



**COMMUNITY
HEALTH CARE
ASSOCIATION
of New York State**

Maternal Health and Hypertensive Disorders in Pregnancy

**Hypertension Care & Management Webinar Series
August 19th, 2022**

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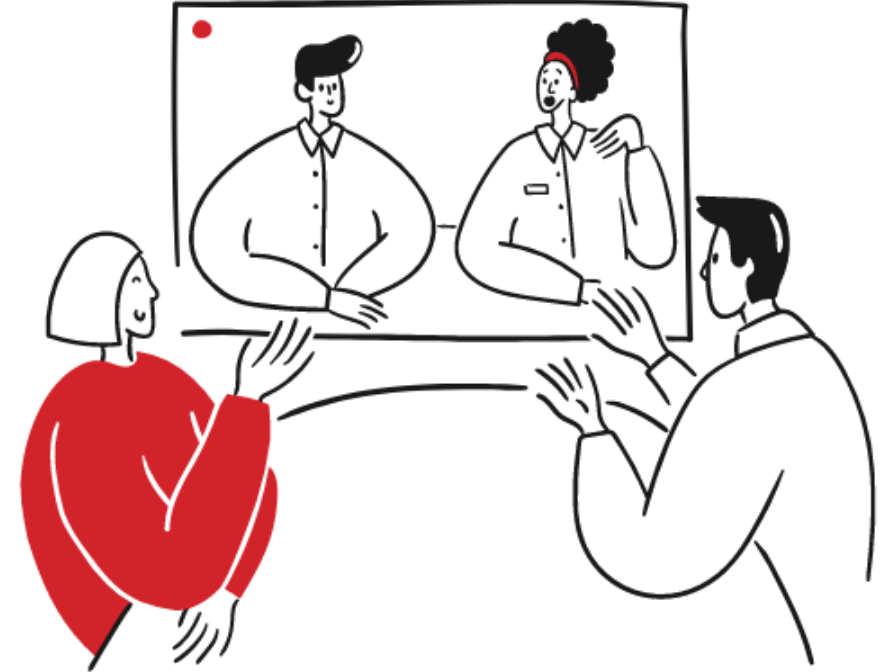
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Housekeeping

- Phones have been muted to prevent background noise.
- Use the chat box to type questions during the webinar.
- This webinar is being recorded and will soon be available to all participants.
- A webinar evaluation will be shared with participants at the end of the meeting. Please provide us with feedback! We need your input to continue to support events like these.



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MEDICINE *of* THE HIGHEST ORDER



Conflicts of Interest

There are no disclosures

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Objectives

1. Introduction (including mortality related to HTN disorders of pregnancy, disparities in prevalence and outcomes).
2. Measurement of blood pressure, staging of HTN and Ambulatory BP monitoring.
Use of HBPM/ABPM in pregnancy.
3. Normal physiology of pregnancy.
4. Hypertensive disorders of pregnancy, definitions, outcomes.
5. Treatment of high BP during pregnancy.

New Definition of Hypertension in pregnancy

The definition of hypertension in pregnancy has not always been standardized, but following the “National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy” recommendation is currently a systolic blood pressure (SBP) ≥ 140 mmHg and/or a diastolic blood pressure (DBP) ≥ 90 mmHg.

Hypertension in Pregnancy

- Hypertension in pregnancy is a condition affecting 5%–10% of pregnancies worldwide.
- Hypertensive disorders of pregnancy constitute one of the leading causes of maternal and fetal morbidity and mortality worldwide.
- It has been estimated that preeclampsia complicates 2–8% of pregnancies globally
- In Latin America and the Caribbean, hypertensive disorders are responsible for almost 26% of maternal deaths, whereas in Africa and Asia they contribute to 9% of deaths.
- Although maternal mortality is much lower in high-income countries than in developing countries, 16% of maternal deaths can be attributed to hypertensive disorders

Hypertension in Pregnancy: Epidemiology

Per pregnancy incidence of 7.5%

Per woman incidence of 15.3%

Contributes to disparities in maternal mortality in the U.S.

- White women: 13 per 100,000 live births
- American Indian and Alaska Native women: 30 per 100,000 live births
- Black women: 41 per 100,000 live births

HDP disproportionately affect Black, American Indian, and Alaska Native women

- Higher odds of HDP in NHB compared to NHW
- Difference eliminated when adjusting for maternal age, pre-pregnancy BMI, smoking, and medical co-morbidities
- Some disparities are explained by higher rates of CVD risk factors

*Garovic VD J Am Coll Cardiol 2020
Grobman WA Obstet Gynecol 2018*

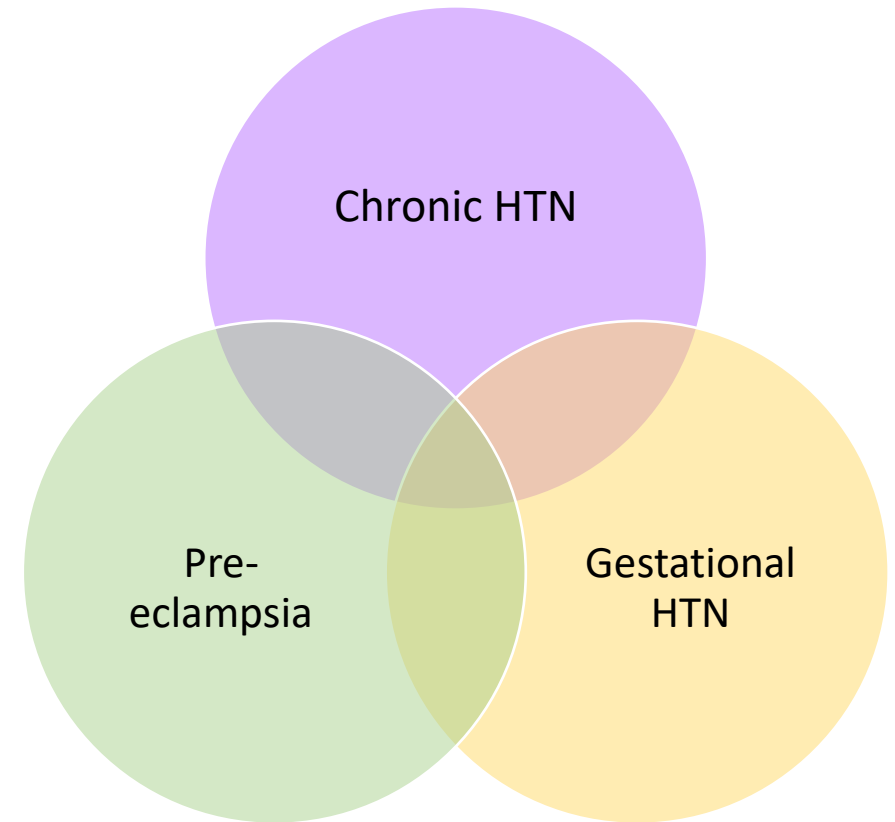
Hypertensive disorders of pregnancy: Overview

HTN in pregnancy is defined as a BP \geq 140/90 mmHg

Hypertensive disorders of pregnancy (HDP) complicate up to 10% of pregnancies.

The **2nd leading cause of global maternal mortality** behind maternal hemorrhage

Significant cause of maternal and offspring **morbidity and mortality**



Garovic VD Hypertension 2021

Hypertensive disorders of pregnancy

- **Preexisting hypertension:** Starts before pregnancy or <20 weeks of gestation, and lasts >6 weeks postpartum with proteinuria.
- **Gestational hypertension:** Starts >20 weeks of gestation, and lasts <6 weeks postpartum.
- **Preexisting hypertension plus superimposed gestational hypertension** with proteinuria.
- **Preeclampsia:** Hypertension with proteinuria (>300 mg/24 h or ACR >30 mg/mmol [265 mg/g]). Predisposing factors are preexisting hypertension, hypertensive disease during previous pregnancy, diabetes, renal disease, first- or multiple pregnancy, autoimmune disease (SLE). Risks are fetal growth restriction, preterm birth.
- **Eclampsia:** Hypertension in pregnancy with seizures, severe headaches, visual disturbance, abdominal pain, nausea and vomiting, low urinary output: Immediate treatment and delivery required.
- **HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome:** Immediate treatment and delivery required.

