Hypertensive Disorders of Pregnancy

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4 Types of Hypertensive Disease

- Gestational hypertension
  —evidence for the preeclampsia syndrome does not develop and hypertension resolves by 12 weeks postpartum
- Preeclampsia and eclampsia syndrome
- Chronic hypertension of any etiology
- Preeclampsia superimposed on chronic hypertension.
- HELLP syndrome: a life-threatening form of preeclampsia (HELLP is an acronym: H = hemolysis; EL = elevated liver enzymes; LP = low platelets)

Gestational Hypertension

- Pregnancy-induced hypertension or PIH, is the new onset of hypertension after 20 weeks of gestation.
- Diagnosis is made in women whose blood pressures reach 140/90 mm Hg or greater for the first time after midpregnancy, but in whom proteinuria is not identified.
- 50% of women subsequently develop preeclampsia syndrome, which includes findings such as headaches or epigastric pain, proteinuria, and thrombocytopenia.
- Requires close monitoring as proteinuria has not developed yet- 10% of eclamptic seizures develop before overt proteinuria can be detected.
- Reclassified by some as transient hypertension if evidence for preeclampsia does not develop and the blood pressure returns to normal by 12 weeks postpartum.

Chronic Hypertension

- High blood pressure that either precedes pregnancy, is diagnosed within the first 20 weeks of pregnancy, or does not resolve by the 12-week postpartum check-up.
- Two categories of severity are recognized:
  - mild (up to 179 mm Hg systolic and 109 mm Hg) and
  - severe (≥ 180 systolic or 110 diastolic).
- Complicates about 5% of all pregnancies, and prevalence rates are increasing due to delayed childbearing.
- Increased risk of superimposed preeclampsia.
- Increased risk of prematurity, birth of infants who are small for their gestational age, intrauterine death, placental abruption, and caesarean delivery.

Chronic Hypertension

- **Drugs to be avoided:**
  - Atenolol and other pure beta-blockers:
    - associated with babies born small for their gestational age.
  - Angiotensin-converting enzyme (ACE) inhibitors :
    - contraindicated in the second and third trimester because they are associated with a myriad of congenital anomalies, including renal failure, oligohydramnios, renal dysgenesis, reduced ossification, pulmonary hypoplasia, and fetal and neonatal death.
  - Angiotensin II receptor antagonists :
    - similar to ACE inhibitors, but there are no data to confirm this
- Patients with severe hypertension in the first trimester have a greater than 50% risk of developing superimposed preeclampsia.
- All hypertensive patients should undergo increased surveillance, serial laboratory tests throughout pregnancy, serial ultrasound scans to follow growth, and antenatal testing.
- The baby should be delivered vaginally if possible.

Preeclampsia

- Pregnancy-specific syndrome that can affect virtually every organ system.
- Hypertension that occurs after 20 weeks of gestation in a woman with previously normal blood pressure. Systolic blood pressure 140 mm Hg or diastolic blood pressure 90 mm Hg on two occasions at least 6 hours apart.
- Complicates 5–7% of all pregnancies.
- Frequency distribution is bimodal, among young, nulliparous women with a second peak occurring in multiparous women greater than 35 years of age.
- Overt proteinuria may not be a feature in some women with the preeclampsia syndrome.
- Evidence of mult-iorgan involvement may include thrombocytopenia, renal dysfunction, hepatocellular necrosis ("liver dysfunction"), central nervous system perturbations, or pulmonary edema.
- **Eclampsia**: severe form of preeclampsia with convulsive seizures and/or coma

Risk Factors

General risk factors

- Thrombophilia (e.g., antiphospholipid syndrome)
- Obesity (BMI ≥ 30)
- Age < 20 or > 40 years
- African-American race
- Diabetes mellitus or gestational diabetes
- Chronic hypertension
- Chronic renal disease (e.g., SLE)

Pregnancy-related risk factors

- Nulliparity
- Previous preeclampsia
- Family history
- Multiple gestation (twins)
- Chromosomal anomalies or congenital structural anomalies
- Hydatidiform moles

Clinical Features

Gestational hypertension

- Asymptomatic hypertension
- Nonspecific symptoms (e.g., morning headaches, fatigue, dizziness) can occur.

