Chapter 4
Hypertensive Disorders of Pregnancy

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Introduction

Hypertension is the most common medical disorder of pregnancy, complicating up to 10% of gestations [1]. Preeclampsia is a leading cause of maternal and perinatal morbidity and mortality and the incidence in increasing [2]. It is estimated that for every preeclampsia-related death, 50–100 women experience a "near-miss" event resulting in significant health risk and morbidity [3, 4]. Many women in the second or third trimester of pregnancy present to the emergency department (ED) for a variety of reasons, and emergency physicians are in a unique position to identify and treat patients with a hypertensive disorder of pregnancy before serious complications occur.

Classification of Hypertensive Disorders of Pregnancy

In 2013, the American College of Obstetricians and Gynecologists' (ACOG) Task Force on Hypertension in Pregnancy released updated evidence-based guidelines for the diagnosis and management of hypertensive disorders of pregnancy [5]. The task force divides hypertension in pregnancy into four categories: (1) preeclampsia/eclampsia, (2) chronic hypertension, (3) chronic hypertension with superimposed preeclampsia, and (4) gestational hypertension (Table 4.1). Hypertension in pregnancy is defined as either a systolic blood pressure of 140 mmHg or greater or a diastolic blood pressure of 90 mmHg or greater. Blood pressure should be elevated on at least two separate occasions more than 4 h apart before the diagnosis of

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Table 4.1 Definitions of the Hypertensive Disorders of Pregnancy

Hypertensive disorder of pregnancy	Diagnostic criteria
Preeclampsia	New-onset hypertension (blood pressure >140 mmHg systolic and/or >90 mmHg diastolic) after 20 weeks and proteinuria Or in the absence of proteinuria: New-onset hypertension after 20 weeks and signs/symptoms of end-organ damage (Box 4.1)
Eclampsia	New-onset seizures in woman with preeclampsia
Chronic hypertension	Hypertension that predates pregnancy or is diagnosed before 20 weeks
Chronic hypertension with superimposed preeclampsia	Patients with chronic hypertension that develop preeclampsia
Gestational hypertension	New-onset hypertension after 20 weeks without proteinuria or signs/symptoms of preeclampsia

Adapted from American College of Obstetricians and Gynecologists, Task Force on Hypertension in Pregnancy. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' task force on hypertension in pregnancy Obstet Gynecol. 2013;122:1122–1131

hypertension is made. However, even an isolated elevated blood pressure reading is concerning, especially if the blood pressure is greater than 160 mmHg systolic and/or 110 mmHg diastolic.

Preeclampsia has traditionally been defined as new onset of hypertension plus proteinuria after 20 weeks of gestation. Proteinuria is defined as excretion of 300 mg or more of protein in a 24-h urine collection or a random protein/creatinine ratio of at least 0.3 mg/dL. Urine dipstick is discouraged to diagnose proteinuria unless other methods are unavailable, in which case a measurement of at least 1+ must be obtained.

Importantly, the task force has eliminated the requirement of proteinuria to make the diagnosis of preeclampsia. In the absence of proteinuria, preeclampsia can be diagnosed in the setting of hypertension after 20 weeks of gestation plus signs or symptoms of end-organ damage, also called "severe features" (Box 4.1). Eclampsia is defined as new-onset grand mal seizures in women with preeclampsia and can occur before, during, or after labor.

HELLP syndrome is an acronym for hemolysis (H), elevated liver enzymes (EL), and low platelets (LP). Many authors consider HELLP syndrome to be a complication of preeclampsia and eclampsia, though some feel HELLP syndrome to be separate entity [6]. Hypertension may be mild or absent in patients with HELLP syndrome (Box 4.2).

Chronic hypertension is hypertension that predates pregnancy or is diagnosed before 20 weeks of gestation. Patients with chronic hypertension may develop preeclampsia, and this is referred to as superimposed preeclampsia. Gestational hypertension is hypertension that occurs after 20 weeks without proteinuria or other signs/symptoms of preeclampsia. However, gestational hypertension is not a benign diagnosis—between 15 and 25% of women with gestational hypertension will develop preeclampsia [7].