Hypertension 2022; 79:e21-e41

Immediate Maternal and Fetal Complications of Hypertensive Disorders of Pregnancy (HDP)

Maternal/Fetal Outcomes	Chronic Hypertension	Preeclampsia
Mortality	aOR 1.7 (1.2-2.4)	aOR 2.6 (2.1-3.4)
Myocardial infarction	aOR 3.4 (2.2-5.1)	aOR 3.0 (2.0-4.6)
Stroke	aOR 3.4 (2.8-4.1)	aOR 7.1 (5.3-9.6)
SGA (birth weight < 10 th %ile)	OR 1.8 (1.2-2.6)*	OR 1.5 (1.0-2.2)
Stillbirth	aOR 1.7 (1.6-1.8)	aOR 1.3 (1.2-1.3)
Preterm delivery (<34 wk)	OR 3.1 (2.0-4.8)*	OR 2.6 (1.6-4.2)
Postpartum hemorrhage	aOR 1.3 (1.2-1.3)	aOR 2.3 (2.2-2.4)

* Severe hypertension

Garovic VD Hypertension 2021

Long-Term Maternal Complications of HDP

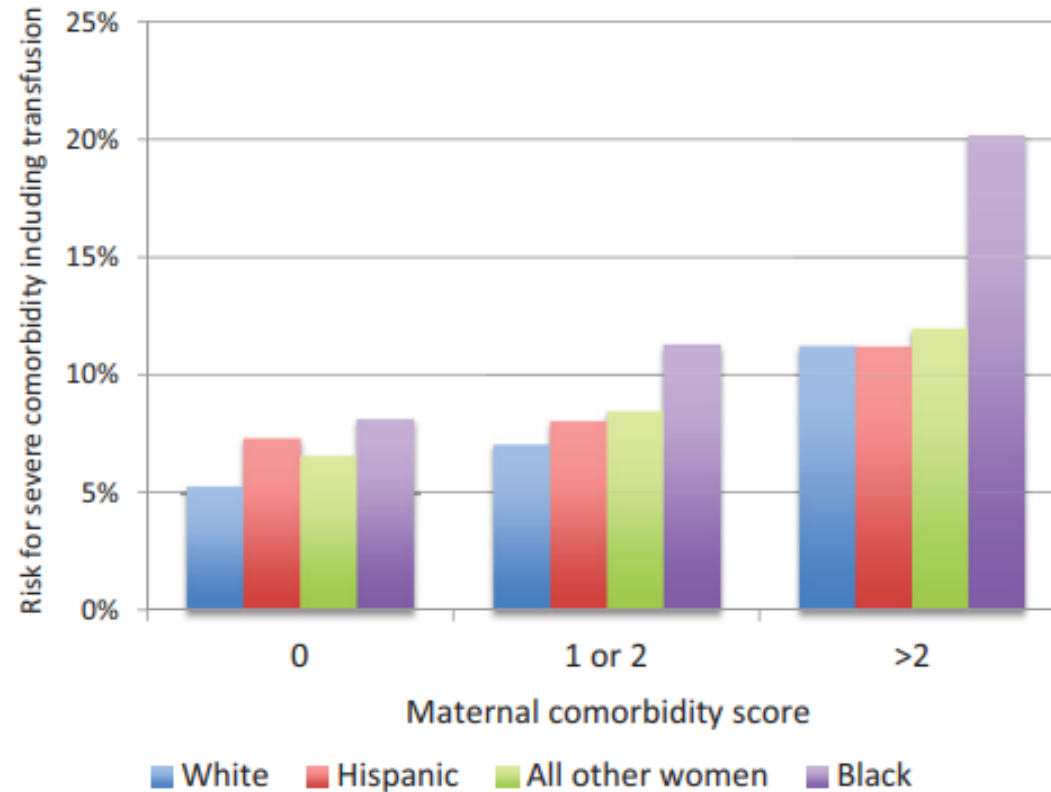
Maternal Outcomes	HDP	Preeclampsia
Chronic hypertension	15% CI 40 years since 1 st birth	7% CI 40 years since 1 st birth
Coronary heart disease	aHR 1.9 (1.4-2.5)	aHR 2.1 (1.4-3.0)
Heart failure	aHR 1.5 (1.3-1.9)	aHR 2.1 (1.6-2.8)
Chronic kidney disease	RR 1.5 (1.1-2.0)*	RR 2.3 (1.5-3.5)
ESRD	RR 3.6 (2.3 -5.7)*	RR 6.6 (2.7-14.8)
Venous thromboembolism	OR 1.5 (1.2-1.9)	aHR 1.6 (1.4-2.0)

CI=cumulative incidence *Gestational hypertension

Hypertension develops **faster** in women with HDP and is **diagnosed up to 10 years earlier** compared with women with normotensive pregnancies

Garovic VD Hypertension 2021

Preeclampsia related severe morbidity is highest in Black women

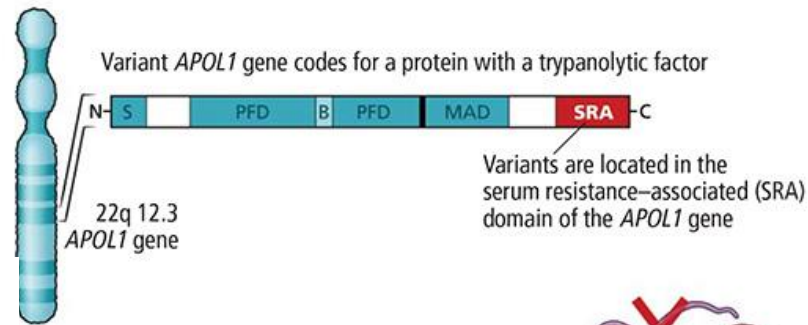


NHB women had higher risk of stroke, pulmonary edema, heart failure, renal failure, and death compared to all other groups

101,741 women aged 15-54 with a dx of PE from a nationwide cohort, 2012-2014

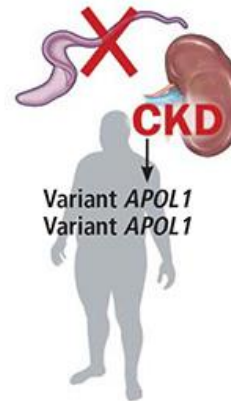
Gyamfi-Bannerman C J Matern Fetal Neonatal Med 2020

Biological factors may increase the risk of PE in Black women



Fetal *APOL1* kidney risk alleles are associated with increased risk for preeclampsia in Black women
OR 3.6 (1.3-9.7)

Hong X AJKD 2020



Having 2 variant alleles confers protection against trypanosomiasis but increases the risk of chronic kidney disease (CKD).

The maternal *HLA-G* 1597 Δ C null mutation is associated with increased risk of pre-eclampsia and reduced *HLA-G* expression during pregnancy in African-American women

Dagan A. Loisel^{1,5}, Christine Billstrand¹, Kathleen Murray¹, Kristen Patterson¹, Tinnakorn Chaiworapongsa^{3,4}, Roberto Romero⁴, and Carole Ober^{1,2,*}

Hispanic women with severe PE appears to have better outcomes than other groups

Table 1
Hypertension (HTN) disorder and race/ethnicity

	White (n = 85) (%)	Black (n = 146) (%)	Hispanic (n = 48) (%)
Gestational HTN	21	7	7
Mild preeclampsia	29	30	65
Chronic HTN	18	24	8
Severe preeclampsia	24	23	21
Chronic HTN with superimposed preeclampsia	8	16	0

Table 2
Hypertension disorder and birth outcomes

	Gestational HTN (%)	Mild Preeclampsia (%)	Severe Preeclampsia (%)
Abruption ^a	No Difference (ND)	ND	ND
Low birth weight ^b	3	3	48
Fetal growth restriction ^b	3	4	51
Admission to neonatal intensive care unit ^b	0	12	56

^a $p < 0.05$; ^b $p < 0.001$.

When women with severe PE were examined separately, negative outcomes were ***highest in Black*** and ***lowest in Hispanic*** women

Carr A J of Neonatal-Perinatal Med 2013

Accurate measurement of BP in pregnancy is essential to appropriate treatment

- ❑ Inadequate treatment increases the risk of placental abruption, stroke
- ❑ Over-treatment can potentially reduce placental perfusion resulting in placental insufficiency, fetal growth restriction



Hemodynamic changes and peripheral edema associated with pregnancy, and PE in particular, may affect the accuracy of algorithms used by oscillometric devices to measure BP

Use of manual BP measurement is the gold standard

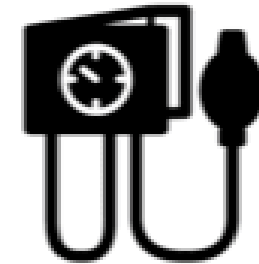
Bello NA Curr Hypertens Rep 2018

Oscillometric Devices Validated in Pregnancy



Device Type	Device	Study Population
Ambulatory	BP Lab ²⁸	Normotensive (without preeclampsia) and hypertensive (with and without preeclampsia)
	Welch Allyn QuietTrak ⁶⁰	Normotensive and hypertensive
Home	Microlife WatchBP Home ³²	Normotensive and hypertensive, without preeclampsia
	Omron MIT ³⁵	Normotensive and hypertensive, without preeclampsia
Clinic	A&D UM-101 ³⁴	Normotensive (without preeclampsia) and hypertensive (with and without preeclampsia)
	Dinamap ProCare 400 ³⁶	Normotensive and hypertensive, without preeclampsia
	Nissei DS-400 ³⁷	Normotensive and hypertensive, with and without preeclampsia
	Omron HEM907 ³⁴	Normotensive (without preeclampsia) and hypertensive (with and without preeclampsia)
Home/Clinic	Omron MIT Elite ²³	Normotensive and hypertensive, without preeclampsia

Manual BP measurement remains the gold standard for BP measurement in pregnancy



Bello NA Hypertension 2018

Home BP Monitoring

- No current guidelines recommending the use of out of office BP measurement as a screening tool for HDP
- May play an important role in post-partum BP monitoring, however not currently standard of care
- Two studies found office and home measurements to be similar (*Tucker KL BMC Pregnancy and childbirth 2017; Naef RW J Perinatol 1998*)
- One study found home measurements to be higher (*Lo C Am J of Obstetrics & Gynecol 2002*)
- Mikami et al recommended trimester specific BP cut-off values