Preeclampsia without severe features

- Onset: 90% occur after 34 weeks of gestation
- Usually asymptomatic
- Nonspecific symptoms may include:
- Headaches
- Visual disturbances
- RUQ or epigastric pain
- Rapid development of edema
- Hypertension
- Proteinuria

Preeclampsia with severe features

- Severe hypertension (systolic ≥ 160 mmHg or diastolic BP ≥ 110 mmHg)
- Proteinuria, oliguria
- Headache
- Visual disturbances (e.g., blurred vision, scotoma)
- RUQ or epigastric pain
- Pulmonary edema
- Cerebral symptoms (e.g., altered mental state, nausea, vomiting, hyperreflexia, clonus)

Clinical Features

HELLP syndrome

- Onset: most commonly > 27 weeks gestation (30% occur postpartum)
- Preeclampsia usually present (~ 85%)
- Nonspecific symptoms: nausea, vomiting, diarrhea
- RUQ pain (liver capsule pain; liver hematoma)
- Rapid clinical deterioration (DIC, pulmonary edema, acute renal failure, stroke, abruptio placentae)

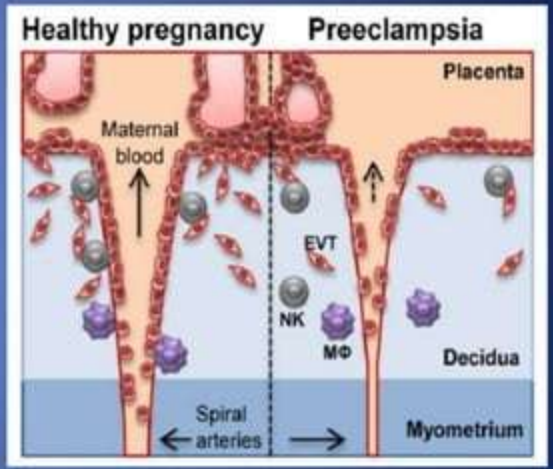
Eclampsia

- Onset: the majority of cases occur in the intra-partum and postpartum period
- Most often associated with severe preeclampsia (but can be associated with mild preeclampsia)
- Eclamptic seizures: generalized tonic-clonic seizures (usually self-limited)

- Deterioration with headaches, RUQ pain, hyper-reflexia, and visual changes are warning signs of a potential eclamptic seizure!
- Hypertensive pregnancy disorders may be intra-partum or postpartum. In some cases, eclamptic seizures may occur postpartum.

Pathogenesis

- "Two-stage disorder" theory of preeclampsia
  - stage 1 is caused by faulty endovascular trophoblastic remodelling that downstream causes the stage 2 clinical syndrome.
- With preeclampsia, there is defective implantation characterized by incomplete invasion of the spiral arteriolar wall by extra villous trophoblasts.
- This results in a small-caliber vessel with high resistance to flow.



