Management of Hypertensive Crisis for the Obstetrician/Gynecologist



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KEYWORDS

- Hypertension
 Pregnancy
 Hypertensive crisis
 Hypertensive urgency/emergency
- Preeclampsia Eclampsia HELLP syndrome Pregnancy safety bundles

KEY POINTS

- Systolic blood pressure greater than 160 mm Hg is associated with many adverse maternal outcomes, such as stroke and pulmonary edema.
- Blood pressure measurements greater than or equal to 160/110 mm Hg lasting longer than 15 minutes warrant immediate medical therapy.
- Hydralazine, labetalol, and nifedipine are currently considered first-line treatment options for the emergent reduction of blood pressure in pregnancy.
- Early maternal warning signs, such as a systolic blood pressure greater than 160 mm Hg, tachycardia, and oliguria, allow timely diagnostic and therapeutic interventions.
- Health care providers taking care of obstetric patients should familiarize themselves with the most updated classifications and management of hypertensive disorders of pregnancy.

INTRODUCTION

Hypertensive disorders of pregnancy are considered among the leading causes of maternal and fetal morbidity and mortality. Complicating approximately 10% of pregnancies, they are responsible for an estimated 50,000 to 60,000 preeclampsia-related deaths per year worldwide, many of which are preventable. ^{1–7}

In pregnancy, irrespective of the underlying cause, a blood pressure measurement greater than or equal to 160/110 mm Hg persisting for more than 15 minutes is considered an obstetric emergency. This condition warrants immediate attention and prompt appropriate therapy.^{1,5,8} Medical professionals taking care of obstetric patients must

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Obstet Gynecol Clin N Am 43 (2016) 623–637 http://dx.doi.org/10.1016/j.ogc.2016.07.005 0889-8545/16/© 2016 Elsevier Inc. All rights reserved. have a good understanding of maternal physiology, as well as the classification and management of hypertensive disorders encountered during pregnancy and the puerperium. They should also be familiar and comfortable with the most up-to-date and evidence-based guidelines. Adherence to these guidelines is of paramount importance, because it has been shown in numerous studies to reduce the incidence of adverse maternal and fetal outcomes. The improvement in maternal outcomes is mainly secondary to a reduction in cerebral and respiratory complications. 1,5,7–11 Prompt medical treatment is extremely important in cases of hypertensive urgency/ crisis because the timing of initiation of therapy can alter morbidity and mortality risk.

WHY ARE HYPERTENSIVE DISORDERS IN PREGNANT AND POSTPARTUM PATIENTS IMPORTANT?

Hypertensive disorders are a leading cause of preventable maternal and fetal morbidity and mortality. Hypertensive disorders in pregnancy are often complex, and usually involve multiple organ systems and may be related to the secondary causes. Optimizing blood pressure remains of paramount importance, especially the control of systolic pressure, given its direct association with stroke and pulmonary edema. ^{1,5,7,11} However, treatment and management go beyond controlling the blood pressure. The entire disease spectrum needs to be taken into consideration to achieve desired outcomes and avoidance of complications. Optimal delivery timing needs to be considered as well as the treatment of any underlying disorder when applicable. Treatment with other necessary medications, such as betamethasone and magnesium sulfate, to prepare the fetus for delivery or to stabilize the mother must also accompany blood pressure control. ^{1,5}

COMMON COMPLICATIONS ASSOCIATED WITH HYPERTENSIVE DISORDERS OF PREGNANCY

These complications can be divided into maternal and fetal types and include 1,2,5,12-16:

Maternal

- Increased risk of:
 - Hemorrhagic stroke
 - Pulmonary edema
 - o Acute renal failure or accelerated end-organ damage
 - Gestational diabetes
 - Heart failure/cardiopulmonary decompensation
 - Hypertensive encephalopathy
 - Retinopathy
 - Cesarean delivery
 - o Postpartum hemorrhage
 - Maternal mortality

Fetal

- Increased risk of:
 - Abruptio placenta
 - Fetal growth restriction (intrauterine growth restriction [IUGR])
 - Preterm delivery
 - Intrauterine fetal demise
 - Perinatal mortality
 - Complications of prematurity
 - Potential teratogen exposure from hypertensive medications

DEFINITION OF HYPERTENSION IN PREGNANCY

Hypertensive disorders in pregnancy can be classified according to the degree of blood pressure increase (Table 1). 1,2,5

