Pre-eclampsia (Toxemia): Symptoms and Treatment

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Pre-eclampsia is a condition characterized by elevated blood pressure and proteinuria that occurs after 20 weeks of gestation. Women with pre-eclampsia can also develop hemolysis, thrombocytopenia, HELLP syndrome, or microangiopathic hemolytic anemia. Due to wide-spread endothelial dysfunction, they may also develop cerebral edema and eclampsia. Laboratory investigations show thrombocytopenia, proteinuria > 30 mg/day, hemolysis, and elevated liver enzymes. The only known cure for pre-eclampsia is the pre-term delivery of the fetus.

Pregnancy-induced Hypertension

Mild pre-eclampsia	hypertension > 140/90 mm Hg + proteinuria > 0.3 g/24 h after 20th week of gestation
Severe pre-eclampsia	hypertension > 160/110 mm Hg + proteinuria > 5 g/24 h + oliguria/HEELP/headache/blurred vision/peripheral edema
Eclampsia	mild or severe pre-eclampsia + grand mal convulsions
Chronic hypertension	• Hypertension that is not pregnancy-induced (as essential hypertension) • Diagnosed when: 1) hypertension exists prior to pregnancy or 2) appears < 20th GA • Proteinuria during pregnancy: **chronic hypertension with superimposed pre-eclampsia**
Transient hypertension	• Occurs in the second half of pregnancy or during labor and delivery • Proteinuria may be present but not > 0.3 g/24 hr; higher levels indicate pre-eclampsia

Definition

Pre-eclampsia occurs after **20 weeks of gestation** and is characterized by the following features:

- Proteinuria > 30 mg/day
- Systolic blood pressure > 140 mm Hg
- Diastolic blood pressure > 90 mm Hg

Untreated cases can be life-threatening.

Epidemiology

Approximately, 8% of pregnant women develop pre-eclampsia; however, it is important to understand that this condition has a wide spectrum in terms of severity. About 15% of maternal deaths are caused due to pre-eclampsia and thus, accurate diagnosis is important to exclude this condition in patients who present with **pregnancy-induced hypertensive disorders**.

Women who developed pre-eclampsia in a previous pregnancy are five times more likely to develop this disease in subsequent pregnancies. Pre-eclampsia is more common in **nulliparous women.** A history of kidney disease, chronic hypertension, diabetes, obesity, and age > 35 years are considered risk factors for this condition.

Being a **multisystemic and vascular disease,** pre-eclampsia puts the mother at risk of developing chronic hypertension, ischemic heart disease, or stroke after delivery.

Pathophysiology

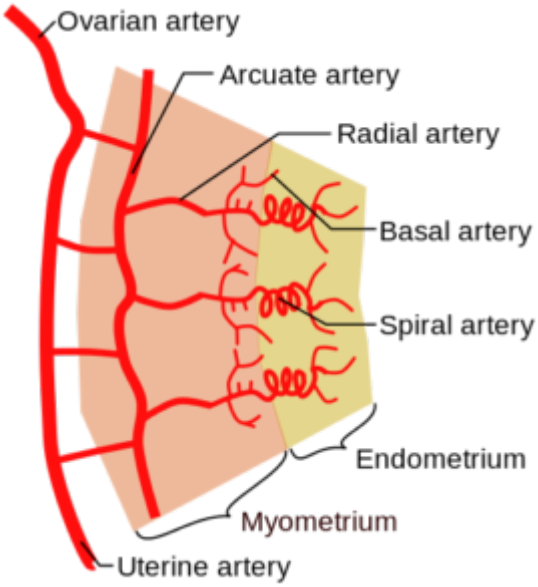

Image: “Arterial vasculature of the non-pregnant uterus.”
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Pre-eclampsia might be related to chronic hypertension, diabetes, or other vasculopathies, but is of unknown etiology in most patients. Regardless, several risk factors described above have been linked to a higher risk of developing pre-eclampsia.

An abnormal placental implantation site may predispose pregnant women to pre-eclampsia. This abnormal implantation may result in an abnormal invasion of the spiral arteries by the **cytotrophoblasts**. Cytotrophoblasts and spiral arteries are usually insensitive to vasodilators such as **nitric oxide**. In pre-eclampsia, spiral arteries regain sensitivity to the vasodilative effects of nitric oxide, which leads to **vasodilation** and **ischemic placental injury**.