Ambulatory BP Monitoring

- Only current recommended use is to confirm a suspected diagnosis of white coat hypertension prior to initiating medication
- WCH may affect up to 30-70% of pregnant women

Bello NA Curr Hypertens Rep 2018

Cardiovascular Physiology of Pregnancy

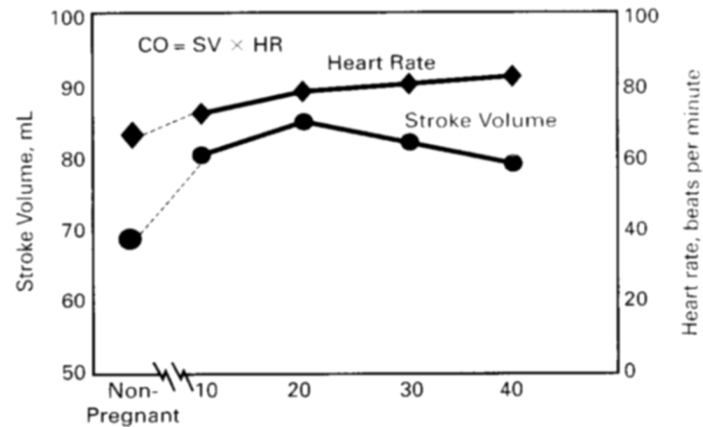
Normal pregnancy is associated with an increase of 30 to 50 % in **blood volume**.

Blood volume increases, starting at the sixth week and rising rapidly until mid pregnancy; the levels peak by 20 to 24 weeks of pregnancy and then are either sustained until term or decrease

An estrogen-mediated stimulation of the renin-angiotensin system results in sodium and water retention appears to be the mechanism underlying the blood volume increase. It occurs early in pregnancy, with increases in plasma volume starting at 6 to 8 weeks and rising progressively until 28 to 30 weeks.

Hemodynamic changes during normal pregnancy

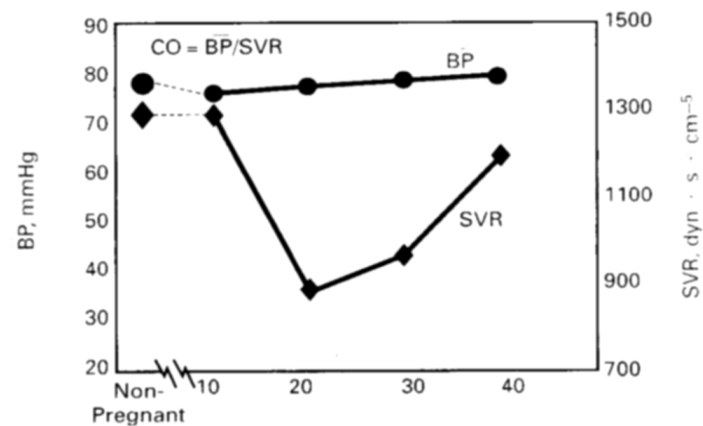
Increased blood volume (30-50%)
alters stroke volume (SV) and
cardiac output (CO).



Increased CO in the 1st trimester is due to increased SV.

Increased CO in the 3rd trimester is due to increased HR.

21% decrease in SVR (vasodilatation)- There is a physiological drop in BP, often detectable before the end of the first trimester.

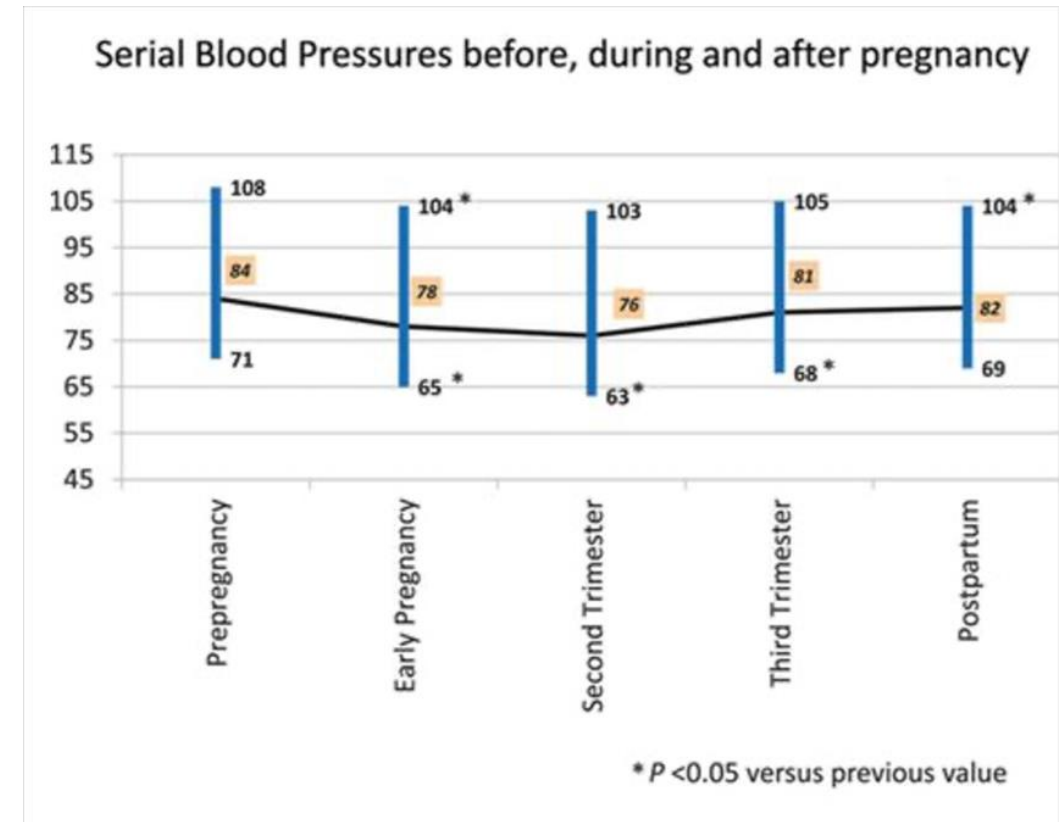
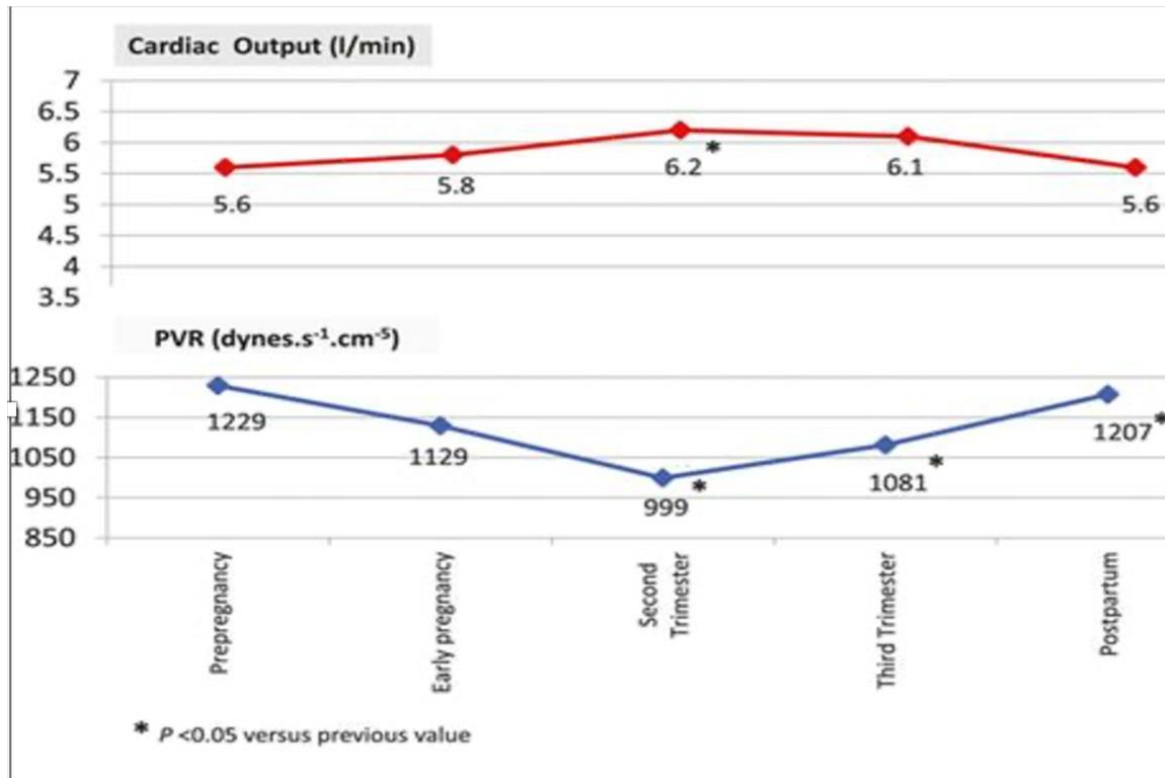


34% decrease in PVR

Increase in heart rate (about 10 BPM).