CLASSIFICATION OF HYPERTENSIVE DISORDERS OF PREGNANCY

Hypertensive disorders of pregnancy can either precede pregnancy or be pregnancy specific (first encountered during pregnancy) and are classified as follows¹:

Pregnancy specific

- Gestational hypertension:
 - Increase of blood pressure that is first encountered in pregnancy with absence of the diagnostic criteria for preeclampsia.
- Preeclampsia:
 - Increase of blood pressure with proteinuria or evidence of multisystem involvement fulfilling the diagnostic criteria for preeclampsia.
 - o Preeclampsia is further divided into:
 - Preeclampsia without severe features
 - Preeclampsia with severe features
- Superimposed preeclampsia:
 - A chronic hypertensive patient who at some point in pregnancy has an escalation of the disease process fulfilling the diagnostic criteria for preeclampsia.
- Hemolysis, elevated liver enzymes, low platelet (HELLP) syndrome:
 - Specific form of preeclampsia/eclampsia that is characterized by the presence of:
 - Hemolysis
 - Increased liver enzyme level
 - Low platelet level
- Eclampsia:
 - The occurrence of new-onset grand mal seizures in a pregnant woman that cannot be attributed to another cause.

Gestational trophoblastic diseases and mirror syndrome are rare pregnancyspecific causes of hypertensive disorders of pregnancy. Usually they occur in the first

Mild	Severe
Systolic blood pressure • ≥140- <160 mm Hg Or Diastolic blood pressure • ≥90 to <110 mm Hg. Or increase in both • At least 2 increased blood pressure measurements • Taken correctly • At least 4 h apart	Systolic blood pressure

2 trimesters of pregnancy. Ultrasonography and human chorionic gonadotropin levels help differentiate them from other possible causes.^{1,2}

Non-pregnancy specific

- Essential hypertension:
 - Blood pressure increase identified before pregnancy with no identifiable underlying cause.
- Secondary hypertension: (potentially curable):
 - o Blood pressure increase with an identifiable secondary cause.
 - Includes conditions such as^{1,2,17}:
 - Renal disease
 - Obstructive sleep apnea
 - Cushing syndrome
 - Renal artery stenosis
 - Pheochromocytoma
 - Coarctation of the aorta
 - Primary aldosteronism
 - Thyroid dysfunction
 - Lupus flare
 - Illicit drugs and medications
 - Cardiac causes
 - Adrenal disease

DEFINITIONS OF HYPERTENSIVE URGENCY/EMERGENCY/CRISIS IN NONPREGNANT VERSUS PREGNANT PATIENTS

The definition and diagnostic parameters of hypertension are similar in both pregnant and nonpregnant patients. However, a major difference lies in what constitutes a hypertensive crisis/urgency. In pregnancy and in the postpartum period (up to 6 weeks) asymptomatic or symptomatic increase of blood pressure greater than or equal to 160/110 mm Hg is considered an emergency that requires immediate evaluation and treatment. ^{1,5} Before pregnancy and beyond 6 weeks postpartum, when to immediately treat an asymptomatic patient with increased blood pressure remains a topic of controversy. However, most authorities agree that a systolic blood pressure of greater than 180 to 200 mm Hg and a diastolic blood pressure greater than 110 to 120 mm Hg warrants treatment. The major difference between hypertensive urgency and emergency is the symptoms and the susceptibility to intracranial hemorrhage at lower systolic blood pressures than nonpregnant and nonpostpartum patients. Patients with hypertensive emergency are usually symptomatic and have multisystem involvement with evidence of end-organ damage. ¹⁸

WHAT IS THE PATHOPHYSIOLOGY OF HYPERTENSIVE CRISIS IN PREGNANT PATIENTS WITH PRECLAMPSIA?

The exact pathophysiology of hypertensive disorders and their interaction with various organ systems and blood biomarkers is complex and remains elusive. The disease process is thought to originate from some form of placental insult that leads to placental ischemia, which many clinicians consider the trigger for the disease process. 19-21

Ischemia results in the release of a variety of placental factors, such as the soluble fms-like tyrosine kinase-1 (sFlt-1), the angiotensin II type-1 receptor autoantibody, and cytokines such as tumor necrosis factor alpha. These placental factors are thought to

trigger widespread maternal vascular dysfunction. 19-21 The circulating levels of sFlt-1 have been shown to be proportionately increased in relation to maternal hypertension. 19-21

BASIC EMERGENT LABORATORY EVALUATION AND IMAGING

New-onset hypertension in pregnancy, or worsening hypertension in a known hypertensive patient, is of great concern and warrants immediate attention and bedside evaluation. Once the initial evaluation is performed, appropriate laboratory evaluation and imaging as needed are initiated to determine the disease severity and diagnosis. Correct management is then guided based on the classification of the hypertensive disorder and its severity.