Box 4.1 Severe features of preeclampsia

• Systolic blood pressure >160 mmHg or diastolic >110 mmHg
• Thrombocytopenia (platelet count <100,000/μL)
• Impaired liver function (twice normal)
• Severe persistent right upper quadrant or epigastric pain unresponsive to medication
• Renal insufficiency (creatinine >1.1 mg/dL or doubling of creatinine in absence of other renal disease)
• Pulmonary edema
• New-onset cerebral or visual disturbances

Adapted from American College of Obstetricians and Gynecologists, Task Force on Hypertension in Pregnancy. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' task force on hypertension in pregnancy. Obstet Gynecol. 2013;122:1122–11

Box 4.2 Diagnosis of HELLP syndrome

• Evidence of hemolysis:
– Schistocytes on peripheral smear
– Lactate dehydrogenase >600 IU/L
– Total bilirubin 1.2 mg/dL)
• Elevated aspartate aminotransferase (>70 IU/L)
• Thrombocytopenia (platelets <100,000/μL)

Adapted from Olsen-Chen C, Seligman NS. Hypertensive emergencies in pregnancy. Crit Care Clin. 2016;32:29–41

Pathophysiology

The concept of preeclampsia/eclampsia has been recognized since ancient times [8], yet the exact mechanisms leading to the disorder still remain unclear. Some women may be genetically predisposed to developing the disease. Recent research suggests that poor placentation can lead to placental hypoxia and insufficiency causing a complex cascade of endothelial dysfunction leading to many of the clinical features observed in preeclampsia [9, 10].

Emergency Department Management

Evaluation

Pregnant patients that are greater than 20 weeks of gestational age presenting to the emergency department (ED) for any reason and are noted to be hypertensive must be evaluated for signs and symptoms of end-organ damage to rule out preeclampsia. Patients should be asked about the presence of headache, visual changes, abdominal pain (specifically right upper quadrant or epigastric pain), chest pain, and shortness of breath. As many women with preeclampsia may have no symptoms [11],

laboratory tests are necessary. Minimum laboratory test includes complete blood count to evaluate for thrombocytopenia, complete metabolic panel to assess creatinine level and liver enzymes, and urinalysis or urine protein/creatinine ratio to evaluate for proteinuria. Additional tests can include lactate dehydrogenase to evaluate for hemolysis if there is concern for HELLP syndrome, coagulation studies, and baseline magnesium level. Serum uric acid may also be ordered as elevated levels have been associated with adverse maternal and fetal outcomes and may help identify women with gestational hypertension who will progress to preeclampsia [12, 13].

Treatment

Delivery is the definitive treatment for preeclampsia, eclampsia, and HELLP syndrome. Timing of delivery is dependent on maternal condition and gestational age of the fetus. Emergency department treatment of the preeclamptic or eclamptic patient includes controlling blood pressure, initiating seizure prophylaxis, treating seizures if they occur, and obtaining emergent obstetric consultation.

Control of Blood Pressure

Pregnant women with blood pressure >160 mmHg systolic or >110 mmHg diastolic require antihypertensive therapy to reduce the risk of stroke and other maternal complications. The goal is to stabilize blood pressure around 140/90 mmHg, not to normalize blood pressure [14]. Sudden drops in blood pressure should be avoided so as not to cause additional complications such as fetal distress.

There is no consensus on an ideal agent for treating blood pressure in preeclampsia [15]. Clinicians should select a drug based on maternal characteristics/contraindications and their own familiarity and experience with a medication. All antihypertensive drugs used in pregnancy cross the placenta, so possible effects on the fetus should also be taken into consideration. The most commonly used agents are labetalol, hydralazine, and nifedipine. All three drugs may be considered first-line therapy. Suggested dosing regimens and drug characteristics are outlined in Tables 4.2 and 4.3, respectively. Magnesium is not recommended as an antihypertensive agent [14].

Seizure Prophylaxis and Treatment

For women with preeclampsia with severe features, magnesium sulfate should be given as prophylaxis against eclampsia [5]. The suggested dose for seizure prophylaxis is 4 g IV over 5 min, followed by 1 g/h infusion. Treatment with magnesium sulfate has been shown to reduce the risk of eclampsia by half [16].

Table 4.2 Initial approach for management of severe antepartum, intrapartum, or postpartum hypertension

Labetalol	Hydralazine	Nifedipine
If BP remains >160 mmHg systolic or >110 diastolic for more than 15 min:		
Give 20 mg IV over 2 min Repeat BP in 10 min	Give 5–10 mg IV over 2 min Repeat BP in 20 min	Give 10 mg orally Repeat BP in 20 min
If BP remains >160 mmHg systolic or >110 diastolic:		
Give 40 mg IV over 2 min Repeat BP in 10 min	Give 10 mg IV over 2 min Repeat BP in 20 min	Give 20 mg orally Repeat BP in 20 min
If BP remains >160 mmHg systolic or >110 diastolic:		
Give 80 mg IV over 2 min Repeat BP in 10 min	Give labetalol 20 mg IV over 2 min Repeat BP in 10 min	Give 20 mg orally Repeat BP in 20 min
If BP remains >160 mmHg systolic or >110 diastolic:		
Give hydralazine 10 mg IV over 2 min Repeat BP in 20 min	Give labetalol 40 mg IV over 2 min Repeat BP in 10 min	Give labetalol 40 mg IV over 2 min Repeat BP in 10 min
If BP remains >160 mmHg systolic or >110 diastolic:		
Obtain emergent consultation from obstetrics, maternal-fetal medicine, or critical care subspecialists and treat as recommended		
Once target BP reached, repeat BP every 10 min for 1 h, then every 15 min for 1 h, then every 30 min for 1 h, then every hour for 4 h		