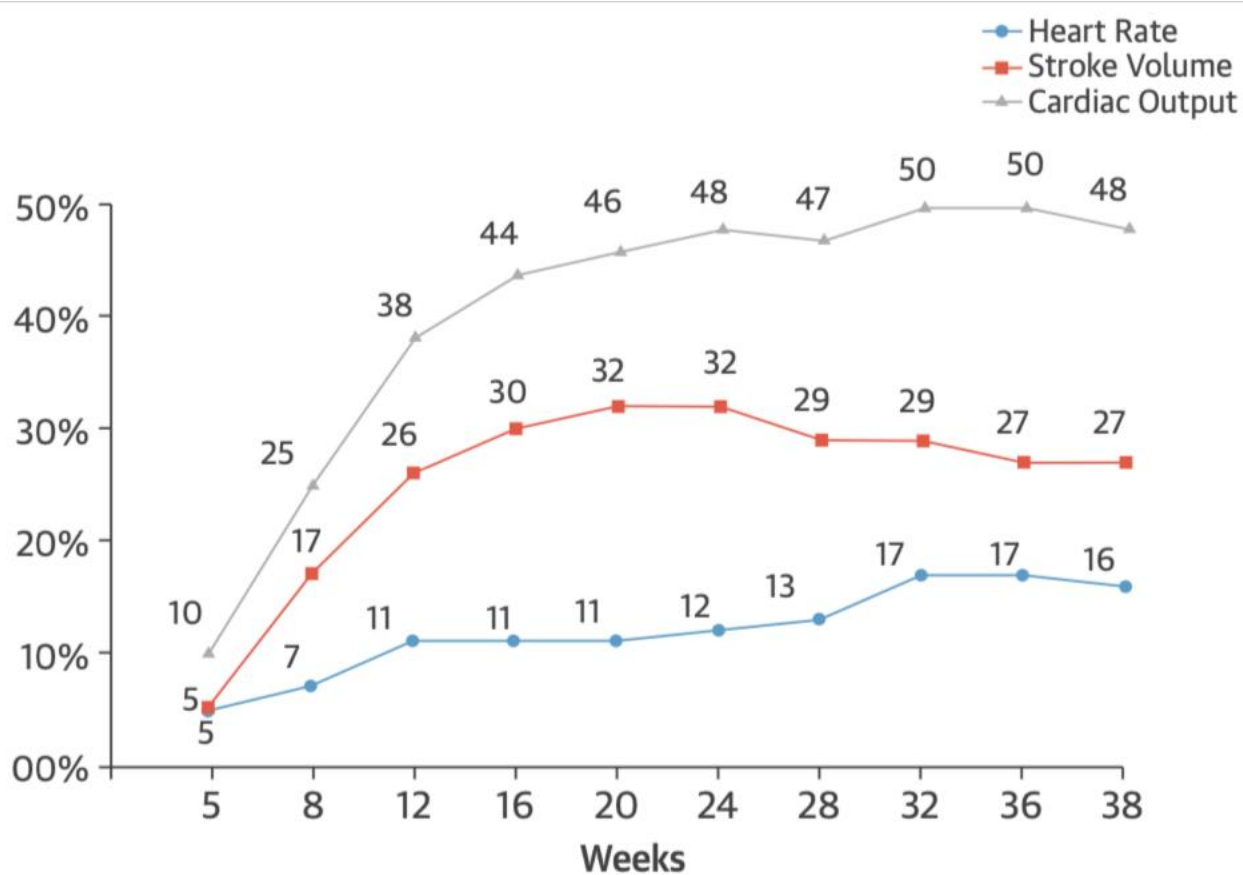
**Increase of CO 30-50%
(peak at 16-28 weeks).**

Usually well tolerated



Monika Sanghavi. Circulation. Cardiovascular Physiology of Pregnancy, Volume: 130, Issue: 12, Pages: 1003-1008.

Hemodynamic changes during pregnancy



Percent changes in heart rate, stroke volume, and cardiac output measured in the lateral position throughout pregnancy compared with pre-pregnancy values. Adapted from Elkayam and Gleicher (1) and Robson et al. (103).

- ↑ blood volume ≈ 50%.
- ↑ cardiac output 30-50% maximum between, 5th and 8th months.
- ↓ systolic and diastolic blood pressure.
- ↓ systemic arterial resistance (hormones, placenta).

Thorne Heart 2004;90:450-6

Increase in CO begins to rise in first trimester and steadily rises to peak at 32 weeks by 30 to 50%.

Elkayam et. Al. JACC VOL. 68, NO. 4, 2016

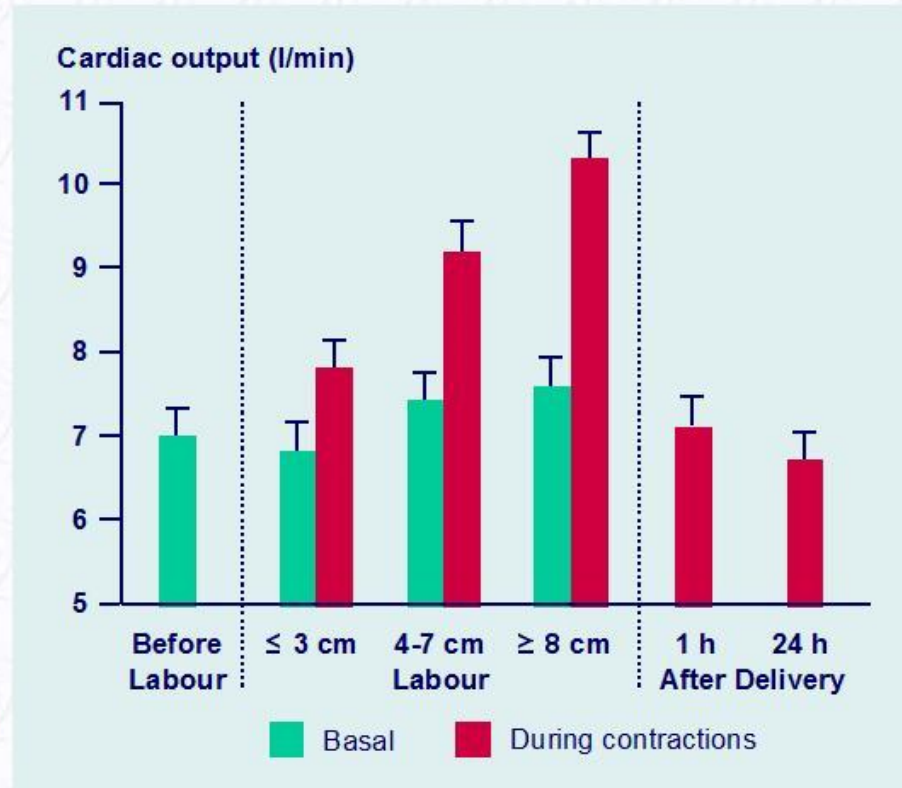
Haemodynamic Changes During Delivery

- Labour:

- ↑ O_2 consumption,
- ↑ baseline cardiac output,
- ↑ cardiac output and blood pressure during uterine contractions, depending on modalities of delivery (epidural analgesia, Cesarean section)

- Post-partum:

- ↑ blood shift from placenta,
- ↑ preload and cardiac output.



Hunter et al. *Br Med J* 1992;68:540-3

After delivery venous return increases because of relief from fetal compression on the IVC.

Immediately postpartum: extra preload may cause clinical deterioration.

Hypertensive disorders of pregnancy (HDP)

The incidence of HDP continues to increase as a result of advanced age at first pregnancy and increased prevalence of obesity, sleep apnea, and other cardiometabolic risk factors. CVD, including cerebrovascular accidents and cardiomyopathy, now accounts for up to half of all maternal deaths.

Pregnancy-related stroke hospitalizations increased >60% from 1994 to 2011, and HDP-associated stroke rates increased 2-fold compared with non-HDP-related stroke.

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Hypertensive disorders of pregnancy

- **Preexisting hypertension:** Starts before pregnancy or <20 weeks of gestation, and lasts >6 weeks postpartum with proteinuria.
- **Gestational hypertension:** Starts >20 weeks of gestation, and lasts <6 weeks postpartum.
- **Preexisting hypertension plus superimposed gestational hypertension** with proteinuria.
- **Preeclampsia:** Hypertension with proteinuria (>300 mg/24 h or ACR >30 mg/mmol [265 mg/g]). Predisposing factors are preexisting hypertension, hypertensive disease during previous pregnancy, diabetes, renal disease, first- or multiple pregnancy, autoimmune disease (SLE). Risks are fetal growth restriction, preterm birth.
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Hypertension 2022; 79:e21-e41

