



APEC Chronic Hypertension in Pregnancy Guidelines

Chronic hypertension (CHTN) is present in as many as 5% of pregnant women with the highest rates noted in women 30 years of age and over and in African Americans. CHTN in pregnancy is defined as elevated blood pressure documented either: 1) prior to pregnancy; 2) before the 20th week of pregnancy; or 3) continues more than 12 weeks postpartum.(ACOG, 2013; Sibai, 2010) Hypertension is defined as a systolic blood pressure of ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg or both documented on at least 2 occasions and measured at least 4-6 hours apart.(ACOG, 2013; Sibai, 2010) Elevation of either the diastolic or systolic component alone is sufficient to make a diagnosis. CHTN is subdivided into primary (essential) and secondary. 90% of CHTN is primary with the remaining 10% secondary to one or more underlying diseases such as renal disease, collagen vascular disease, endocrine disorders, or coarctation of the aorta. (Sibai, 2010)

CHTN in pregnancy can be subcategorized as either mild or severe. Current guidelines define **mild CHTN** as a systolic BP 140-159 mm Hg and/or diastolic BP 90-109 mm Hg documented on at least 2 occasions and measured at least 4-6 hours apart. This definition is analogous to that used for categorization of pre-eclampsia. **Severe CHTN** is defined as systolic BP ≥ 160 mm Hg and/or diastolic BP ≥ 110 mm Hg documented on at least 2 occasions and measured 4-6 hours apart. Patients with CHTN can be classified as either low-risk or high-risk for adverse outcomes depending on the severity of their disease and prior history. Low-risk pregnant CHTN patients are those with mild essential HTN and no history of perinatal loss or end organ involvement. Pregnant women with CHTN at high risk include those with secondary HTN, evidence of end organ damage (e.g. renal insufficiency, retinal changes), previous perinatal loss, or baseline BP $\geq 160/110$ on or off medications.

Management of patients with CHTN diagnosed and treated prior to pregnancy is fairly straightforward, but undiagnosed CHTN in pregnant women who present later for care can be confused with pre-eclampsia or gestational hypertension (GHTN). In the absence of a preconceptional diagnosis of CHTN, measuring blood pressure before 12 weeks is optimal since the normal gestational decrease of blood pressure occurs at 16-18 weeks and may mask undiagnosed CHTN. Pre-eclampsia can be distinguished from CHTN in that it usually appears after 20 weeks gestation in previously normotensive women and is usually, but not always, accompanied by proteinuria; if severe, there will often be signs and symptoms of organ involvement including hemolysis, elevated liver enzymes, elevated serum creatinine, low platelet count, headache, or epigastric pain. Oliguria and elevated Hgb and Hct levels

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usually indicate hemoconcentration, another factor further indicative of pre-eclampsia. Systemic lupus erythematosus or primary renal disease should be considered if the diagnoses of CHTN or pre-eclampsia do not apply. (ACOG, 2013) Risks of CHTN in pregnancy include superimposed pre-eclampsia, abruption, premature delivery, intrauterine growth restriction, perinatal mortality, and cesarean delivery. (ACOG, 2013; Sibai, 2010)

HTN that presents in the third trimester without signs and symptoms of pre-eclampsia is often diagnosed as gestational hypertension (GHTN). Up to 40% of pregnant women with CHTN or GHTN will ultimately develop pre-eclampsia. (ACOG, 2013; Sibai, 2010) Signs of superimposed pre-eclampsia may include: 1) the acute onset of proteinuria or a sudden increase over baseline proteinuria; 2) an increase in BP over baseline; 3) onset of symptoms of pre-eclampsia; and 4) development of laboratory abnormalities consistent with organ involvement. (ACOG, 2013; Sibai, 2010) HTN that persists beyond 12 weeks postpartum is reclassified as chronic. (ACOG, 2013)

All women with a diagnosis of CHTN should have laboratory studies obtained at the time of their initial presentation to establish a baseline status and define the severity of the underlying disease.