Placental ischemia results in **intrauterine growth retardation**. Additionally, the involvement of free radicals, the presence of inflammatory cytokines, and an elevation of

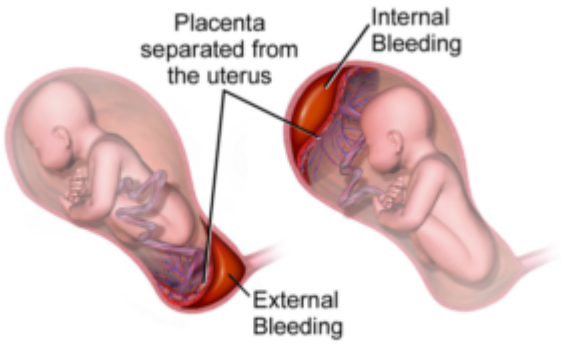
vascular endothelial growth factor-1 are observed in the mother. This eventually causes **endothelial dysfunction** due to thrombophilia and increased vascular permeability. Endothelial dysfunction is responsible for the complicated presentation of pre-eclampsia known as **HELLP syndrome,** which is an acronym for hemolysis, elevated liver enzymes, and low platelet count.

Additionally, alterations in the cerebral vascular bed result in **neurologic symptoms and convulsions**. Endothelial dysfunction is also implicated in causing a decrease in glomerular filtration rate, which manifests as **proteinuria**.

In addition to abnormal placentation, certain **genetic mutations** are known to increase the risk of pre-eclampsia. This is more evident in women with a maternal history of pre-eclampsia, who are approximately five times more likely to develop this condition during their first pregnancy.

The involvement of specific genes **such as 1-q-42–43,** and **eNOS on 7q36 and other loci** also increase the risk of pre-eclampsia. Pre-eclampsia is sometimes considered an autoimmune disorder; placental necrosis can occur when fetoplacental cells are identified as foreign in origin, as implicated in some cases.

Clinical Presentation



Abruptio Placenta (Placental Abruption)

Image: "Placental Abruption." by Blausen.com staff. "Blausen gallery 2014". Wikiversity Journal of Medicine. DOI:10.15347/wjm/2014.010. ISSN 20018762. – Own work.
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Patients present with headaches, visual disturbance, oliguria, frothy urine, or edema. In more severe presentations patients can develop brisk tendon reflexes, neurologic alterations due to cerebral edema, HELLP syndrome, and vaginal bleeding.

Patients with pre-eclampsia and vaginal bleeding should be evaluated for possible **placental abruption**. Screening for systolic and diastolic hypertension is also an important aspect in the diagnosis of pre-eclampsia.

Patients who display neurological signs that are not responsive to medical treatment may develop **eclampsia**, a complication to pre-eclampsia.

Physical examination reveals a **systolic blood pressure > 140 mm Hg** and/or **diastolic blood pressure > 90 mm Hg**. Patients with access to their serial weight measurements will notice an **increase in weight** due to edema. Additionally, **ankle edema** and respiratory crackles due to **pulmonary edema** may develop.

Diagnostic Work-up

Laboratory investigations are helpful in the diagnosis of pre-eclampsia. Patients have a low platelet count and elevated haptoglobin and lactate dehydrogenase levels due to hemolysis. Additionally, bilirubin, aspartate, and alanine aminotransferase levels are evaluated to exclude HELLP syndrome, which results in liver dysfunction.

Renal injury can occur in patients with pre-eclampsia; therefore, serum electrolytes, urea, and creatinine levels should be monitored. A 24-hour urine assessment for proteinuria is essential to confirm the diagnosis of pre-eclampsia. get their Additionally, the prothrombin, activated thrombin, and fibrinogen levels in women with pre-eclampsia should be regularly monitored to exclude **microangiopathic hemolytic anemia**.

Fetal Doppler ultrasound combined with **cardiotocography** is indicated to evaluate ischemic complications and fetal well-being including health, weight, size, and growth.