Abbreviations: BP blood pressure, *IV* intravenous. Adapted from American College of Obstetricians and Gynecologists. Committee Opinion No 623: emergent therapy for acute-onset, severe hypertension during pregnancy and the postpartum period. Obstet Gynecol. 2015;125:521–525

Table 4.3 Characteristics of antihypertensive drugs commonly used for severe hypertension in pregnancy

Drug	Mechanism	Contraindications/cautions
Labetalol	Nonselective beta-blocker, some alpha-blocking activity	Avoid in women with asthma, heart disease, congestive heart failure May cause neonatal bradycardia and hypoglycemia
Hydralazine	Direct vasodilator, relaxes arteriolar smooth muscle	May cause maternal hypotension, tachycardia, headache, flushing, nausea/vomiting, palpitations
Nifedipine	Calcium channel blocker	May cause maternal tachycardia, flushing, palpitations, headache

Adapted from Olsen-Chen C, Seligman NS. Hypertensive emergencies in pregnancy. Crit Care Clin. 2016;32:29–41

If seizures develop, magnesium sulfate is still the drug of choice and has been shown to be superior to diazepam, phenytoin, and lytic cocktail in reducing maternal death and further seizures [17–19]. If magnesium has not been started yet, give 4 g IV over 5 min, then 1 g/h infusion. If the patient is already receiving magnesium and seizes, give an additional 2–4 g IV over 5 min and increase the infusion to 2 g/h [20]. Eclamptic seizures are generally short in duration (<1 min) [21]. Cerebral

imaging should be considered for patients with prolonged or repeated seizures and for patients with a focal neurologic deficit to rule out possible intracranial hemorrhage or other neurologic complication.

Patients receiving magnesium should be closely monitored for signs of magnesium toxicity. Symptoms of magnesium toxicity include loss of deep tendon reflexes, respiratory depression, somnolence, and cardiac arrest. If magnesium toxicity is suspected, the infusion should be stopped immediately and 10 mL of 10% calcium gluconate can be administered [22]. There is theoretical concern that treatment with both nifedipine and magnesium sulfate could result in increased risk of magnesium-related maternal side effects such neuromuscular blockade and severe hypotension, but this has not been shown to be the case [23].

Disposition

The progression of preeclampsia is unpredictable and can be rapid; therefore, hospital admission to an obstetrics unit is usually indicated. The emergency physician must decide if the current facility has the capacity and capability to provide the level of maternal-fetal-neonatal care needed or if the patient would benefit from transfer to a higher level of care. Transfer of patients to a facility with sufficient obstetric and neonatal resources has been shown to reduce maternal, fetal, and neonatal morbidity and mortality [24]. Since the definitive treatment of preeclampsia and eclampsia is delivery, the decision of when and where to transfer is often based on gestational age and the need for obstetric and neonatal specialists [25]. Neonatal mortality is significantly lower if preterm babies are delivered at highly specialized hospitals rather than being transported there after birth [26, 27]. For this reason, every effort should be made to transfer a pregnant patient with preeclampsia/eclampsia to a tertiary care facility prior to delivery, especially if she is far from term.

The Emergency Medical Treatment and Active Labor Act (EMTALA) imposes specific obligations on healthcare providers to perform a medical screening examination and to provide stabilizing treatment to any patient with an emergency medical condition [28]. In pregnant women, this includes both the mother and fetus. According to EMTALA, a woman in labor is considered unstable until both the baby and the placenta have been delivered. However, a patient in labor may still be transferred if there is felt to be adequate time before delivery or if the benefits of transfer outweigh the risks. Several steps must be taken before transfer can take place: (1) assessment of fetal viability, gestational age, and well-being; (2) stabilizing treatment with control of blood pressure and convulsions and seizure prophylaxis with a loading dose of magnesium sulfate if appropriate; (3) maternal laboratory assessment (complete blood count and platelet count, liver enzymes, creatinine, urine protein); (4) fetal monitoring if available; (5) consultation of obstetric/perinatal team; and (6) transmission of all records for review [27].

Special Considerations

Postpartum Preeclampsia

The majority of hypertensive emergencies associated with pregnancy occur antepartum or within the first 48 h after delivery [29]. Eclampsia that occurs greater than 48 h after delivery is known as late postpartum eclampsia (LPPE) [30]. The incidence of LPPE appears to be increasing and now represents about 13–16% of all cases of eclampsia [31–34]. Blood pressure has been shown to rise over the first week after delivery and peaks on postpartum days 3–6 [35, 36]. This is likely due to physiologic fluid mobilization and volume expansion. The use of medications such as nonsteroidal anti-inflammatory pills, ergot derivatives, and decongestants may also contribute to postpartum hypertension [36, 37].