Hypertensive disorders of pregnancy

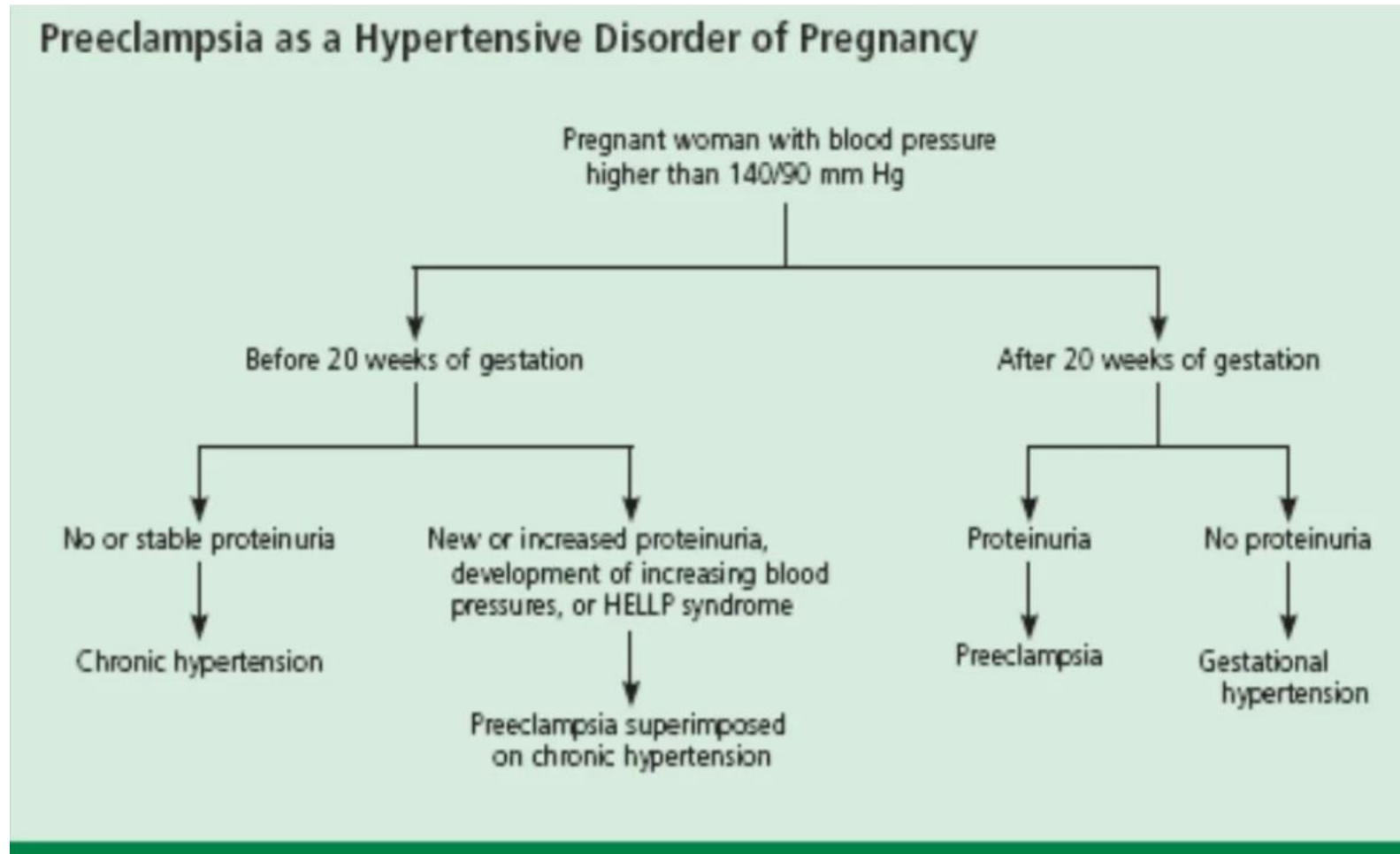


Figure 1. An algorithm for differentiating among hypertensive disorders in pregnant women (HELLP = *hemolysis, elevated liver enzymes, low platelet count*)

CHRONIC HYPERTENSION in pregnancy

Incidence of chronic HTN 0.5-4%

80% essential HTN

20% due to renal disease

CHRONIC HYPERTENSION

BP \geq 140/90 mm Hg before pregnancy or diagnosis before 20 weeks of gestation

Persists after 6 weeks postpartum

Symptoms & signs

↑risk in ➡ Age > 30, obese, multipara, DM, renal disease, black race, family Hx

Difficult to differentiate HPT with superimposed pre-eclampsia from HTN with renal disease

➡both have proteinuria

Secondary HTN

Most ($\approx 90\%$) women with chronic hypertension have primary hypertension. Secondary hypertension may occur in a small proportion of women and is associated with worse maternal and fetal outcomes. It should be considered if maternal age is <35 years, hypertension is severe or resistant, there is no family history of hypertension, or there are suggestive laboratory features such as hypokalemia, elevated creatinine, or albuminuria early in pregnancy.

Obesity and obstructive sleep apnea may play an increasing role in secondary hypertension among pregnant women.

Gestational hypertension

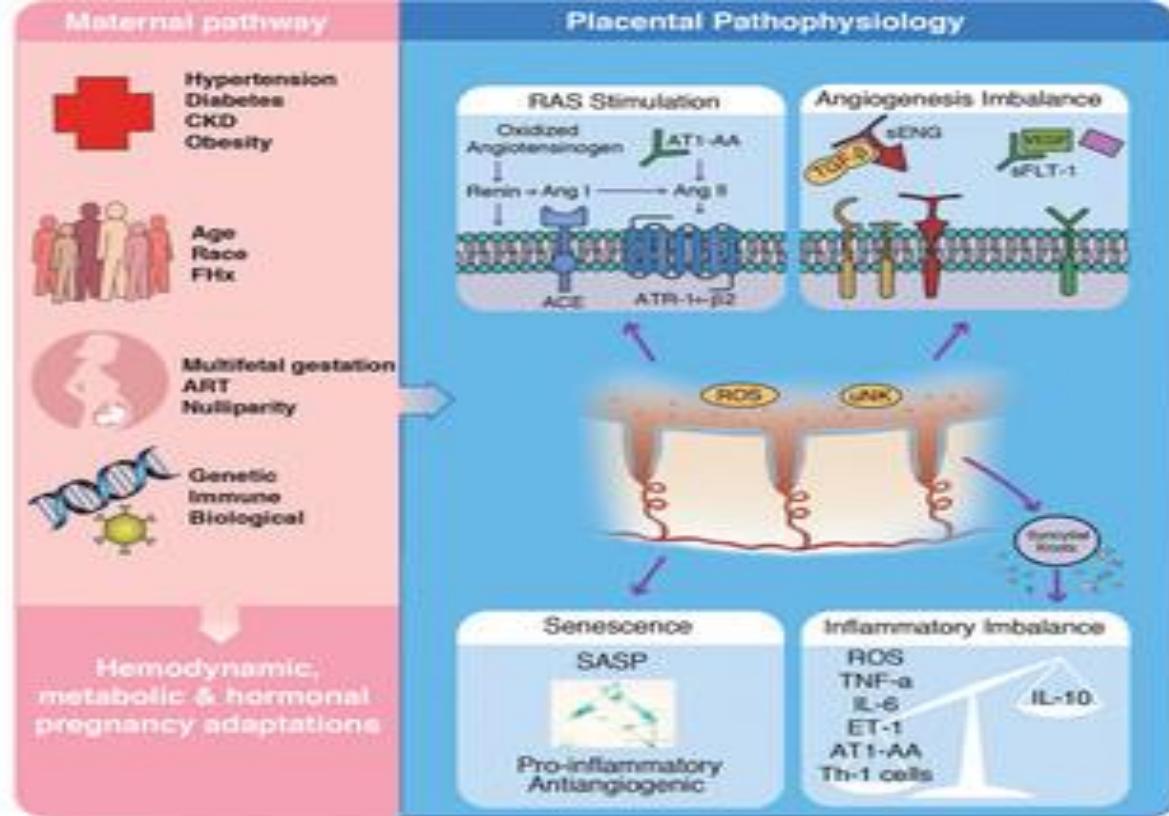
BP \geq 140/90 mm Hg for the first time during pregnancy

