe administer
Nifedipine 20 mg PO

Repeat BP in 20 min
if remains severe
obtain MFM consult
and repeat BP in 20
min

Hold IV Labetalol for maternal
pulse under 60

IV LABETALOL
20 mg over 2 min

Repeat BP in 10 min
if severe administer
Labetalol 40 mg

Repeat BP in 10 min
if severe administer
Labetalol 80 mg

Repeat BP in 10 min
if severe administer
Labetalol 20 mg

Seizure Prophylaxis

Mag Sulfate bolus
dose 4-6 g over 15
min, remain with pt

Mag Sulfate
maintenance dose
1-2 g/hr

Complete mag
assessment per
protocol and check
serum mag levels if
indicated

IV HYDRAZINE
5-10 mg over 2
minutes

Repeat BP in 20 min
if severe administer
Hydralazine 10 mg

Repeat BP in 20 min
if severe administer
Labetalol 10 mg

Repeat BP in 10 min
if severe administer
Labetalol 40mg AND
obtain MFM consult

Once BP thresholds are achieved, repeat BP:
- Every 10 min x 1 hour
- Then q15 min x 1 hour
- Then q30 min x 1 hour
- Then q1 hr for 4 hours