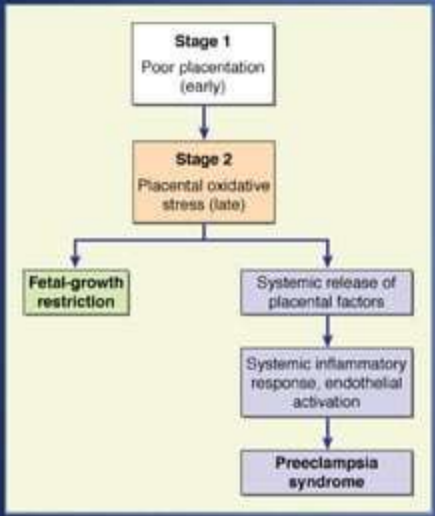
Pathogenesis

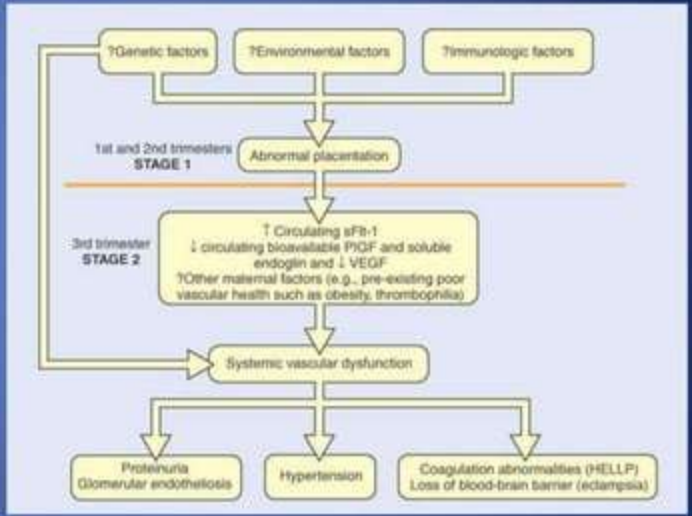
- Multiple maternal, fetal, and placental factors are involved in placental hypoperfusion, which leads to maternal hypertension and other consequences.
- Abnormal placental (or trophoblast) implantation or development in the uterus → hypoperfusion of placenta and fetus
- Arterial hypertension with systemic vasoconstriction causes placental hypoperfusion → release of vasoactive substances → ↑ maternal blood pressure to ensure sufficient blood supply of the fetus
- Systemic endothelial dysfunction causes placental hypoperfusion → ↑ placental release of factors → endothelial lesions that lead to microthrombosis

Consequences of vasoconstriction and micro-thrombosis

- Organ ischemia and damage
- Preeclampsia:
  - multi-organ involvement (primarily renal)
- Eclampsia:
  - predominantly cerebral involvement
- HELLP syndrome:
  - severe systemic inflammation with multi-organ hemorrhage and necrosis (particularly liver involvement)
- Chronic hypo-perfusion of the placenta →
  - insufficiency of the utero-placental unit and fetal growth restriction

Pathogenesis





Multi-organ Involvement

Heart

- With the clinical onset of preeclampsia, cardiac output declines, due at least in part to increased peripheral resistance.
- When assessing cardiac function in preeclampsia, consideration is given to echocardiographic measures of myocardial function and to clinically relevant ventricular function.
- Serial echocardiographic studies have documented in preeclampsia evidence for ventricular remodelling that is accompanied by diastolic dysfunction in 40 percent of women.
- Ventricular remodelling is an adaptive response to maintain normal contractility with the increased afterload of preeclampsia.

Eyes

- Retinal vasospasm, retinal edema, serous retinal detachment, and cortical blindness may occur in the setting of preeclampsia. Blindness is uncommon and usually transient, resolving within hours to days of delivery.

Multi-organ Involvement

Organ	Pathomechanism	Disorder	Occurrence
Kidney	• Glomerular endothelial dysfunction and hypertension–induced vasoconstriction	• Edema • Proteinuria • Impaired renal function	• **Preeclampsia** • Eclampsia • HELLP syndrome
Lung	• Increased systemic vascular resistance and volume overload → left ventricular dysfunction → ↑ pulmonary capillary hydrostatic pressure, ↑ capillary permeability , and ↓ albumin	• Pulmonary edema • Respiratory distress	• Severe preeclampsia • HELLP syndrome
Liver	• Vasoconstriction and microthrombotic obstruction of liver sinusoids → liver cell damage	• Liver impairment and liver swelling	• **HELLP syndrome** • Severe preeclampsia • Eclampsia
CNS	• Hypertension–induced vasoconstriction and endothelial damage → disruption of cerebral microcirculation with microthrombi → vasospasms in the CNS	• Seizures	• **Eclampsia**
Blood	• Systemic microthrombi and vasoconstriction → overactivation of the coagulation system and platelet consumption • Microangiopathic hemolysis	• Disseminated intravascular coagulopathy (DIC) • Thrombocytopenia • Anemia	• **HELLP syndrome** • Severe preeclampsia