Baseline CHTN Tests

- Serum creatinine to assess renal function. An initial creatinine of ≥ 1.1 mg/dL should be repeated each trimester.
- Random urine protein/creatinine ratio to assess for proteinuria. Any woman with a ratio of ≥ 0.3 should be evaluated with a 24 hr urine collection.
- Women with long-standing hypertension (>4 yrs), poorly controlled BP or evidence of end organ damage, should also have an EKG to assess for left ventricular hypertrophy. If there is concern for left ventricular hypertrophy, or if there is prior evidence of ventricular dysfunction, an echocardiogram should be performed.
- Women with hypertension resistant to 2 or more medications, hypokalemia (not caused by a diuretic), creatinine >1.1 mg/dL, or a strong family history of kidney disease should be assessed for secondary causes of hypertension. Secondary hypertension is most commonly of renal origin and is assessed through urinalysis and renal ultrasound.

Recommendations

- Pregnant women with systolic BP persistently ≥ 160 mm Hg or diastolic BP ≥ 105 mm Hg should be treated with antihypertensive therapy to achieve a target $< 160/105$ mm Hg.
- Pregnant women receiving monotherapy, without comorbidities, consideration can be given to discontinuation of therapy if BP $< 150/100$ mm Hg and gestational age < 20 weeks. Currently,

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ACOG does not recommend treatment of CHTN or initiation of drug therapy unless there is severe HTN. It is unknown whether there is benefit to tighter control of blood pressure during pregnancy and what the risks are. In the recently completed CHIPS trial, which included patients with GHTN in addition to those with CHTN, there was an increased risk of progression to severe HTN in those with less tight control but there was no difference in any of the other outcomes examined. (Magee et al., 2015) More evidence is needed to make definitive recommendations.

- Pregnant women with DM class D, F, H, R, or T, known renal disease, cardiomyopathy, history of CAD, prior stroke, sickle cell disease, or connective tissue disorders, antihypertensive therapy should be initiated to maintain BP <140/90. (ACOG, 2013)
- Pregnant women on multiple anti-hypertensive agents, the regimen should be adjusted to include agents preferred during pregnancy with a BP goal < 160/105 mm Hg. Pregnant women on anti-hypertensive therapy should have their dose titrated down if the BP is <110/60 or the MAP <60.
- Pregnant women with mild-moderate HTN (<160/105) antihypertensive therapy should be withheld until BP becomes severe (approximately 10-20% of women). (ACOG, 2013).
- Medications should not be initiated or increased for newly elevated or worsening BP after 32 weeks of gestation due to the risks of masking superimposed preeclampsia.
- Smoking cessation should be encouraged.
- Low-dose (81 mg everyday) aspirin should be recommended in women with CHTN for preeclampsia prevention.
- Weekly antenatal testing beginning at 32 weeks of gestation.
- Serial ultrasounds every 4 to 6 weeks beginning at 28 weeks to assess for fetal growth restriction.
- Weekly visits beginning at 32 weeks of gestation.
- Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers are teratogenic and are contraindicated during all trimesters of pregnancy.

Fetal Surveillance

Pregnant women with CHTN are at increased risk for uteroplacental insufficiency and therefore at risk for fetal growth disturbance, oligohydramnios, and IUFD. Antenatal surveillance is indicated to identify signs of these problems that would allow intensified surveillance and delivery prior to fetal jeopardy. All women on therapy and any women with a history of CHTN who is not on therapy but has BP >140/90 should undergo antenatal testing:

- Initial assessment of fetal growth and fluid at 18-22 weeks.
- Repeat US for fluid and growth at 28-32 weeks and every 4-6 weeks until delivery.
- NST, BPP, CST or modified BPP weekly beginning at 32-34 weeks. Women with more severe disease or end organ damage may need twice weekly testing. While the evidence is clear that antenatal testing results in a decrease in perinatal morbidity and mortality, it is unclear that any

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one form of antenatal testing offers a distinct improvement in outcome versus any other. Therefore, the choice of the method of antenatal testing can be individualized to the practice setting, resource availability, and individual patient as needed.