No proteinuria

BP returns to normal < 12 Wk postpartum

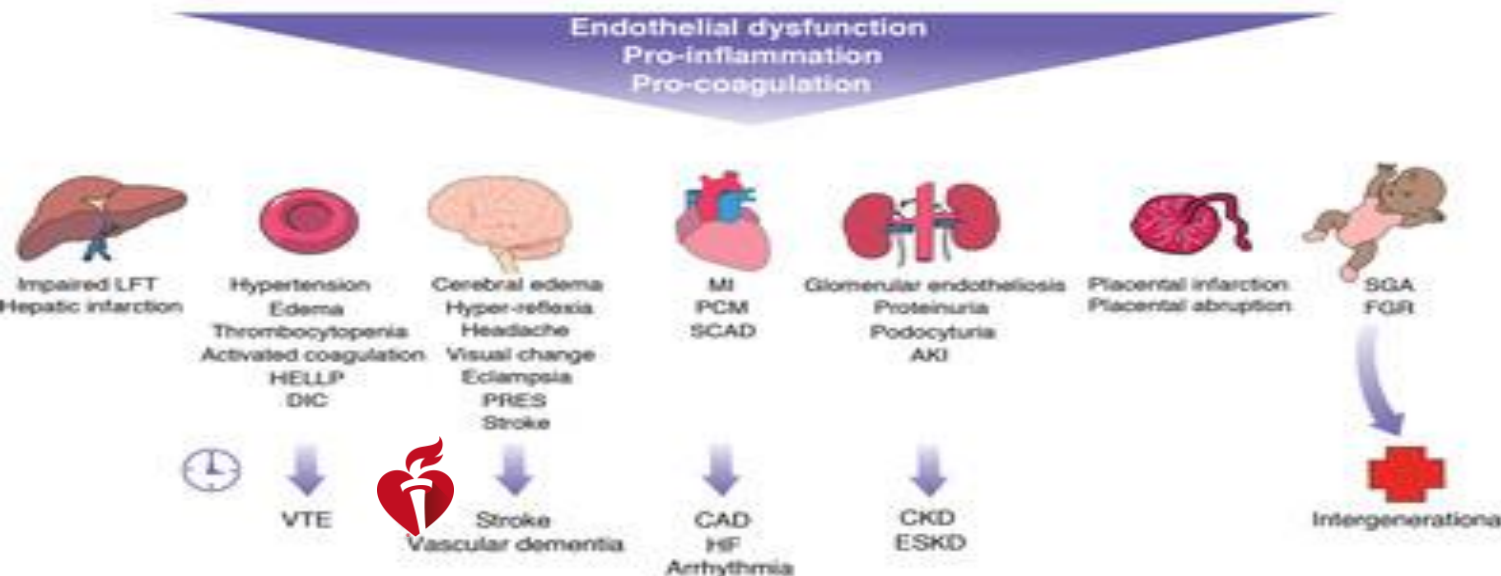
Final Dx made only postpartum

	Pre-eclampsia	Pre-existing (chronic) Hypertension
Parity	usually primigravida	usually multigravida.
Past History	of pre-eclampsia may be present	of hypertension in between pregnancies.
Hypertension	after the 20th week of pregnancy (except in vesicular mole) and disappears within 6 weeks postpartum	before pregnancy, during the first 20 weeks and persists after 6 weeks postpartum.
Proteinuria	If present, it develops after hypertension	If present, it develops before hypertension due to underlying renal disease.



Pathophysiology of pre-eclampsia:

- Vasoconstriction
- Platelet activation with intravascular coagulation.
- Endothelial dysfunction.

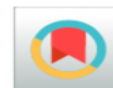


Vesna D. Garovic. Hypertension. Hypertension in Pregnancy: Diagnosis, Blood Pressure Goals, and Pharmacotherapy: A Scientific Statement From the American Heart Association, Volume: 79, Issue: 2, Pages: e21-e41, DOI: (10.1161/HYP.0000000000000208)

THE PRESENT AND FUTURE

JACC STATE-OF-THE-ART REVIEW

Preeclampsia—Pathophysiology and Clinical Presentations



JACC State-of-the-Art Review

Christopher W. Ives, MD,^a Rachel Sinkey, MD,^{b,c} Indranee Rajapreyar, MD,^d Alan T.N. Tita, MD, PhD,^{b,c} Suzanne Oparil, MD^d

ABSTRACT

Preeclampsia is a hypertensive disorder of pregnancy. It affects 2% to 8% of pregnancies worldwide and causes significant maternal and perinatal morbidity and mortality. Hypertension and proteinuria are the cornerstone of the disease, though systemic organ dysfunction may ensue. The clinical syndrome begins with abnormal placentation with subsequent release of antiangiogenic markers, mediated primarily by soluble fms-like tyrosine kinase-1 (sFlt-1) and soluble endoglin (sEng). High levels of sFlt-1 and sEng result in endothelial dysfunction, vasoconstriction, and immune dysregulation, which can negatively impact every maternal organ system and the fetus. This review comprehensively examines the pathogenesis of preeclampsia with a specific focus on the mechanisms underlying the clinical features. Delivery is the only definitive treatment. Low-dose aspirin is recommended for prophylaxis in high-risk populations. Other treatment options are limited. Additional research is needed to clarify the pathophysiology, and thus, identify potential therapeutic targets for improved treatment and, ultimately, outcomes of this prevalent disease.

(J Am Coll Cardiol 2020;76:1690–702) © 2020 by the American College of Cardiology Foundation.

HTN and pre-eclampsia

Hypertension in pregnancy is defined as elevated systolic BP ≥ 140 mm Hg and/or diastolic BP ≥ 90 mm Hg on 2 measurements 4 h apart at rest.

Hypertension is a necessary diagnostic criterion for the preeclampsia syndrome

Compared with normotensive pregnant control patients, hypertension in preeclampsia occurs in the setting of increased systemic vascular resistance and afterload, and decreased cardiac output and intravascular volumes.

Am Coll Cardiol. 2020 Oct, 76 (14) 1690–1702

Incidence and risk factors for preeclampsia

Preeclampsia occurs in 2-8% of pregnancies worldwide

RISK FACTORS

Extremes of reproductive age 15 < & >35 Y

Nulliparity (first pregnancy)

Black race

FH of Preeclampsia in a 1st degree female relative

Hx of preeclampsia in prior pregnancy

Diabetes Mellitus

Obesity ➡ 4.3% ➡ BMI < 19.8 kg/m²

➡ 13.3% ➡ BMI ≥ 35 kg/m²

Pre-existing cardiovascular disease likely plays a role in the development of preeclampsia.

Chronic renal disease

Chronic HTN

Multiple gestations ➡ twins 13 vs 6%

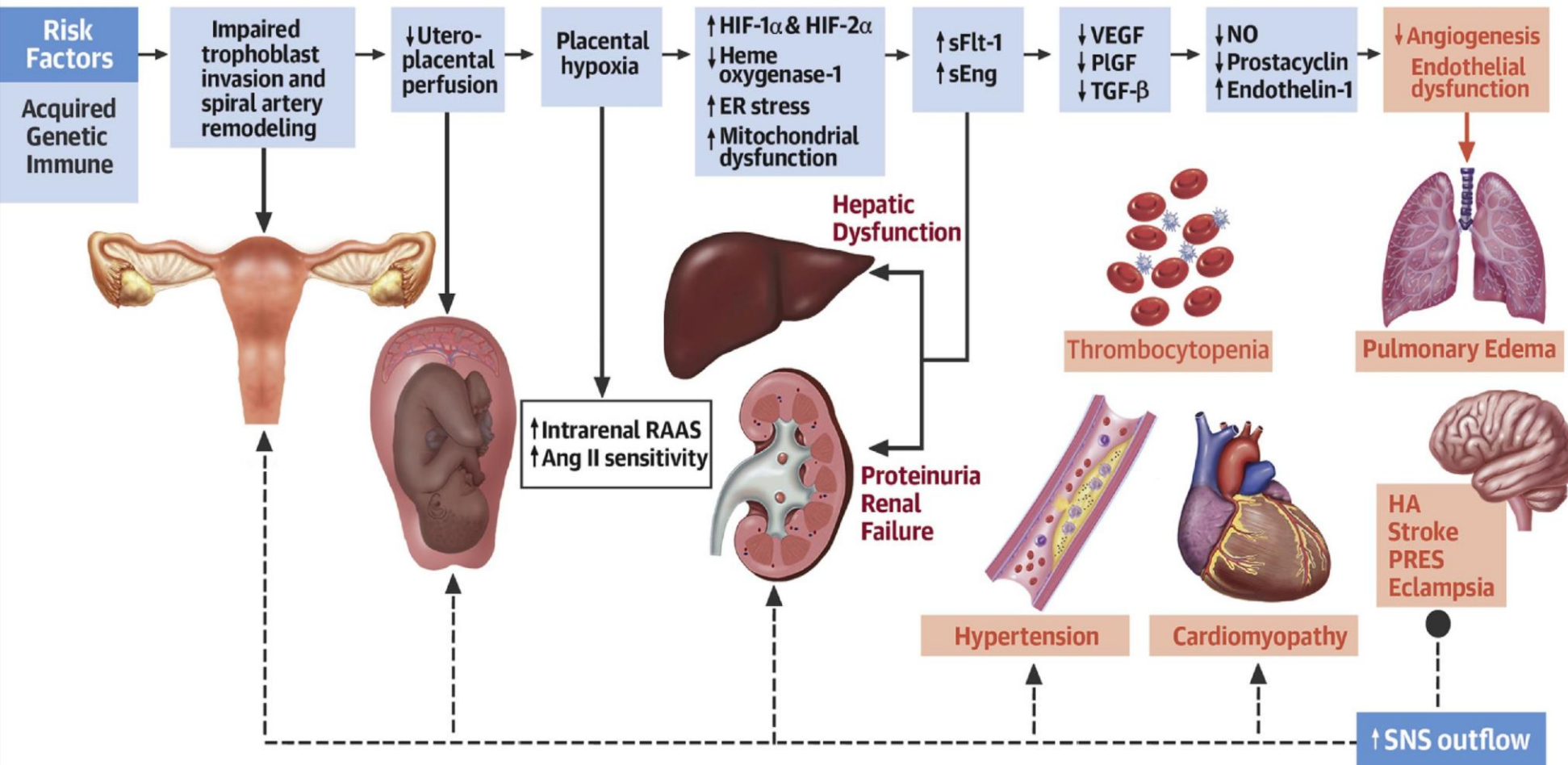
Hypertension. 2022;79:e21–e41.

