Approximately 7 to 10% of all pregnancies are complicated by hypertensive disease, 70% of which are gestational hypertension-preeclampsia related and 30% are due to chronic hypertension. (Sibai, 2010b) In the past, elevated blood pressure of more than 30 mm Hg systolic or more than 15 mm Hg diastolic above the patient's baseline was used to diagnose preeclampsia , however, this definition has not been shown to be a good prognostic indicator and is no longer recommended. ("Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy," 2000). Although no longer considered diagnostic of preeclampsia, women demonstrating elevations of this magnitude should be carefully monitored for worsening. In addition, in recognition of the syndromic nature of preeclampsia, the ACOG Task Force on Hypertension in Pregnancy has eliminated the requirement for proteinuria to make the diagnosis. (ACOG, 2013)

The California Maternal Quality Care Collaborative (CMQCC) developed a toolkit entitled "Improving Healthcare Response to Preeclampsia" which can be found at https://www.cmqcc.org/preeclampsia_toolkit . The toolkit includes a compendium of best practice publications; care guidelines in the form of tables, charts, and forms; and a slide set for professional education. This resource is an excellent instrument to assist providers with developing systems of care for women with preeclampsia.

Definitions

High blood pressure in pregnancy is classified by four categories:

1. Chronic hypertension (CHTN)
2. Gestational hypertension
3. Preeclampsia-eclampsia
4. Preeclampsia superimposed on chronic hypertension

Hypertension is defined as a systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg observed on at least 2 occasions ≥ 4 hours apart, but no more than 7 days apart. **CHTN** in pregnancy is defined as elevated blood pressure documented either prior to pregnancy or before the 20th week of pregnancy, or continuing more than 12 weeks postpartum. (Sibai, 2010a) **Gestational hypertension** is defined as onset of high blood pressure after 20 weeks gestation without proteinuria, thrombocytopenia, impaired liver function, the new development of renal insufficiency, pulmonary edema, or new-onset cerebral or visual disturbances. **Preeclampsia-eclampsia** is a syndrome unique to

pregnancy characterized by new onset hypertension and proteinuria or, in the absence of proteinuria, new-onset hypertension with the new onset of any of the following: thrombocytopenia; renal insufficiency, impaired liver function; pulmonary edema; or cerebral or visual symptoms (Table 1).(ACOG, 2013) **Preeclampsia superimposed on chronic hypertension** is chronic hypertension in association with preeclampsia. (ACOG, 2013)

The etiology of preeclampsia is not known. Preeclampsia appears to be a disease that involves a number of maternal, placental, and fetal factors. These include: placental implantation with abnormal trophoblastic invasion of uterine vessels; abnormal immunological tolerance to placental and fetal tissues; maternal maladaptation to cardiovascular or inflammatory changes of normal pregnancy; and genetic factors. (Cunningham et al., 2010)

Preeclampsia is defined (Table 1) as a systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg on 2 occasions at least 4 hrs apart after 20 weeks gestation in women with a previously normal blood pressure or ≥160 mm Hg systolic or ≥110 mm Hg diastolic, confirmed within a short interval (minutes) to facilitate timely antihypertensive therapy and proteinuria ≥ 300 mg/24 hrs or a protein/creatinine ratio ≥ 0.3 mg/dL or a dipstick reading of ≥ 1+ (dipstick used only if other quantitative methods not available). In the absence of proteinuria, preeclampsia is diagnosed as new-onset hypertension with the new onset of any of the following: thrombocytopenia, renal insufficiency, impaired liver function, pulmonary edema, or cerebral or visual symptoms. (ACOG, 2013)