Preeclampsia and eclampsia may occur up to 6 weeks postpartum. Women who develop postpartum preeclampsia and eclampsia may have had no evidence of the disease during their pregnancy [38]. Many women in the postpartum period may present to the emergency department for evaluation instead of being seen by their obstetric provider. Early treatment of preeclampsia, eclampsia, and HELLP syndrome in the postpartum patient hinges on whether the clinician recognizes late presentations of these disorders. The criteria for diagnosing postpartum preeclampsia, eclampsia, and HELLP syndrome are the same as in the antepartum period.

In the postpartum period, headache is the most common presenting symptom of preeclampsia [38]. It should be noted that headache could also herald other potentially serious conditions. An estimated 10–11% of postpartum patients with headache have critical conditions such as intracranial bleed, stroke, mass, or cerebral venous sinus thrombosis [39]. Patients with postpartum preeclampsia may also present with abdominal pain, chest pain, shortness of breath, visual changes, or increased swelling, similar to antepartum patients.

Preeclampsia and eclampsia in the postpartum period should be managed the same as antepartum period by controlling blood pressure and initiating magnesium sulfate for seizure prophylaxis/control.

HELLP syndrome may develop first in the postpartum period in up to 30% of cases and should be considered in any patient with abdominal pain, nausea, or vomiting [40]. Management is similar to treatment in the antepartum period and includes magnesium sulfate, blood pressure control, and close monitoring of vital signs and laboratory values [37]. The use of steroids for the treatment of HELLP syndrome is conflicting. Some reports have shown improvement in platelet counts following treatment with steroids. However, a 2010 Cochrane review found no evidence of steroids improving in the clinical outcome [41]. The decision to initiate steroid treatment for HELLP syndrome should be made in consultation with an obstetrician.

Preeclampsia Less Than 20 Weeks of Gestation

As stated, preeclampsia is defined as occurring after 20 weeks of gestation. Very rarely, preeclampsia can occur before 20 weeks, usually in abnormal pregnancies complicated by triploidy, trophoblastic disease, or antiphospholipid antibody syndrome [42, 44–47]. Case reports have been published describing preeclampsia before 20 weeks without these abnormalities, and authors refer to this occurrence as "pure" preeclampsia [48, 49]. This is an extremely unusual phenomenon and not likely to be diagnosed in the emergency department. A much more common scenario—and potential pitfall for emergency physicians—would be a patient presenting with signs/symptoms of preeclampsia who is farther along in her pregnancy than previously thought (incorrect dates) and is in fact greater than 20 weeks of gestation. Emergency physicians should confirm the gestational age of any patient pregnant presenting to the ED with hypertension and ensure the most accurate pregnancy dating method was used.

Chronic Hypertension with Superimposed Preeclampsia

Pregnant patients with chronic hypertension presenting to the ED can be especially challenging for emergency physicians. These patients are at risk for developing superimposed preeclampsia, and clinicians should not be reassured that the patient's blood pressure is "always high." Indeed, 13–40% of patients with chronic hypertension will go on to develop superimposed preeclampsia [50, 51], and these women have higher rates of adverse maternal-fetal outcomes [5]. Superimposed preeclampsia should be suspected when there is a sudden increase in blood pressure that was previously well controlled, new-onset proteinuria or sudden increase in proteinuria, or if any other signs/symptoms of end-organ damage are present. Emergency department management of chronic hypertensive patients with superimposed preeclampsia is the same as patients with preeclampsia.

Summary

Hypertension complicates many pregnancies and is a leading cause of maternal and fetal morbidity and mortality. It is critical that emergency physicians assess the blood pressure of pregnant patients presenting to the ED for any reason and screen for signs/symptoms of end-organ damage. Early identification and appropriate management of the hypertensive disorders of pregnancy can improve outcomes for both mother and baby. Treatment of preeclampsia and eclampsia can begin in the ED and includes blood pressure control and seizure prophylaxis with magnesium sulfate. The definitive treatment of preeclampsia, eclampsia, and HELLP syndrome is delivery. Depending on maternal condition and gestational age, transfer to a tertiary facility may be required.

Key Points

- Pregnant patients that are greater than 20 weeks of gestational age presenting to the ED for any reason and are noted to be hypertensive must be evaluated for signs and symptoms of end-organ damage to rule out preeclampsia.
- Proteinuria is no longer required to make the diagnosis of preeclampsia.
- Labetalol, hydralazine, and nifedipine are all considered first-line treatment for severe hypertension in pregnancy.
- Patients with preeclampsia with severe features require magnesium sulfate therapy for prophylaxis against eclampsia.
- Magnesium sulfate is the drug of choice for treatment of eclamptic seizures.

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