Prenatal Screening/ Initial Workup

Prenatal Screening

- Early detection to prevent maternal and fetal complications.
- Maternal blood pressure
- Maternal weight
- Maternal urine status (urine dipstick)

Initial Workup

- Blood Pressure
- Urine tests to determine proteinuria
- 24-hour urine collection (gold standard): ≥ 300 mg/24 h
- Urine dipstick: 1–2 + protein
- **Laboratory analysis**
- CBC (RBC, platelets)
- Liver function tests (transaminases)
- Kidney function tests (creatinine)
- Peripheral smear (assess for hemolysis) and coagulation studies are indicated if HELLP syndrome is suspected (i.e., thrombocytopenia and/or liver function impairment are present

Diagnostic Criteria

		Diagnostic criteria
Gestational hypertension		• Hypertension (> 140/90 mmHg) diagnosed after 20 weeks gestation

Preeclampsia	**Preeclampsia without severe features**	• Hypertension (> 140/90 mmHg)
		• Proteinuria ≥ 300 mg/24 h
		• If proteinuria is absent, at least one of the following must be present:
		  ◦ Thrombocytopenia
		  ◦ Impaired renal function
		  ◦ Impaired liver function
		  ◦ Visual or neurologic changes
		  ◦ Pulmonary edema

	Preeclampsia with severe features	• One or more of the following symptoms:
		  ◦ Severe hypertension (> 160 mmHg systolic or > 110 mmHg diastolic)
		  ◦ Thrombocytopenia < 100,000/μL
		  ◦ Impaired renal function (serum creatinine > 1,1 mg/dL or doubling of serum creatinine)
		  ◦ Impaired liver function (elevated transaminases)
		  ◦ Pulmonary edema
		  ◦ Cerebral or visual symptoms

	HELLP syndrome	• The following features must be present:
		  ◦ **H** = **H**emolysis
		  ◦ **EL** = **E**levated **L**iver enzymes
		  ◦ **LP** = **L**ow **P**latelets

Eclampsia		• Primarily a clinical diagnosis: patient with preeclampsia presenting with new-onset grand mal seizures
Chronic hypertension		• Hypertension diagnosed < 20 weeks gestation or before pregnancy

Differential Diagnosis

Eclampsia

- Seizure disorders during pregnancy
- Epilepsy
- Encephalitis
- Metabolic disorders (e.g., hypoglycemia, hyponatremia)
- Hemorrhagic stroke
- Ischemic stroke
- Withdrawal syndromes

HELLP Syndrome

- Causes of thrombocytopenia and liver impairment during pregnancy
- Thrombotic microangiopathy (TTP, HUS)
- Fulminant viral hepatitis

Classification

Mild Preeclampsia	Severe Preeclampsia
Blood pressure ≥ 140/90 mm Hg but < 160/110 mm Hg on two occasions at least 6 hours apart while the patient is on bed rest	Blood pressure ≥ 160 mm Hg systolic or ≥ 110 mm Hg diastolic on two occasions at least 6 hours apart while the patient is on bed rest
Proteinuria ≥ 300 mg/24 h but < 5 g/24 h	Proteinuria of 5 g or higher in 24-hour urine specimen or 3+ or greater on two random urine samples collected at least 4 hours apart
Asymptomatic	Oliguria < 500 mL in 24 hours
	Cerebral or visual disturbances
	Pulmonary edema or cyanosis
	Epigastrica or right upper quadrant pain
	Impaired liver function
	Thrombocytopenia
	Fetal growth restriction

Management (without severe features)