Initial laboratory evaluation includes^{1,2}:

- Quantitative assessment of urine protein (ie, 12-hour or 24-hour urine collection or a protein/creatinine ratio)
- Renal function tests
- Complete blood count with platelet count
- Glucose
- Electrolytes
- Uric acid
- Liver enzymes

Depending on the degree of blood pressure increase, clinical assessment, symptoms, and laboratory evaluation, further laboratory tests or diagnostic imaging may be warranted, including 1,2:

- Chest radiograph
 - Recommended in the presence of shortness of breath, decreased oxygen saturation, or abnormal pulmonary examination.
- Electrocardiogram (ECG) and possible echocardiogram
 - Recommended in presence of shortness of breath, decreased oxygen saturation, or abnormal cardiac examination.
 - o If chest pain is present, cardiac enzymes may need to be checked.
- Thyroid-stimulating hormone
- Head imaging
 - Evaluation for intracranial hemorrhage, cerebral thrombosis, or posterior reversible encephalopathy syndrome.
 - o MRI and computed tomography scan are usually the modalities of choice.
- Abdominal imaging
 - Recommended in the presence of persistent abdominal pain.
 - o Useful in the diagnosis of liver hematoma.

TARGETS OF TREATMENT

The ultimate goal of treatment is to minimize both maternal and fetal risk, while safely guiding both the mother and fetus through pregnancy and beyond. Management decisions are altered based on the following factors^{1,2,5,8,12}:

- Type of hypertensive disorder and underlying cause
- · Gestational age
- Disease severity
- Severity of hypertension
- Maternal and fetal clinical status

- Maternal response to intervention
- Maternal comorbidities

Factors that can influence the occurrence of complications are varied and include 1,2,5,8,12:

- Achieving the correct diagnosis
- Early identification of the highest risk patients
- Prompt and appropriate administration of medications
- Timing of delivery
- Compliance with prenatal care
- · Correct and accurate gestational age
- Disease severity
- Other comorbidities (eg, diabetes mellitus, obesity)

The treatment targets should focus on the following areas:

- 1. Blood pressure control
- 2. Maternal well-being
- 3. Fetal well-being and delivery preparation

Blood Pressure Control

Blood pressure targets differ slightly for postpartum patients compared with undelivered mothers. A brief overview is summarized here:

Antepartum¹:

- Reduce blood pressure to achieve ranges consistently below the severe range (<160/110 mm Hg) as so-called high-normal levels.
- Therapy should be given within 1 hour of persistent severe-range blood pressures (ideally within 15 minutes).
- Blood pressure should be reduced to approximately 140 to 150 over 90 to 100 mm Hg and not any lower to avoid hypoperfusion of the fetus and maternal organs.

Postpartum¹:

- Therapy should be given within 1 hour of persistent severe-range blood pressures.
- Reduce blood pressure to achieve levels consistently less than 150/90 mm Hg.
- Blood pressure should be monitored closely for the first 72 hours postpartum.
- Outpatient surveillance should be considered for those discharged before 72 hours (eg, home nursing visit).
- Reevaluate the patient within 7 to 10 days of discharge.
- Avoid nonsteroidal antiinflammatory drugs in the hypertensive postpartum patient.

Blood pressure control is extremely important to reduce the adverse outcomes seen in hypertensive disorders in pregnancy and the postpartum period. One element of particular interest is the association between systolic blood pressure severity and stroke. In a study involving 28 patients who had strokes associated with hypertensive disorders of pregnancy, all but 1 had a systolic blood pressure in the severe range. In that same study, baseline maternal pulse pressure (the difference between systolic and diastolic pressure in millimeters of mercury) was doubled just before the occurrence of stroke. The association between stroke and systolic hypertension has also been shown in studies outside of pregnancy. 22

Maternal Well-Being

Maternal well-being is of utmost importance and outcomes can be improved by appropriate and timely intervention. Listed here are some key points that need to be taken into consideration when caring for hypertensive pregnant patients:

- Close observation of maternal vital signs, including oxygen saturation.
- Appropriate and timely treatment of hypertension.
- Appropriate laboratory evaluation and treatment as needed.
- Appropriate and timely administration of magnesium sulfate for seizure prophylaxis (magnesium sulfate is not used for blood pressure control).
- Strict input and output documentation.
- Appropriate use of imaging modalities.
- Appropriate transfer to the intensive care unit (ICU) when indicated.
- Transfer to a facility that has the necessary and appropriate level of care (adequate maternal and neonatal intensive care resources).
- Safe transport should be arranged when higher level of care is needed.
- Involvement of subspecialists when indicated.

