

## An Overview of Hypertension in Pregnancy: Risk to the Mother and the Fetus

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Hypertension, Blood pressure, Cardiovascular disease, Pregnancy.

### What is Hypertension?

Hypertension as defined by World Health Organization is blood pressure (BP) equal to or greater than 140/90 mm Hg, whereas normal and optimal levels are 130/85 mm Hg and 120/80 mm Hg, respectively [1,2]. Recently, American College of Cardiology and American Heart Association have revised the criteria for diagnosis and management of BP. Normal BP is less than 120/80 mm Hg and is considered elevated when it rises above this value. Stage I hypertension is defined as systolic BP of 130-139 mm Hg and/or diastolic BP of 80-89 mm Hg, while stage II is when BP is equal or higher than 140/90 mm Hg [3]. Hypertension is one of the known major risk factors for cardiovascular disease.

Currently, the rates of hypertension are lower in women than in men; however, women may have higher rates of hypertension in the future [2]. Likewise the prevalence of hypertension in pregnancy has increased by 67% in the last decade [4]. In pregnancy, hypertension is defined as BP >140/90 mm Hg on two occasions at least 4 hours apart. Not surprisingly, about 5% and 7% of all pregnancies are complicated by hypertension. Hypertension remains one of the major causes of maternal and fetal morbidity and even mortality [5] (Table 1).

Maternal Risks	Fetal Risks
Cerebrovascular accident	Stillbirth
Pulmonary edema	Preterm birth
Myocardial infarction	Restriction of growth
Renal failure	
Postpartum hemorrhage	

**Table 1:** Maternal and Fetal Risks in Hypertensive complications of pregnancy.

### What are the types of hypertension in pregnancy?

Hypertension in pregnancy is categorized into chronic hypertension, preeclampsia-eclampsia, chronic hypertension with superimposed preeclampsia, and gestational hypertension [6]. Preeclampsia-eclampsia and chronic hypertension with superimposed preeclampsia usually lead to the highest maternal-fetal risk (Table 2).

Types of Hypertension	Diagnosis	Associated Features
Chronic hypertension	<ul style="list-style-type: none"> <li>Hypertension either present before pregnancy or diagnosed prior to 20 weeks of gestation</li> <li>BP &gt; 140 mm Hg systolic and/or 90 mm Hg diastolic</li> </ul>	<ul style="list-style-type: none"> <li>Renal disease</li> <li>Vascular disease</li> <li>Retinopathy</li> <li>Left ventricular hypertrophy</li> </ul>
Preeclampsia	<ul style="list-style-type: none"> <li>New-onset hypertension, usually after 20 weeks of gestation</li> <li>BP &gt; 140 mm Hg systolic and/or 90 mm Hg diastolic and</li> <li>More than 300 mg of protein in 24-hour urine collection or Protein/creatinine ratio greater than 0.3 mg/dL</li> <li>or any of the following in the absence of proteinuria</li> <li>Thrombocytopenia</li> <li>Creatinine &gt;1.1 mg/dL or doubling of baseline</li> <li>Elevated AST/ALT twice normal</li> <li>Pulmonary edema</li> </ul>	<ul style="list-style-type: none"> <li>Hemoconcentration</li> <li>Thrombocytopenia</li> <li>Hemolysis</li> <li>Disseminated intravascular coagulation</li> <li>Renal failure</li> <li>Pulmonary edema</li> <li>Cerebral edema</li> <li>Visual disturbances</li> <li>Liver hematoma</li> <li>Placental abnormalities</li> </ul>
Chronic hypertension with superimposed preeclampsia	<ul style="list-style-type: none"> <li>Preeclampsia in women with preexisting chronic hypertension</li> </ul>	<ul style="list-style-type: none"> <li>As above</li> </ul>
Gestational hypertension	<ul style="list-style-type: none"> <li>BP &gt; 140 mm Hg systolic and/or 90 mm Hg diastolic without features of preeclampsia</li> </ul>	<ul style="list-style-type: none"> <li>Higher risk of preeclampsia</li> <li>Higher risk of hypertension in future</li> </ul>

**Table 2:** Hypertensive Disorders in Pregnancy.

In order to diagnose hypertension in pregnancy, two readings must be taken four hours apart above the cutoff [5]. BP should be measured after a minimum of 10 minutes of rest. It is important that the patient has not consumed caffeine or tobacco in the last 30 minutes as they can temporarily increase BP. In clinical practice, another error commonly encountered is the wrong BP cuff size. Appropriate cuff size covers 40% of the arm length and is 1.5 times the circumference of the arm positioned at the level of the heart [7].