- Initial antepartum evaluation: assess maternal and fetal status and necessity for hospitalization and delivery
  - Laboratory analysis: CBC, platelet count, serum creatinine, liver enzyme levels
  - Urine protein test
  - Monitor for symptoms of severe preeclampsia
  - Fetal ultrasound (estimate fetal weight and amniotic fluid volume)
  - Non-stress test (NST)
  - Biophysical profiling if NST is nonreactive
- Hospitalization and delivery indicated if:
  - Pregnancy ≥ 37 weeks gestation
  - Suspected placental abruption
  - Pregnancy ≥ 34 weeks gestation plus one of the following
    - Labor or rupture of membranes
    - Fetal weight < 5thpercentile
    - Oligohydramnios
    - Abnormal maternal or fetal test results

Cont'd

- In all other cases, continue outpatient monitoring
- Maternal monitoring: (1–2 x/week): blood pressure, urine dipsticks, blood analysis (platelet count, liver enzymes, renal function)
- Fetal monitoring: ultrasound every 3 weeks and NST 1–2x weekly
- Patient education
  - Recognize signs of severe preeclampsia or fetal distress (e.g., reduced fetal movement, vaginal bleeding)
- Avoid physical exertion

- Antihypertensive drug therapy for severe hypertension (systolic BP ≥ 160 mmHg or diastolic BP ≥ 110 mmHg)
- First-line agents
  - Labetalol
  - Hydralazine
  - Nifedipine
  - Methyldopa
- ACE inhibitors and angiotensin-receptor blockers (ARB) are contraindicated during pregnancy due to their teratogenic effect!
- Preeclampsia without severe features can progress to preeclampsia with severe features within days! Close monitoring is vital!

Drugs

EMERGENCY PARENTERAL THERAPY FOR SEVERE HYPERTENSION DURING PREGNANCY

Agent	Action	Dose	Side Effects	Comments
Hydralazine	Direct vasodilator	5 mg IV over 1-2 min, then 5-10 mg IV every 20-40 min until blood pressure is 130-150/80-100 mm Hg. If no response after 20-25 mg, switch to another drug. Alternatively, give continuous IV infusion of 0.5-10 mg/hr.	Headache, tachycardia, flushing, vomiting	Increases cardiac output and probably uterine renal blood flow; has historically been drug of choice for short-term control.
Labetalol hydrochloride	Nonselective α_1-blocker β_1-blocker	Start with 10-20 mg IV bolus. If response is inadequate after 10 min, give 20-80 mg IV every 20-30 min if needed to lower blood pressure to 130-150/80-100 mm Hg. Total dose not to exceed 300 mg. Alternatively, give a continuous IV infusion of 1-2 mg/min.	Nausea, vomiting, heart block, bronchoconstriction, dizziness	Current drug of choice in many centers. Avoid if evidence of asthma or acute heart failure.
Nifedipine	Calcium channel blocker	10-20 mg orally; repeat in 30 min if inadequate response, then 10-20 mg every 2-6 hours if needed to lower blood pressure to 130-150/80-100 mm Hg.	Reflex tachycardia and headaches	

Management (with severe features)

- **Delivery** (only curative option!) is indicated if:
  - Pregnancy is ≥ 34 weeks gestation
  - Pregnancy is < 34 weeks gestation with maternal or fetal instability
- Immediate delivery after stabilization (IV magnesium sulfate prophylaxis, antihypertensive drugs, corticosteroids) if one of the following is present:
  - Pulmonary edema
  - Eclampsia (cerebral symptoms)
  - Disseminated intravascular coagulation (DIC)
  - Placental abruption
  - Severe, uncontrollable hypertension
  - Nonreassuring signs of fetal distress
  - Fetal demise
- Delivery 24–48 hours after corticosteroid administration and initial stabilization if one of the following is present:
  - Labor or premature rupture of membranes
  - HELLP syndrome
  - Fetal growth restriction (< 5thpercentile)
  - Severe oligohydramnios
  - Umbilical cord artery doppler showing reversed end-diastolic flow
  - New-onset or worsening renal impairment
- **Procedure**: vaginal delivery should be conducted if possible, but often cesarean delivery is needed for younger gestational age, immature cervix, or poor maternal or fetal condition.

