

## Pre-eclampsia (Toxemia) — Symptoms and Treatment

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



## Pregnancy-Induced Hypertension

<b>Mild Pre-eclampsia</b>	Hypertension > 140/90 mmHg + Proteinuria > 0.3g/24 h After 20th week of gestation
<b>Severe Pre-eclampsia</b>	Hypertension > 160/110 mmHg + Proteinuria > 5g/24 h + Oliguria / HELLP / headache, blurred vision / peripheral edema
<b>Eclampsia</b>	Mild or Severe preeclampsia + Grand mal convulsions
<b>Chronic hypertension</b>	<ul style="list-style-type: none"> <li>• Hypertension that's not pregnancy induced (as essential hypertension). -</li> <li>• It's diagnosed when: 1- hypertension exists prior to pregnancy or 2- when appears &lt; 20th GA.</li> <li>• If proteinuria occurred during pregnancy: <b>chronic hypertension with superimposed pre-eclampsia.</b></li> </ul>
<b>Transient hypertension</b>	<ul style="list-style-type: none"> <li>• It occurs in the second half of pregnancy or during labor &amp; delivery.</li> <li>• Proteinuria may present BUT doesn't exceed 0.3g/24hr if exceeded, diagnosis: pre-eclampsia.</li> </ul>

## Definition of Pre-eclampsia

Pre-eclampsia is a condition that occurs after **20 weeks of gestation** characterized by the features, Proteinuria > 30 mg/day, a systolic blood pressure > 140 mmHg or a diastolic blood pressure > 90 mmHg and untreated cases can be life-threatening.

# Epidemiology of Pre-eclampsia

Approximately, 8% of pregnant women develop pre-eclampsia, but it is important to understand that this condition has a wide spectrum in terms of severity. 15% of maternal deaths are caused by pre-eclampsia making it a very important diagnosis to exclude in any patient who presents with **pregnancy-induced hypertension disorder**.

**Maternal history of pre-eclampsia** increases the risk by 5 times and the condition is more common in **nulliparous women**. A previous history of [kidney disease](#), chronic [hypertension](#), [diabetes](#), obesity and age > 35 years are also risk factors for pre-eclampsia.

Pre-eclampsia also puts the mother at risk of developing chronic hypertension after delivery, ischemic heart disease and [stroke](#) because it is a **multisystemic and vascular disease**.

## Pathophysiology of Pre-eclampsia

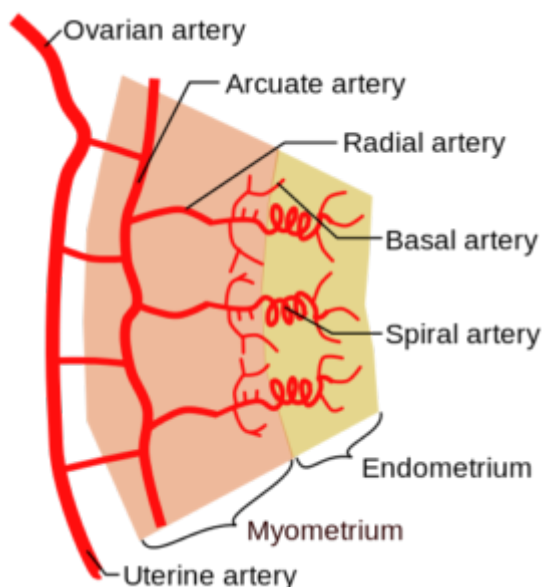


Image: "Arterial vasculature of the non-pregnant uterus."  
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Pre-eclampsia might be related to chronic hypertension, diabetes or other vasculopathies, but is of unknown etiology in the majority of the patients. Regardless, several risk factors described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

**Abnormal placental implantation site** might predispose to pre-eclampsia. This abnormal implantation might result in an abnormal invasion of the spiral arteries by the **cytotrophoblasts**. Cytotrophoblasts and the spiral arteries are usually insensitive to vasodilative substances, such as **nitric oxide**. In pre-eclampsia, the spiral arteries regain sensitivity to vasodilative effects for nitric oxide and this leads to **vasodilation** and **ischemic placental injury**.