Fetal Well-Being and Delivery Preparation

It is desirable to prolong the pregnancy as much as the maternal and fetal conditions allow in preterm patients. However, there are certain conditions when pregnancy prolongation is not possible. Fetal well-being needs to be periodically assessed using fetal surveillance tools such as the nonstress test and/or the biophysical profile. Once the maternal condition allows, detailed ultrasonography should be performed to help assess whether pregnancy prolongation is an option.

In order to potentially optimize neonatal outcomes, the following should be administered based on gestational age and likelihood of delivery within the next 72 hours¹:

- Magnesium sulfate to help decrease the incidence of moderate to severe cerebral palsy if the gestational age is less than 32 weeks.^{23,24}
- Corticosteroids from 24 to 34 weeks of gestation (may be considered at 23 weeks) to help enhance fetal lung maturity.²⁵

ANTIHYPERTENSIVE MEDICATIONS IN PREGNANCY

In the continued absence of reliable noninvasive tests or biomarkers to identify hypertensive patients at immediate risk of adverse outcomes, blood pressure remains the most commonly gauged parameter and is the cornerstone that guides treatment.

The choice of antihypertensive medication in pregnancy depends on 1:

- · Pregnancy safety profile
- Urgent control versus long-term control
- Evidence-based guidelines/institutional policies
- Medicine availability
- Clinical scenario
- Patient-specific comorbidities and contraindications to certain medications
- Comfort level of provider
- Availability of intravenous (IV) access

There is a lack of quality pregnancy literature evaluating racial and ethnic variations in response to antihypertensive therapy. However, some literature outside of pregnancy suggests that ethnicity may play a role in response to treatment. For example, some studies have shown that African Americans are less responsive to β -blockers

than white people. This finding should be taken in consideration when choosing therapy. 18,26

Blood pressure control in pregnancy is divided into 2 stages. The first is directed at acute blood pressure control. The second is directed at long-term blood pressure control throughout the remainder of the pregnancy.

Immediate Control

- First-line pharmacologic therapy used in pregnancy for immediate/urgent control of blood pressure includes (Fig. 1)^{1,5,27}:
 - Labetalol (IV)
 - Hydralazine (IV)
 - Nifedipine (oral)
- Second-line pharmacologic therapy used in pregnancy for immediate/urgent control of blood pressure includes^{5,28}:
 - Esmolol
 - Nicardipine (infusion pump)
 - Labetalol (infusion pump)
 - Sodium nitroprusside

Sodium nitroprusside should be used as a last resort and for the shortest time possible because it can worsen maternal cerebral edema. There is also concern for maternal and fetal cyanate and thiocyanate toxicity.⁵

When second-line therapy is needed, it should be done in conjunction with a specialist (maternal-fetal medicine, anesthesia, internal medicine, or critical care).

Long-Term Control

- First-line pharmacologic therapy used in pregnancy for long-term control of hypertension in pregnancy^{1,2}:
 - o Methyldopa (oral)
 - Labetalol (oral)
 - Nifedipine (oral)
- Second-line therapy and ancillary medications:
 - Diuretics (thiazide diuretics)

Thiazide diuretics are generally considered safe to use in pregnancy. However, they should be used with caution secondary to the potential concern for intravascular volume depletion and hypokalemia.¹

Drugs to Avoid in Pregnancy

- 1. Angiotensin-converting enzyme inhibitors^{1,2,29}
- 2. Angiotensin receptor blockers

These drugs are known teratogens and are associated with fetal renal agenesis and dysfunction.

Commonly used antihypertensive medications include:

Methyldopa^{1,30-32}

- Mechanism of action: central-acting alpha-2 adrenergic agonist.
- Use in pregnancy: long term only, not for immediate control of blood pressure (used for gradual blood pressure control).
- Dose: 0.5 to 3 g/d by mouth 2 to 3 times daily. Maximum dose 3 g/d.