Mild pre-eclampsia is defined as having systolic blood pressure > 140 mm Hg or diastolic blood pressure > 90 mm Hg, and when proteinuria > 30 mg/day in pregnant women after 20 weeks of gestation.

Severe pre-eclampsia is diagnosed when systolic blood pressure is > 160 mm Hg or diastolic blood pressure > 110 mm Hg, proteinuria > 5 g/day, oliguria, creatinine > 120 micromol/L, HELLP syndrome, thrombocytopenia with platelet count < 100,000/cc, intrauterine fetal growth restriction, **oligohydramnios,** or **intrauterine fetal death**.

A **brain CT scan** might be indicated to exclude brain edema in patients with severe pre-eclampsia or eclampsia. A **chest X-ray** may be indicated to rule out pulmonary edema. However, these tests should be reserved for patients with severe disease as radiations can be **harmful to the fetus**.

Treatment

The only cure for pre-eclampsia is **delivery,** which is usually based on the severity of the condition and the current gestational age, i.e. fetal viability.

Management of severe pre-eclampsia is straightforward as the life-threat to the mother is more evident. The aim is to prevent its progression to eclampsia and avoid hypertension-related end-organ damage.

Women beyond 35 weeks of gestation who develop pre-eclampsia should have the fetus delivered. Additionally, patients who develop pre-eclampsia before 24 weeks of gestation should have their pregnancy terminated due to the high risk of complications associated with treatment. Unfortunately, this results in a wide time span between 25–35 weeks of gestation that falls under a grey area.

Patients with uncontrolled severe hypertension, eclampsia, acute pulmonary edema, placental abruption, severe thrombocytopenia with platelet count < 50,000/cc, or subcapsular hepatic hematoma should have an immediate delivery of the pre-term fetus regardless of the gestational age.

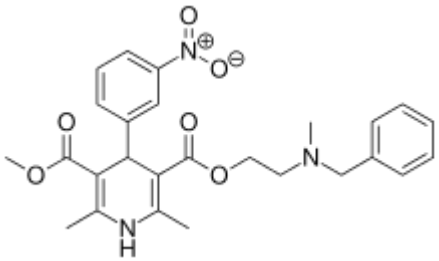

Image: “Chemical structure of nicardipine – a dihydropyridine L-type calcium channel blocker.” by Autor/Fotograf, MD. License: Public Domain

Treatment of hypertension in pre-eclampsia is only indicated when systolic blood pressure is > 160 mm Hg or diastolic blood pressure is > 110 mm Hg. The **calcium channel blocker** nicardipine, **beta-blocker** labetalol, clonidine, and dihydralazine can be used for pre-eclampsia-associated hypertension.

If the gestational age is above 30 weeks, 12 mg of **betamethasone,** in two separate doses 24 hours apart, is indicated to induce fetal pulmonary maturity if delivery is planned.

Patients with severe pre-eclampsia may benefit from **magnesium sulfate (MgSO4),** which is also used in **eclampsia-related convulsions**. Additionally, the use of MgSO4 in pre-eclampsia has been shown to prevent eclampsia; if indicated, the patient should be admitted to the **intensive care unit** due to the high risk of end-organ failure associated with its use.

A **cesarean section** is indicated for delivery in patients with eclampsia.

Approximately 20% of women who develop pre-eclampsia eventually develop **chronic hypertension** or **microalbuminuria** that does not resolve after delivery. Accordingly, they should be monitored for the first 72 hours after delivery as an improvement in condition may be observed. A follow-up visit to monitor **blood pressure** and for the **assessment of proteinuria** is also indicated.

Complications

- Chronic hypertension
- Proteinuria and other renal pathologies resulting from damage to the renal tubules
- Bleeding disorders
- Neurological events such as seizures, strokes, and hemorrhages

Prognosis

- Pre-eclampsia is responsible for 14% of all maternal deaths
- An infant born to a mother having pre-eclampsia has the risk of developing autism and delayed developmental milestones
- There is a 10% chance of recurrent pre-eclampsia in subsequent pregnancies

References

Uzan J, Carbonnel M, Piconne O, et al (2011) Pre-eclampsia: Pathophysiology, diagnosis,

and management. Vasc Health Risk Manag 7:467–474. doi: 10.2147/VHRM.S2018

Notes