### Chronic hypertension

Chronic hypertension complicates 0.8-1.5% pregnancies. Secondary causes of hypertension are identified only in 11-14% of these young women, i.e. renal, adrenal, endocrine, autoimmune, and vascular. However, 85-89% cases of hypertension that are of unknown etiology are referred to as having “Essential Hypertension” [4].

Diagnosis of chronic hypertension during pregnancy is based on BP > 140/90 mm Hg on two separate occasions at least 4 hours apart prior to 20 weeks. Severe if BP is > 160/110 mm Hg, and diagnosis can be confirmed within minutes to facilitate timely treatment [5]. Clinicians should keep in mind that a subset of patients may have “White coat hypertension” a phenomenon of elevated BP in the presence of health care providers. Although the cause may seem benign, 8% of white coat hypertension cases lead to preeclampsia and 40% to gestational hypertension [8].

A study involving nearly 30,000 pregnant women who had chronic hypertension illustrated that the risk of cerebrovascular accidents, pulmonary edema, renal failure, or maternal morbidity were five to six times higher than in normal women [9]. Additionally, women with chronic hypertension are 1.8 times as likely to have a planned cesarean delivery prior to onset of labor, and have twice the risk of postpartum hemorrhage [10,11]. Chronic hypertension is also associated with fetal risks including preterm delivery in 28% and low birth weight in 17% of infants born to hypertensive mothers [12].

Longstanding hypertension may affect various organ systems in the body including vasculature, kidneys, heart, eyes and brain. Kidneys typically first affected by high BP and therefore, assessment of renal function and degree of proteinuria are indicated as the initial test. Women with chronic hypertension in pregnancy should undergo additional baseline laboratory tests including complete blood count, serum creatinine and blood urea nitrogen, serum electrolytes, serum aspartate aminotransferase and alanine aminotransferase, spot urine protein/creatinine ratio, and an electrocardiogram/echocardiogram [5].

Thresholds for use of anti-hypertensive drugs in pregnant women is a subject of controversy, due to the effects that it may have on the fetus. In mild cases, the risk benefit ratio for pharmacological therapy to treat hypertension remains inconclusive [13]. However in women with significantly elevated BP >160/110 mm Hg, prompt treatment is indicated during pregnancy. The balanced goal

of anti-hypertensive therapy is to prevent both maternal and fetal complications.

### Preeclampsia

Preeclampsia complicates 2-8% of pregnancies and the rates have increased by 25% in the last two decades [14,15]. Preeclampsia is defined as elevated BP of >140/90 mm Hg on two occasions at least 4 hours apart along with proteinuria and/or evidence of end organ involvement. End organ involvement may manifest as: i) symptoms of severe headaches, visual disturbances, vomiting, abdominal pain, swelling of hands, face or feet, hyperreflexia, or ii) Abnormal laboratory tests such as elevated liver enzymes, low platelets, or elevated creatinine [16]. Risk factors for development of preeclampsia include prior history of preeclampsia, chronic hypertension, multifetal gestations, pre-gestational/gestational diabetes, thrombophilia, systemic lupus erythematosus, obesity, antiphospholipid antibody syndrome, advanced maternal age, underlying kidney disease, assisted reproductive technology, and obstructive sleep apnea [17-20]. Preeclampsia with severe features carries the highest risk of maternal-fetal complications thereby necessitating delivery planning. These features include a systolic blood pressure over 160 mm Hg or a diastolic blood pressure above 110 mm Hg, thrombocytopenia, impaired liver function, renal insufficiency, pulmonary edema, sudden headaches unresponsive to medication, or visual disturbances [21]. Preeclampsia with severe features is especially likely to cause hematologic effects, such as thrombocytopenia and hemolysis [22].

Many studies have been undertaken to find a preventative strategy for preeclampsia, but most remain inconclusive. Cochrane review analyzed 13 and concluded that increased calcium intake did have a significant effect on reducing preeclampsia [23]. American College of Obstetrics and Gynecology recommend use of daily low dose aspirin 81 mg starting between 12-28 weeks until delivery to prevent preeclampsia in high risk women [24].