Risk factors	Effect estimate (95% CI)
High*	
Prior preeclampsia	RR, 8.4 (7.1–9.9) ⁷³
Chronic stage 2 hypertension† (≥140/90 mm Hg)	RR, 5.1 (4.0–6.5) ⁷³
Pregestational diabetes	RR, 3.7 (3.1–4.3) ⁷³
Multifetal pregnancy	RR, 2.9 (2.6–3.1) ⁷³
Antiphospholipid syndrome	RR, 2.8 (1.8–4.3) ⁷³
Systemic lupus erythematosus	RR, 2.5 (1.0–6.3) ⁷³
Chronic kidney disease	OR, 10.4 (6.3–17.1) ⁷⁴
Moderate*	
Maternal age >35 y	RR, 1.2 (1.1–1.3) ⁷³
Prepregnancy BMI >30 kg/m ²	aOR, 3.7 (3.5–3.9) ⁷⁵ RR, 2.8 (2.6–3.1) ⁷³
Family history (first-degree relative)	RR, 2.9 (1.7–4.9) ⁷⁶
Race (Black)	aHR, 1.6 (1.5–1.6) ⁷⁷ HR, 2.2 (1.9–2.6), early onset ⁷⁸ HR, 1.3 (1.2–1.4), late onset ⁷⁸
Low socioeconomic status	aOR, 4.91 (1.9–12.5) ⁷⁹
Nulliparity	RR, 2.1 (1.9–2.4) ⁷³
History of adverse pregnancy outcome:	
Stillbirth	RR, 2.4 (1.7–3.4) ⁷³
Placental abruption	RR, 2.0 (1.4–2.7) ⁷³
Other	
Chronic hypertension (130–134/80–84 mm Hg)	aOR, 2.2 (1.9–2.5), mild ⁸⁰ aOR, 2.7 (2.0–3.5), severe ⁸⁰
Chronic hypertension (135–139/85–90 mm Hg)	aOR, 2.7 (2.3–3.2), mild ⁸⁰ aOR, 3.8 (2.8–5.1), severe ⁸⁰
Severe hypertension	OR, 6.1 (4.4–8.5) ¹⁹
White coat hypertension	RR, 2.4 (1.2–4.8) ⁸¹
Prepregnancy BMI >25 kg/m ²	RR, 2.1 (2.0–2.2) ⁷³
Insulin resistance >75th centile	aOR, 1.9 (1.1–3.2) ⁸²
Gestational diabetes	aOR, 1.6 (1.4–1.9) ⁸³
Recovered acute kidney injury	aOR, 2.9 (1.9–4.4) ⁸⁴
Hyperthyroidism	aOR, 1.8 (1.1–2.9) ⁸⁵
Hydatidiform mole	OR, 10.1 (3.4–30.0) ⁸⁶
Fetus with trisomy 13	Incidence with 24%–44% vs without 2%–8% ⁸⁷

Pre-eclampsia

Hypertension and proteinuria are the cornerstone of the disease.

CENTRAL ILLUSTRATION: Pathogenesis of Preeclampsia



Christopher W. Ives et al. *J Am Coll Cardiol* 2020; 76:1690-1702.

Pre-eclampsia can be associated with systemic organ damage (severe forms of preeclampsia can be complicated by renal, cardiac, pulmonary, hepatic, and neurological dysfunction; hematologic disturbances; fetal growth restriction; stillbirth; and maternal death).

TABLE 1 Highlights of Clinical Features of Preeclampsia

Clinical Feature	Underlying Abnormalities	Clinical Consequences
Hypertension	Increased SVR and afterload Decreased CO and intravascular volumes Activation of RAAS, ET-1, SNS AT1R down-regulated, placental hypoxia, and AT1R autoantibodies Increased vasoconstrictors, decreased vasodilators Increased sFlt-1 and sEng, oxidative stress	Heart failure Pulmonary edema Renal dysfunction Neurological injury
Proteinuria	Glomerular endotheliosis Disruption of filtration barrier Increased tubular permeability	Hypertension Ischemic heart disease Stroke Chronic kidney disease End-stage renal disease
Renal dysfunction	Decreased RBF and GFR Glomerular endotheliosis Increased tissue factor expression Thrombotic microangiopathy	Hypertension Chronic kidney disease End-stage renal disease
Neurological abnormalities	Headache: loss of fenestrae on choroid plexus, periventricular edema, vasogenic edema in posterior cerebral circulation Visual disturbances: retinopathy, retinal detachment, cortical blindness, central serous chorioretinopathy, hypertensive retinopathy, diabetic retinopathy	Seizures PRES Permanent blindness
Eclampsia	Unknown (potentially vasogenic or cytotoxic edema)	Permanent neurological dysfunction
Cardiac dysfunction	Increased SVR, afterload Concentric LV hypertrophy, LA enlargement Increased RVSP, increased LV filling pressures, LV diastolic dysfunction,	Heart failure Peripartum cardiomyopathy
Pulmonary edema	Increased vascular permeability Cardiac dysfunction Corticosteroids/tocolytics Iatrogenic volume overload	Acute hypoxemic respiratory failure
Hepatic dysfunction	Hepatic microcirculatory deterioration, hepatocellular injury	Liver failure, hepatic rupture
Hematologic dysfunction	Procoagulant state	Thrombocytopenia, DIC
Fetal growth restriction	Incomplete spiral artery remodeling Decidual vasculopathy Uterine and placental dysfunction	Fetal growth <10th percentile

This table depicts the key aspects underlying the pathophysiology of each clinical feature of preeclampsia. Subsequent clinical consequences that can be observed with each feature are listed.

AT1R = angiotensin II receptor type 1; CO = cardiac output; DIC = disseminated intravascular coagulation; ET = endothelin; GFR = glomerular filtration rate; LA = left atrial; LV = left ventricular; PRES = posterior reversible encephalopathy syndrome; RAAS = renin-angiotensin-aldosterone system; RBF = renal blood flow; RVSP = right ventricular systolic pressure; sEng = soluble endoglin; sFlt = soluble fms-like tyrosine kinase; SNS = sympathetic nervous system; SVR = systemic vascular resistance.

Pre-eclampsia is a hypertensive disorder of pregnancy (HDP) defined as gestational hypertension with proteinuria >0.3 g/24 h, It is the most common cause of prematurity. It occurs more frequently during the first pregnancy.

Diagnostic criteria:

Always necessary. . .
Hypertension <ul style="list-style-type: none">• SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg on 2 occasions at least 4 h apart after 20 weeks' gestation in a woman with previously normal BP• SBP ≥ 160 mm Hg or DBP ≥ 110 mm Hg on 1 occasion
. . .And 1 of the following
Proteinuria <ul style="list-style-type: none">• ≥ 300 mg per 24-h urine collection (or extrapolated from timed collection), or• Protein/creatinine ratio of ≥ 0.3 mg/dl, or• Dipstick reading of 2+ (used only when other methods not available)
OR any 1 of the following (in the absence of proteinuria)
Thrombocytopenia <ul style="list-style-type: none">• Platelet count $<100,000/\text{mm}^3$
Renal insufficiency <ul style="list-style-type: none">• Serum creatinine concentration >1.1 mg/dl or a doubling of serum creatinine concentration in the absence of other renal disease
Impaired liver function <ul style="list-style-type: none">• Elevated concentration of liver transaminases to $2\times$ normal• Severe persistent right upper quadrant or epigastric pain unresponsive to medication
Pulmonary edema <ul style="list-style-type: none">• Diagnosed by physical examination or chest x-ray
Neurological signs <ul style="list-style-type: none">• New-onset headache unresponsive to medication and not accounted for by alternative diagnoses or visual symptoms• Visual disturbances
Fetal growth restriction* <ul style="list-style-type: none">• Estimated fetal weight $<10\text{th}$ percentile

Adapted from ACOG Practice Bulletin No. 202 (3) and ISSHP recommendations (7). *Included in ISSHP definition of preeclampsia though not in ACOG definition.

ACOG = American College of Obstetricians and Gynecologists; BP = blood pressure; DBP = diastolic blood pressure; ISSHP = International Society for the Study of Hypertension in Pregnancy; SBP = systolic blood pressure.

Symptoms and signs of pre-eclampsia

↑ BP

Proteinuria

Edema of the face & hands (but it has been dropped of the definition due to poor predictive value). Signs of pulmonary edema. Abnormal weight gain.

Headache

Visual disturbances

Reduced urine output

Epigastric or RUQ pain

Exaggerated reflexes

Lower abdominal pain/bleeding (?placental abruption).