Delivery Plan

- Uncomplicated mild HTN with normal antenatal testing: plan delivery at term
 - Well-controlled patients (on or off meds) with mild or severe hypertension at baseline with normal fetal growth and antenatal testing should be delivered at 39 weeks and no later than 40 weeks
- Patients with HTN with prior adverse pregnancy outcome (stillbirth) are candidates for earlier delivery at 37-38 weeks.
- Patients with severe hypertension refractory to medical treatment but without evidence of pre-eclampsia should be delivered at 37 weeks if antenatal testing and fetal growth are normal.
- In patients with CHTN who develop superimposed pre-eclampsia, management depends on the gestational age at diagnosis
 - For patients diagnosed prior to 34 weeks, consultation with Maternal-Fetal Medicine specialists is recommended to formulate an evaluation and management strategy that optimizes the risk-benefit ratio for the mother and the fetus. If any severe symptoms or significant laboratory abnormalities are present, delivery at an appropriate level facility is likely indicated.
 - For patients diagnosed at 34-36 weeks, decisions on delivery should be individualized based on the severity of the BP elevations, the presence of laboratory abnormalities and the results of fetal testing. If BP elevations are mild, labs are normal and testing is reassuring, delivery may be able to be delayed until 36-37 weeks.
 - For patients diagnosed after 36 weeks, delivery is indicated at the time of diagnosis.

Diagnosis of superimposed preeclampsia

There is often ambiguity in the diagnosis of superimposed preeclampsia. Superimposed preeclampsia may be suspected when a patient who is compliant with her antihypertensive medication (or did not previously require antihypertensive therapy) and has newly elevated or worsening blood pressures after 20 weeks of gestation with associated new or worsening proteinuria. In these patients, the following work up should be performed:

- Serial sitting blood pressures-3 blood pressures with the appropriate sized cuff, 5 minutes apart.
- History and physical to assess for signs and symptoms of severe preeclampsia: headache, vision changes, right upper quadrant/epigastric pain, nausea/vomiting, vaginal bleeding, hyper-reflexia/clonus, or decreased fetal movement.

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- Lab evaluation: CBC, transaminases, creatinine, and urine protein/creatinine ratio or 24 hour urine collection if protein previously elevated.
- Antenatal testing if ≥ 32 weeks.
- Ultrasound for fluid and growth if not performed within the last 4 weeks.

Quality Indicators/Benchmarks

- Baseline creatinine
- 24 hr urine protein or spot urine for protein/creatinine ratio and creatinine clearance
- Ultrasound for growth @ 28-32 weeks
- Antenatal testing by 34 weeks

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Pharmacologic Agents

Oral Antihypertensive Drugs	Dosage	Maternal Adverse Effects
<u>Primary Agents</u>		
Labetalol (mixed alpha and beta blocker)	200-2,400mg/day in 2-3 divided doses	Headache
Nifedipine (calcium channel blocker)	30-120mg/day slow-release preparation	Headache
Methyldopa (centrally acting sympatholytic)	0.5-3.0 grams/day in 2-3 divided doses	Maternal sedation, elevated LFTs, depression
<u>Adjunctive agents</u>		
Hydralazine (direct vasodilator)	50-300 mg/day in 2-4 divided doses	Should not be used as a sole agent due to reflex tachycardia; use with a beta-blocker
Hydrochlorothiazide (diuretic and venodilation)	12.5-50 mg/day but minimal benefit above 25 mg	Can cause volume depletion and electrolyte disorders; rarely initiated in pregnancy, but if patient taking prior to pregnancy may continue

Acute Severe HTN

Severe hypertension can be encountered anytime during pregnancy, but most often occurs when patients present with superimposed pre-eclampsia. Prompt attention to control of marked elevations in the BP are required to prevent symptoms of hypertensive urgency and stroke, but care must be taken to not lower the blood pressure too rapidly and cause neither loss of cerebral perfusion in watershed areas or interfere with uteroplacental perfusion. The goal of acute treatment should be to lower the blood pressure to 140-150/90-100 mm Hg.

Pharmacologic Agents for Treatment of Severe Acute HTN

	Dosage	Maternal Adverse Effects
Hydralazine	5 mg IV or IM, then 5-10 mg every 20-40 minutes IV	Maternal hypotension, fetal bradycardia; maternal tachycardia often dose-limiting side effect
Labetalol	10-20 mg IV, then 20-80 mg every 20-30 minutes, up to a max of 300 mg	Maternal tachycardia and arrhythmia
Nifedipine	10-20 mg PO (NOT sublingual), repeat in 30 minutes if needed	Only used in absence of parenteral options

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References

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