Risk factors associated with preeclampsia include: nulliparity, obesity, multiple gestation, family history of preeclampsia or eclampsia, preexisting hypertension or renal disease, previous preeclampsia or eclampsia, diabetes mellitus, nonimmune hydrops, antiphospholipid antibody syndrome, age 35 years or older, African-American race, and molar pregnancy. It is extremely rare for preeclampsia to develop before 20 weeks gestation, but when it does occur it is usually associated with renal disease or molar pregnancy. (Sibai, 2010b) Signs and symptoms of preeclampsia include elevated blood pressure, proteinuria, nondependent edema, visual disturbances, headache, and epigastric pain. Laboratory abnormalities occur with preeclampsia and are reflective of the end organ injury that can occur in preeclampsia. They include hemoconcentration (due to poor volume expansion, may manifest as increased hemoglobin/hematocrit), elevated serum creatinine and liver enzymes (due to vasospasm with decreased organ perfusion), and hemolysis and thrombocytopenia (due to severe vasospasm with endothelial injury and subsequent cell damage/destruction).

Table 1. Diagnostic Criteria for Preeclampsia (ACOG, 2013)

Blood Pressure	• ≥ 140 mm Hg systolic or ≥ 90 mm Hg diastolic one 2 occasions at least 4 hrs apart after 20 wks GA in women with a previously normal BP • ≥ 160 mm Hg systolic or ≥ 110 mm Hg diastolic, confirmed within a short interval (minutes) to facilitate timely antihypertensive therapy
And	
Proteinuria	• ≥ 300mg per 24-hr urine collection (or this amount extrapolated from a timed collection) **Or** • Protein/creatinine ratio ≥ 0.3 mg/dL • Dipstick reading of ≥ 1+ (used only if other quantitative methods not available)
Or in the absence of proteinuria, new-onset hypertension with the new onset of one or more of the following:	
Thrombocytopenia	• Platelet count < 100,000/µL
Renal insufficiency	• Serum creatinine > 1.1 mg/dL or a doubling of the serum creatinine in the absence of other renal disease
Impaired liver function	• Elevated blood levels of liver transaminases to twice normal concentrations
Pulmonary edema	
Cerebral or visual symptoms	

Severe preeclampsia is defined by the presence of one or more of the following(ACOG, 2013)

- Systolic BP ≥ 160 mm Hg or diastolic ≥ 110 mm Hg on 2 occasions 4 hours or more apart while the patient is on bed rest.
- Thrombocytopenia (platelet count < 100,000/µL).
- Impaired liver function as indicated by abnormally elevated blood levels of liver enzymes (to twice normal concentration), severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by alternative diagnoses, or both.
- Progressive renal insufficiency (serum creatinine > 1.1 mg/dL or a doubling of the serum creatinine in the absence of other renal disease.
- New-onset cerebral or visual disturbances.
- Pulmonary edema.

Eclampsia is defined as the presence of new-onset grand mal seizures in women with preeclampsia, although in up to 20-25% of patients the presenting signs and symptoms may be seizure activity.

HELLP Syndrome

A particularly severe and serious form of preeclampsia is HELLP syndrome characterized by hemolysis, elevated liver enzymes, and low platelets. Prompt recognition is vital to improving outcomes. Due to the different number of assays used to measure liver enzymes, clinicians should be familiar with the upper limit values used in their own laboratory. Criteria for HELLP syndrome are: LDH > 600 IU/L (more than 2 times the upper limit of normal values) or bilirubin > 1.2 mg/dL, AST > 70 IU/L (more than 2 times the upper limit of normal values), and platelets < 100,000/µL.(Sibai, 2004) Proteinuria may or may not be present with HELLP syndrome.

Management

Preeclampsia is a clinical diagnosis, there is no single test for preeclampsia that has been found to be reliable and cost-effective; delivery is the only available cure. In addition, preeclampsia is a multisystemic, dynamic process that is progressive at variable rates. Clinicians must weigh maternal and fetal risks when deciding between immediate delivery and expectant management. Clinical assessment includes frequent evaluation of maternal and fetal conditions, gestational age, presence of labor, severity of the disease process, Bishop Score, and maternal preferences.

Management of preeclampsia without severe features:

Women with mild gestational hypertension or preeclampsia without severe features at or beyond 37 weeks of gestation:

- **Delivery** rather than continued observation is suggested. (ACOG, 2013)
- Once delivery planned, MgSO4 for seizure prophylaxis (Table 2).