Thrombocytopenia

Complications of pre-eclampsia

- Eclampsia
- HELLP syndrome (hemolysis, elevated liver enzymes, low platelets).
- Maternal end-organ damage and dysfunction: (pulmonary edema, renal failure, stroke, liver issues).
- Placental abruption
- Intrauterine growth retardation
- Stillbirth

Treatment and prevention of pre-eclampsia

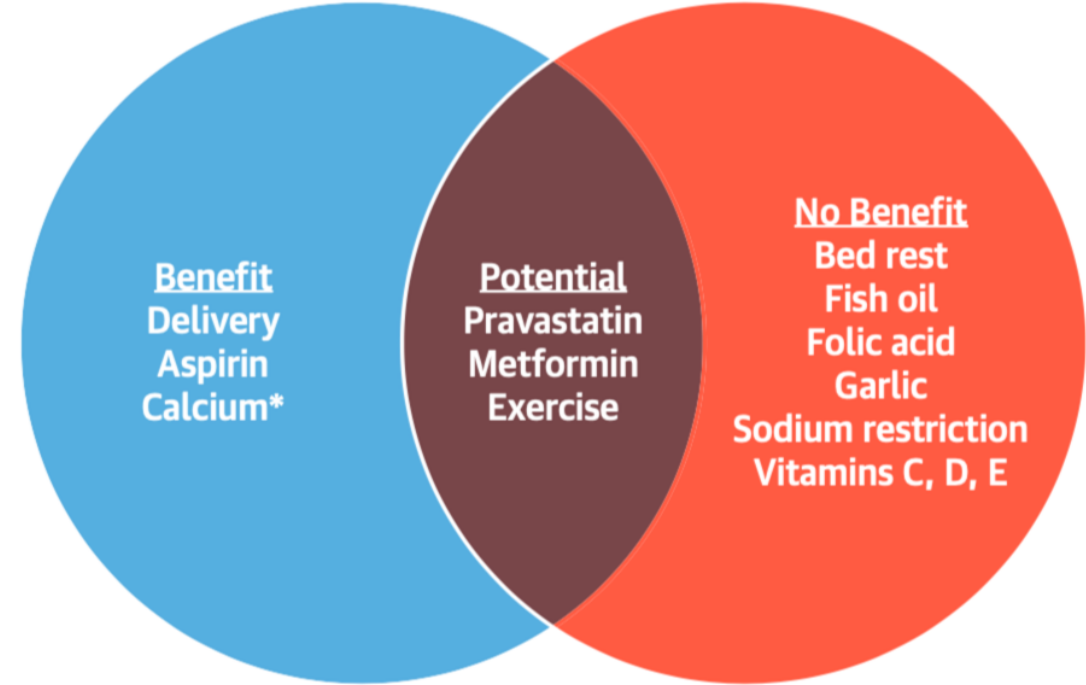
Delivery is the only definitive treatment .

Indications: progressive maternal organ dysfunction, inability to control BP, fetal well-being.

.

Low-dose aspirin is recommended for prophylaxis in high-risk women.

A recent Cochrane review summarized evidence from 60 trials including 36,716 women and found an 18% reduced risk of preeclampsia with aspirin prophylaxis (relative risk: 0.82; 95% confidence interval: 0.77 to 0.88).



Overview of evidence of treatments to reduce risk of preeclampsia. Interventions with proven benefit are delivery for treatment, and aspirin and calcium for prophylaxis. Pravastatin, metformin, and exercise are currently being investigated and are showing promise. *Only in nutritional deficiency in low-middle income countries.

Eclampsia

Eclampsia is defined as new-onset tonic-clonic, focal, or multifocal seizures in the setting of HDP in the absence of other causes. **Seizures define onset of eclampsia.**

1% of patient with pre-eclampsia develop eclampsia.

A Cochrane review of medications for preeclampsia found that intravenous magnesium sulfate reduced the risk of eclampsia by 59%, superior to phenytoin.

Hypertension in Pregnancy

- Maternal risks include placental abruption, stroke, multiple organ failure (liver, kidney), disseminated vascular coagulation.

FETAL COMPLICATIONS

Elevated systolic BPs throughout pregnancy, even below the diagnostic threshold for hypertension, also are associated with increased risk of preterm delivery and infants who are small for gestational age and have low birth weight.

Fetal risks include intrauterine growth retardation (IUGR 10-15%), preterm birth (25-30%), and intrauterine death (stillbirth & fetal distress due to abruptio placentae or chronic intrauterine asphyxia).

Hypertension. 2022;79:e21–e41.

HTN in pregnancy

While the benefits of antihypertensive therapy for mild-to-moderate gestational hypertension (<160/110 mmHg) have not been demonstrated in clinical trials, there is consensus that drug treatment of severe hypertension in pregnancy is beneficial.

Treatment for Mild Chronic Hypertension during Pregnancy

Tita AT et al. DOI: 10.1056/NEJMoa2201295

CLINICAL PROBLEM

Chronic hypertension during pregnancy increases risk of poor pregnancy and birth outcomes. Although pharmacologic antihypertensive therapy is standard treatment for severe hypertension during pregnancy, its benefits and safety are unclear for mild chronic hypertension in pregnant women.

CLINICAL TRIAL

Design: A U.S. multicenter, open-label, randomized, controlled trial assessed whether treatment of mild chronic hypertension in pregnant women, as compared with no treatment, would reduce adverse pregnancy outcomes without harming fetal growth.

Intervention: 2408 women with a known or new diagnosis of mild chronic hypertension and a singleton fetus at <23 weeks' gestation were randomly assigned to receive either active treatment with antihypertensive medications approved for pregnancy or standard treatment — i.e., no treatment, unless systolic blood pressure was ≥ 160 mm Hg or diastolic blood pressure was ≥ 105 mm Hg. The primary outcome was a composite of preeclampsia with severe features, medically indicated preterm birth at <35 weeks, placental abruption, fetal death, or neonatal death.

RESULTS

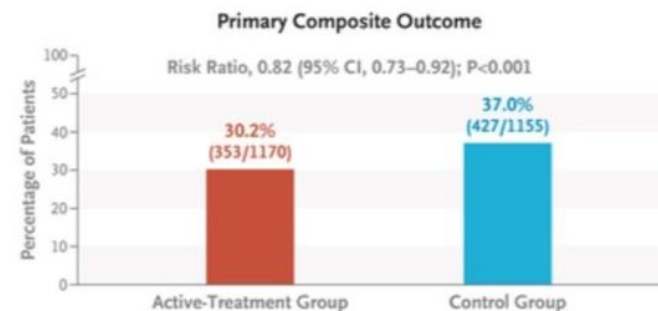
Efficacy: Active treatment of mild chronic hypertension reduced the frequency of primary outcome events.

Safety: The percentage of infants who were small for gestational age (<10th percentile) was similar in the active-treatment and control groups.

LIMITATIONS AND REMAINING QUESTIONS

- Patients were aware of their treatment group.
- There was a high ratio of women screened to women enrolled (12:1).
- The study was not powered to assess treatment effects across subgroups.

Links: Full Article | NEIM Quick Take | Editorial



CONCLUSIONS

Treating mild chronic hypertension in pregnancy reduced adverse pregnancy outcomes without impairing fetal growth.

HTN in pregnancy

SAFER TO USE

MMILD TO MODERATE HTN
(BP <160/110 mm Hg)

MMETHYLDOPA

Drug of first choice; Proven safety record

Do not appear to alter maternal CO or BF to the uterus or kidneys

LLABETALOL

Also considered as 1st choice, Safety similar to methyldopa
Rapid acting, Oral/IV,

NNIFEDIPINE

Nifedipine is another popular drug; widely used.
Long-term effects not known. Preferred in late gestation.

HYDRALAZINE

CLONIDINE/PRAZOSIN

(C.S.) BETA BLOCKERS

SEVERE HTN/ HTN EMERGENCIES
(BP ≥160/110 mm Hg)

H

HHYDRALAZINE (IV)

Drug of first choice in severe hypertension/emergencies;
Widely used; given IV; long safety experience

LLABETALOL (IV)

NNIFEDIPINE (Oral)

NNITROPRUSSIDE (IV)

Drugs to avoid in pregnancy

Drugs to avoid	Teratogenicity
ACE inhibitors, ARBs, direct renin inhibitors	Teratogenic: oligohydramnios [8, 11]
Mineralocorticoid receptor antagonists	Antiandrogen effects cause feminization of male fetus
Nitroprusside	Fetal cyanide poisoning
Atenolol	Intrauterine growth retardation, preterm delivery [12]

Drugs to avoid in pregnancy

ACE INHIBITORS (PRILs)	<u>CONTRAINDICATED</u> In 2 nd & 3 rd trimesters of pregnancy • May cause foetal hypotension, anuria, malformations or death In 1 st trimester • Increased risk of CVS and CNS malformations
ARBs (SARTANs)	
ATENOLOL	<u>AVOIDED</u> Associated with foetal growth impairment, if used in early pregnancy
BETA BLOCKERS (Non selective)	<u>AVOIDED</u> Propranolol has been implicated to cause low birth weight, neonatal bradycardia, hypoglycaemia etc.
DIURETICS	<u>AVOIDED</u> Diuretics are generally avoided, as they prevent the volume expansion seen in normal pregnancy & may decrease placental perfusion.

Hypertension and preeclampsia in pregnancy have been recognized as important risk factor for cardiovascular disease (CVD) in women in the future independent of traditional cardiovascular disease risks: failed stress test of pregnancy.

It is well accepted, that hypertension develops significantly more frequently after HDP, but studies indicate that hypertension also develops faster in women with HDP and is diagnosed up to 10 years earlier compared with women with normotensive pregnancies.

Hypertension. 2022;79:e21–e41.

Conclusions

- Hypertension in pregnancy is a condition affecting 5%–10% of pregnancies worldwide.
- It has been estimated that preeclampsia complicates 2–8% of pregnancies globally
- Hypertensive disorders of pregnancy constitute one of the leading causes of maternal and fetal morbidity and mortality worldwide.
- Preeclampsia, a hypertensive disorder of pregnancy, affects 2% to 8% of pregnant women and causes considerable mortality.
- Prevention and treatment of HDP is important to prevent complications of HDP.

Questions?



Please fill out our survey!

Please find the survey link in the chat. You will also be prompted in an e-mail post-session, along here via this link

<https://bit.ly/3bTG2WE>

Completing the survey helps us to provide the health center network with relevant and impactful information, and meet our own HRSA deliverables. Thank you in advance!





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