### Chronic Hypertension with superimposed Preeclampsia

Pregnant women with chronic hypertension at increased risk of developing preeclampsia. Preeclampsia may complicate 20-50% of women with chronic hypertension, a rate that is five times more compared to an otherwise healthy pregnant woman [9,25,26]. Superimposed preeclampsia can be difficult to diagnose, as complications from a worsening of chronic hypertension can be confused with superimposed preeclampsia. Superimposed preeclampsia should be suspected if there is a sudden increase in a previously well-controlled hypertensive patient along with a new or an increase in proteinuria or other organ system involvement. Laboratory test abnormalities seen in superimposed preeclampsia may include elevated hematocrit, thrombocytopenia, hyperuricemia, worsening proteinuria, elevated serum creatinine and higher levels of liver transaminases [27].

Interestingly, women who develop superimposed preeclampsia on chronic hypertension are more likely to encounter severe complications compared to women who have either condition alone. The risk of fetal growth restriction may be as high as 50%,

along with an increased risk of preterm delivery and placental abruption [28,29].

### Gestational Hypertension

Gestational hypertension is characterized by a mildly elevated BP >140/90 mm Hg, usually near term without features of preeclampsia, i.e. organ system involvement. The cause remains unclear, however, women with gestational hypertension tend to develop hypertension later on in life and are likely to experience it again during another pregnancy [16].

### Antihypertensive Medications in Pregnancy

The goal of antihypertensive therapy in pregnancy is a modest decrease in BP. Antihypertensive therapy is indicated for persistently high BP of 160/110 mm Hg or more. In a study comparing less intensive (<100 mm Hg) vs. intensive (<85 mm Hg) control of diastolic BP. Intensive control of hypertension does not improve fetal complications but only marginal decrease in progression to severe hypertension [30].

Commonly used medications in pregnancy to treat hypertension include labetalol, nifedipine, methyldopa, and hydrochlorothiazide (Table 3). Labetalol and nifedipine are two of the most commonly used drugs used and are considered first line agents if long-term care is required. Methyldopa is generally not used as much as it can be less effective compared to the other drugs, and has many side effects [13]. Diuretics such as hydrochlorothiazide are not typically used as primary agents for the treatment of hypertension [31]. Diuretics may also theoretically have additional side effects such as intravascular volume depletion, fetal growth restriction, or oligohydramnios.

Medications	Mode of action	Dose	Side Effects
Methyldopa	Central alpha adrenergic stimulant	500-3000 mg/day in 2-4 doses orally	Drowsiness, depression, dizziness
Hydrochlorothiazide	Diuretic, second-line or third-line agent	12.5-50 mg/day	Intravascular volume depletion, electrolyte abnormalities
Nifedipine	Calcium channel blocker	30-120 mg/day orally (extended-release)	Avoid in tachycardia. Do not use sublingually

**Table 3:** Common Medications used in Pregnancy.

### Postpartum Considerations

Postpartum care should be customized to incorporate the unique requirements of women with hypertensive complications of pregnancy. Early follow up within a week of discharge is recommended in postpartum women with elevated BP. American College of Obstetrics and Gynecology recommends a comprehensive plan including referral to primary care physician to ensure ongoing surveillance and risk management strategies. Suggested components of a postpartum care plan include an infant feeding plan, follow-up laboratory tests in case of complications, future risk assessment, management of postpartum problems, and ongoing evaluation of chronic health conditions [32]. Counseling regarding short and long term risks, cardiovascular risk assessment,

and implications of hypertensive disease are the key components. Medications should be individualized and adjusted to ensure patient compliance, underlying risk profile and compelling indications if any. Most of the commonly used antihypertensive drugs are safe for treating hypertension in breast feeding women including calcium channel blockers and angiotensin converting enzyme inhibitors. However, diuretics may reduce breast milk quantity and therefore their use should be limited. Methyldopa should ideally be avoided to minimize the risk of depression, as postpartum women are particularly vulnerable during this period [33].

Hypertensive complications in pregnancy may serve as a window to future cardiovascular health and therefore, provide a unique opportunity to impact future health in these young women through counseling, education and appropriate follow up.

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