Women with mild gestational hypertension or preeclampsia prior to 37 weeks of gestation:

- Although most patients with preeclampsia without severe features are best managed with inpatient hospitalization, some patients with stable disease following a period of inpatient admission, may be candidates for close outpatient follow up. These patients should be highly compliant and seen for follow up evaluation in the office at least twice per week with interval evaluations by a home health provider.
- Outpatient monitoring includes: Twice weekly maternal and fetal assessments with the goal of early identification of severe features and subsequent hospitalization and delivery.

Maternal assessment includes: serial assessment of symptoms and fetal movement (daily by woman), serial measurement of BP (twice weekly), weekly proteinuria assessment and labs including CBC with platelet count, AST, ALT, creatinine, bilirubin, and LDH (as indicated).
Fetal assessment includes: NST, BPP, and/or AFI

Hospitalization is often recommended for women with new-onset preeclampsia. Monitoring includes:

- Daily assessment for clinical findings such as headache, visual disturbances, epigastric pain, and rapid weight gain.
- Daily maternal weight and intake and output assessment looking for signs of oliguria.
- Frequent blood pressure readings typically every 4-8 hours.
- Baseline labs: AST, CBC with platelet count, and serum creatinine. Serum uric acid does not add sensitivity or specificity for the diagnosis of preeclampsia and therefore should not be routinely ordered.
- 24 hr urine collection for protein. Once an initial 24 hr urine collection demonstrates that there is significant proteinuria (>300 mg), there is little value to repeat 24 hour measurements. Therefore, repeat 24 hr collections should not be routinely obtained as the results in isolation would not be an indication for delivery.
- For preeclampsia without severe features, repeat lab tests weekly if stable values without progression; sooner if disease progression is questionable or if more significant disease is suspected.
- At least weekly non stress tests or biophysical profiles; twice weekly tests for suspected fetal growth restriction or oligohydramnios.
- Daily fetal movement assessment.
- Ultrasound for fetal growth every 3 weeks.
- Weekly assessment of amniotic fluid (modified BPP).
- A course of corticosteroids should be given to women <34 weeks.

Management of severe preeclampsia:(ACOG, 2011, 2013)

- Women with severe preeclampsia **at or beyond 34 weeks gestation**, and in those with unstable maternal or fetal conditions irrespective of gestational age, should be **delivered** as soon as the maternal status is stabilized. (ACOG, 2013)
- Vaginal delivery should be attempted unless otherwise contraindicated. A diagnosis of preeclampsia is not an indication for cesarean section. Even with an unfavorable cervix, more than 60% of women with severe pre-eclampsia are able to achieve a vaginal delivery.
- Women with severe preeclampsia **less than 34 weeks gestation** with stable maternal and fetal conditions should be **transferred** to a tertiary care facility capable of caring for the infant and consideration should be given to **consultation** with a Maternal Fetal Medicine (MFM) specialist. (ACOG, 2013)
- Avoid aggressive hydration to prevent pulmonary edema-limit IV fluids to 150cc/hr.
- MgSO4 for seizure prophylaxis (Table 2).

- Antihypertensive treatment should be given for women with a systolic blood pressure > 160-165 mm Hg with a goal of < 155 mm Hg or diastolic blood pressure of ≥ 105-110 mm Hg with a goal of < 100-105 mm Hg. (Table 3).
- < 34 weeks: administer a course of betamethasone. Even if steps need to be taken to immediately move to induction of labor due to maternal or fetal status, corticosteroids should be administered because neonatal benefits may begin to accrue as quickly as 12 hours after the initial dose. In women with severe hypertension, but in whom maternal and fetal status is otherwise stable, consideration can be given to delaying the initiation of induction or delivery until 24-48 hours after the initiation of corticosteroids.
- Once a diagnosis of severe pre-eclampsia is made, the plan should be made for delivery. In highly select cases at very early gestational ages, there may be a role for expectant management with initiation of anti-hypertensive agents, but this course of management should only be undertaken with the patient under the direct care of a MFM specialist.