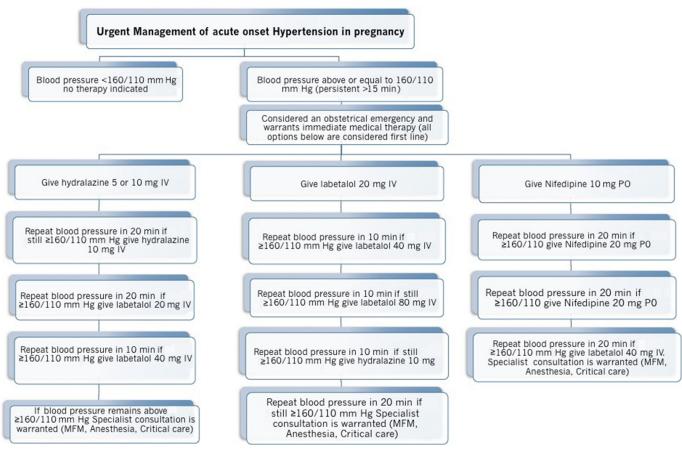


Fig. 1. Acute management of severe pregnancy-associated hypertension. MFM, maternal fetal medicine specialist. (*Data from* American College of Obstetrics and Gynecology Committee opinion no. 623: emergent therapy for acute-onset, severe hypertension during pregnancy and the postpartum period. Obstet Gynecol 2015;125(2):521–5.)

Side effects:

- Fetal: no known fetal adverse effects. There are long-term postdelivery data up to 7 years of age.
- o Maternal: hepatic dysfunction and necrosis, hemolytic anemia.
- Comments:
 - May be less effective in controlling severe-range blood pressures than the other commonly used medications.

Labetalol 1,2,5,27,33-36

- Mechanism of action: combined α -blocker and β -blocker.
- Use in pregnancy: can be used for both immediate and long-term control of blood pressure.
- Dose:
 - Immediate control: 20, 40, 80 mg IV given every 10 minutes as needed over a 20-minute period (maximum dose, 300 mg IV). Can give 200 mg orally if unable to achieve IV access. Can also be used as an infusion at a rate of 1 to 2 mg/min IV (second line).
 - Long-term control: 2 to 3 doses divided daily with a daily maximum of 2400 mg.
- · Side effects:
 - o Fetal: possible concern of IUGR (contradictory and inconclusive evidence).
 - Maternal: bronchoconstriction, heart block, orthostatic hypotension, sleep disturbances, fatigue, bradycardia.
- Comments:
 - Avoid in patients with asthma, heart disease, congestive heart failure, or if the maternal heart rate is less than 60 beats/min.

Nifedipine 1,5,27,37

- Mechanism of action: calcium channel blocker.
- Use in pregnancy: can be used for immediate and long-term control of blood pressure.
- Dose:
 - Immediate control: 10, 20, 20 mg orally respectively every 20 minutes if blood pressure is still in the severe range (see Fig. 1).
 - o Long-term control: 30 to 120 mg daily dose of the extended release preparation.
- Side effects: hypotension, headache, reflex tachycardia.
- Comments: should be used with caution in patients receiving magnesium sulfate because there is a theoretic risk of hypotension and neuromuscular blockade when combined.

Hydralazine^{1,2,5,13,27,36}

- Mechanism of action: peripheral vasodilator.
- Use in pregnancy: urgent control of blood pressure.
- Dose: 5 to 10 mg IV over 2 minutes repeated every 20 minutes with a single cumulative dose of a maximum of 20 mg (after that, switching to another agent is recommended).
- Side effects: maternal hypotension, reflex tachycardia, vomiting, headache, and aggravation of angina pectoris.

MATERNAL EARLY WARNING CRITERIA

The National Partnership for Maternal Safety defined a list of abnormal parameters (Box 1) that require immediate bedside evaluation by a health care provider. The

Box 1

Maternal early warning criteria

- Systolic blood pressure of less than 90 or greater than 160 mm Hg
- Diastolic blood pressure of greater than 100 mm Hg
- Heart rate less than 50 or greater than 130 beats per minute
- Oxygen saturation on room air, at sea level less than 95%
- Oliguria (<35 mL/h for 2 hours or more)
- Maternal agitation, confusion, or unresponsiveness (changed mental status)
- Nonremitting headache in patients with hypertensive disease of pregnancy
- Shortness of breath

Modified from Mhyre JM, D'Oria R, Hameed AB, et al. The maternal early warning criteria: a proposal from the National Partnership for Maternal Safety. J Obstet Gynecol Neonatal Nurs 2014;43(6):773; with permission.