Management

- Expectant management: if pregnancy < 34 weeks and mother and fetus are stable
  - Monitor in facilities with maternal and neonatal ICU
  - Daily maternal monitoring: vital signs, laboratory tests, monitor symptoms of severe preeclampsia, contractions, rupture of membranes, vaginal bleeding
  - Daily fetal non-stress test and kick count; twice weekly BPP; ultrasound every two weeks
  - Oral antihypertensive treatment of severe hypertension
  - Magnesium sulfate for prophylaxis of eclampsia
  - Administer corticosteroids for fetal lung maturity
  - Diuretics for pulmonary edema

Management

Eclampsia

- Stabilization
  - Airway management
  - Supplemental oxygenation
- Anticonvulsive therapy
  - Magnesium sulfate IV (first-line)
  - Antidote: calcium gluconate IV if early signs of magnesium toxicity (decreased deep tendon reflexes)
  - Alternative or supportive: lorazepam or diazepam IV if unresponsive to magnesium sulfate
- Position patient on left lateral decubitus position → prevent placental hypoperfusion through compression of the inferior vena cava and reduce the risk of aspiration in the mother
- Delivery: once the mother is stable and seizures have stopped.
  - Delivery is the only cure for eclampsia

HELLP Syndrome

- Stabilization
  - IV fluids
  - Blood transfusions
  - Antihypertensive agents (labetalol, hydralazine)
  - Magnesium sulfate
- Delivery if ≥ 34 weeks gestation or at any gestational age with deteriorating maternal or fetal status (If the fetus is viable, delay labor until 24–48 h after corticosteroid administration)

Complications

Maternal

- Placental abruption
- Cerebral hemorrhage, stroke
- Acute renal failure
- DIC
- Acute respiratory distress syndrome (ARDS)
- Retinal detachment
- Maternal death
- Aspiration pneumonia
- Long-term: increased risk for cardiovascular disease, diabetes mellitus, and chronic kidney disease

Fetal

- Fetal growth restriction
- Preterm birth
- Seizure-induced fetal hypoxia
- Fetal death

Prognosis

- The prognosis of hypertensive pregnancy disorders depends on the severity of the condition and the complications that occur.
- In the majority of cases, the conditions resolve within hours or days after delivery.
- Recurrence rate in following pregnancies
  - Preeclampsia: 10–20%
  - Eclampsia: 2%
  - HELLP syndrome: 5%
- Maternal mortality
  - Eclampsia: 5-10%
  - HELLP syndrome: 2%
- Fetal mortality
  - Eclampsia: 10-12%
  - HELLP syndrome: up to 20%

Prevention

- Prophylactic low-dose ASA PO from 12–14 weeks gestation for patients with a high risk of developing preeclampsia

Risk Level	Risk Factors	Recommendation
High	History of preeclampsia Multifetal gestation Chronic hypertension Type 1 or 2 diabetes Renal disease Autoimmune disease (systemic lupus erythematosus, antiphospholipid syndrome)	Recommend low-dose aspirin if the patient has one or more of these high-risk factors
Moderate	Nulliparity (never having given birth) Obesity (body mass index >30 kg/m^2) Family history of preeclampsia (mother or sister) Sociodemographic characteristics (African American race, low socioeconomic status) Age ≥35 years Personal history factors (e.g., low birthweight or small for gestational age, previous adverse pregnancy outcome, >10-year pregnancy interval)	Consider low-dose aspirin if the patient has two or more of these moderate-risk factors
Low	Previous uncomplicated full-term delivery	Do not recommend low-dose aspirin

Reference

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THANK YOU