Table 2. MgSO4 Seizure Prophylaxis

Renal Function	MgSO4 Loading Dose	Constant infusion rate	Monitoring	Toxicity treatment
Normal, no evidence of pulmonary edema	4-6 grams/20 min	2 grams/hour Continue 24 hours postpartum	Magnesium levels not indicated unless signs of toxicity Monitor for evidence of toxicity: • deep tendon reflex • lethargy • respirations	• Check magnesium level • Discontinue infusion • If respiratory or EKG changed are noted: administer calcium gluconate (1 ampule=4.64 mEq IV x 1 dose)
Mild renal insufficiency	4 grams/20 min	1 gram/hour Continue 24 hours postpartum	Serial magnesium levels every 6 hours, target range 5-7 Monitor for evidence of toxicity: • deep tendon reflex • lethargy • respirations	• Check magnesium level • Discontinue infusion • If respiratory or EKG changed are noted: administer calcium gluconate (1 ampule=4.64 mEq IV x 1 dose)
Significant renal impairment	4 grams/20 min	Individualize, may not be needed	Serial magnesium levels every 6 hours, target range 5-7 Monitor for evidence of toxicity: • deep tendon reflex • lethargy • respirations	• Check magnesium level • Discontinue infusion • If respiratory or EKG changed are noted: administer calcium gluconate (1 ampule=4.64 mEq IV x 1 dose)

Table 3. Antihypertensive Drugs

Drug	Dosage	Repeat	Precautions
Hydralazine	5-10 mg IV over 2 min	May repeat every 20 min	• If after 30-40mg has been administered and the BP remains above the target range, switch to Labetalol. • If maternal heart rate >120 bpm, discontinue hydralazine.
Labetalol	10 mg IV every 10-15 min in a dose-escalating fashion: 10mg followed by 20mg, then 40mg, then 80mg	Repeat every 10-15 min to a maximum total dose of 220mg for initial response	• IM administration should be avoided with a viable IUP due to an inability to titrate dosing effectively. • Once an initial response has been achieved (even if 40 or 80mg were required), subsequent doses should be no greater than 20mg to avoid hypotension.

Post partum

In women with gestational hypertension, preeclampsia, or superimposed preeclampsia, BP should be monitored in the hospital for 48-72 hours and again 7-10 days after delivery or earlier in women with symptoms. Discharge instructions for all women should include information about signs and symptoms of preeclampsia and the importance of prompt reporting of symptoms.

Delivery of the placenta usually halts the disease progression but it does not reverse all of the associated pathophysiological changes of preeclampsia. Moreover, preeclampsia and eclampsia can develop in the postpartum period with 33% of convulsions occurring within the 24-48 hr postpartum period. Thus, seizure prevention with magnesium sulfate infusion should continue through the first 24 hrs postpartum. Patients with persistent blood pressure elevations: systolic > 150-155 mm Hg or diastolic > 90-100 mm Hg, should be treated with hydralazine 20 mg IM or standard IV doses. Conventional oral agents such as nifedipine XL 30mg daily or labetalol 200 mg BID can be initiated to maintain blood pressure at systolic < 150-155 mm Hg and diastolic < 100 mm Hg. Patients discharged home on oral anti-hypertensive therapy require postpartum follow up within 1-2 weeks of discharge.

Thrombotic thrombocytopenic purpura (TTP) and hemolytic-uremic syndrome (HUS) should be considered if the patient continues to have signs, symptoms, and worsening lab parameters after delivery with preeclampsia. Treatment of patients with these disorders should be individualized by a multidisciplinary team of MFM, nephrology, hematology, and transfusion physicians at a tertiary care facility.

Diagnostic criteria of these disorders may include:

- Fever (more common with TTP)
- Anemia (hemolytic)
- Thrombocytopenia
- Renal failure
- Central nervous system symptoms: seizures or severe headache (more common with TTP)

Quality Indicators/Benchmarks

- Antenatal corticosteroids <34 weeks GA
- Delivery at appropriate facility

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