aim of these early warning parameters is to provide timely diagnostic and therapeutic interventions and enhance quality of care. 38,39

STRATEGIES TO IMPROVE MATERNAL AND FETAL OUTCOMES

Early recognition, timely and appropriate intervention, and adherence to guidelines serve as the foundation for achieving optimal and quality care for mothers and fetuses. Implementation of nationwide or institutional guidelines in the United States, United Kingdom, and Canada has shown a decline in complication rates caused by hypertensive disorders. ^{7,40–43} Some suggested strategies for consideration to reduce the rate of potential preventable complications are as follows ^{8,39}:

- Introduction of hospital-wide early warning criteria (including the emergency department) for obstetric patients.
- Guidelines to mandate immediate bedside assessment by an appropriate health care provider if any of the early warning criteria are met (any team member taking care of the patient should be able to escalate).
- Staff training regarding the proper measurement of blood pressure in patients.
- Administration of appropriate antihypertensive medication in a timely fashion in patients with persistent severe-range blood pressures (>160/110 mm Hg).
- Establish institution-wide/hospital-wide evidence-based guidelines and protocols for management of hypertensive disorders of pregnancy.
- Introducing checklists or order sets to standardize management by all providers.
- Periodic drills and simulations for all members of the obstetric team with debriefings and feedbacks.
- Debriefings and team meetings after poor/adverse outcomes or near misses to help avoid these events in the future.
- Early and appropriate involvement of subspecialist care, including maternal-fetal medicine specialists, anesthesia, internal medicine, nephrology, hematology, critical care, and so forth, as needed.

MANAGEMENT BEYOND BLOOD PRESSURE CONTROL

Once the blood pressure has been reduced to target range, a more thorough and detailed evaluation can be undertaken. Management is dictated by the information obtained and ultimately the final diagnosis.

Transfer to the ICU may be indicated in certain patients with a hypertensive disorder of pregnancy either in the antenatal or postpartum period. Such decisions are made collectively as a team and are based on the stability of the patient, physical examination, vital signs, laboratory values, imaging, and degree of anticipated level of care needed. Another determining factor is the level of care available at a local level. If clinically possible, fetal monitoring should be undertaken in certain ICU patients. In the presence of any of the following factors, strong consideration should be given to critical care transfer for the patient to receive a higher level of care. 44,45

- Need for respiratory support and possible intubation.
- Vital sign abnormalities, such as a heart rate greater than 150 beats/min or less than 40 beats/min.
- Tachypnea (respiratory rate >35/min).
- Patients with acid-base imbalance or severe electrolyte abnormalities.
- Need for pressor support or other forms of cardiovascular support.
- Need for more invasive monitoring, such as pulmonary artery catheterization.
- Abnormal ECG findings, especially patients who require further intervention, such as cardioversion or defibrillation.
- Patients refractory to first-line hypertensive medications who require a drip.

Once a diagnosis is made, management is tailored to that specific diagnosis, including the use of other medications. Optimal timing of delivery is decided by multiple factors, including fetal well-being, gestational age, and type of hypertensive disorders. Some hypertensive disorders of pregnancy can potentially be managed expectantly, like preeclampsia, without severe features, whereas others, like eclampsia, require delivery soon after maternal stabilization.

The following points are reemphasized as critically important concepts and components of high-risk pregnancy and postpartum care for hypertensive patients:

- Maternal hypertensive disorders are among the leading causes of maternal and fetal morbidity and mortality.
- Systolic blood pressure greater than 160 mm Hg is associated with many adverse maternal outcomes, such as stroke and pulmonary edema.
- Early recognition and prompt appropriate treatment are essential.
- Blood pressure measurements greater than or equal to 160/110 mm Hg lasting longer than 15 minutes warrant immediate medical therapy.
- Hydralazine, labetalol, and nifedipine are currently considered first-line treatment options for the emergent reduction of blood pressure in pregnancy.
- Methyldopa is not used for urgent reduction of blood pressure.
- Magnesium sulfate is not recommended for use as an antihypertensive agent.
- If first-line treatments fail to reduce blood pressure, then consultation with a specialist is warranted.
- Early maternal warning signs, such as a systolic blood pressure greater than 160 mm Hg, tachycardia, and oliguria, allow timely diagnostic and therapeutic interventions.
- Following evidence-based guidelines has shown a reduction in the incidence of preventable morbidity and mortality.

Health care providers taking care of obstetric patients should familiarize themselves with the most updated classifications and management of hypertensive disorders of pregnancy.

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