Placental ischemia results in **intrauterine growth retardation**. Additionally, free radicals, cytokines and an elevation in the vascular endothelial growth factor 1 occur in the mother.

This eventually causes **endothelial dysfunction** due to thrombophilia and increased

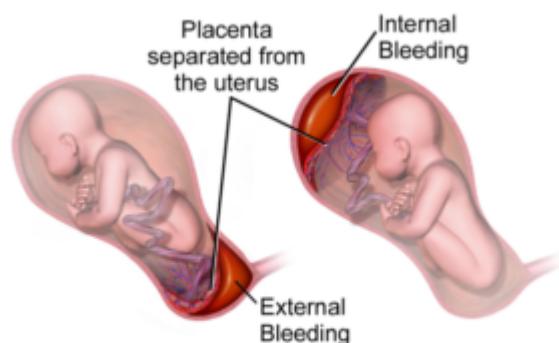
vascular permeability. This endothelial dysfunction is responsible for the complicated presentation of pre-eclampsia known as **HELLP syndrome** which stands for hemolysis, elevated liver enzymes, and low platelet count.

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

In addition to abnormal placentation, certain **genetic mutations** are also 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 pre-eclampsia in their first pregnancy.

Certain specific genes such as **loci 1-q-42-43** and **eNOS on 7q36** also increase the risk of pre-eclampsia. Pre-eclampsia is also partially **autoimmune** as placental necrosis can happen when the mother identifies the fetoplacental cells as foreign in origin which is implicated in some cases.

## Clinical Presentation of Pre-eclampsia



### **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. License: [CC BY 3.0](https://creativecommons.org/licenses/by/3.0/)

Patients can 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**. **Hypertension** is also part of the criteria for the diagnosis of pre-eclampsia which can be either systolic or diastolic.

Patients who develop neurologic signs that are not responsive to medical treatment have **eclampsia**, a complication to pre-eclampsia.

Physical examination reveals a **systolic blood pressure > 140 mmHg** and/or a **diastolic blood pressure > 90 mmHg**. Patients, if they have serial weight measurements, can show **weight gain** due to edema. Additionally, **ankle edema** can be identified. Patients might develop respiratory crackles due to **pulmonary edema**.

## Diagnostic Work-up for Pre-eclampsia

**Laboratory investigations** are helpful in the evaluation of a patient with pre-eclampsia. Patients have a low platelets count, elevated lactate dehydrogenase due to hemolysis, and an elevated haptoglobin. Additionally, bilirubin, aspartate and alanine aminotransferases are checked to exclude HELLP syndrome in which liver dysfunction occurs.

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

**Ultrasonography of the fetus**, with Doppler assessment and combined with **electrocardiography** is indicated to evaluate the fetus' health, weight, size and any ischemic complications such as growth restriction.

**Mild pre-eclampsia** is diagnosed when systolic blood pressure is  $> 140$  or diastolic blood pressure is  $> 90$  mmHg and when proteinuria is more than 30 mg/day in a pregnant woman after 20 weeks of gestation.

**Severe pre-eclampsia** is defined as having systolic blood pressure above 160 mmHg or diastolic blood pressure above 110 mmHg, proteinuria  $> 5$  g/day, oliguria, creatinine  $> 120$  micromol/L, HELLP syndrome, thrombocytopenia  $< 100,000/cc$ , intrauterine fetal growth restriction, **oligohydramnios** or **intrauterine fetal death**.

A **brain CT scan** might be indicated to exclude brain edema in a patient with severe pre-eclampsia or eclampsia and **chest X-ray** to evaluate **pulmonary edema**. These tests should be reserved for patients with severe disease as they are **toxic to the fetus**.

## Treatment of Pre-eclampsia

The only curative treatment 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 more straightforward as the life-threat to the mother is more evident. The aim is to prevent progression into eclampsia and to avoid hypertension related end-organ damage.

Women who are currently after their 35th week 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 with expectant treatment. Unfortunately, this gives a very wide range, 25 to 35 weeks of gestation, where things are grayer.

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

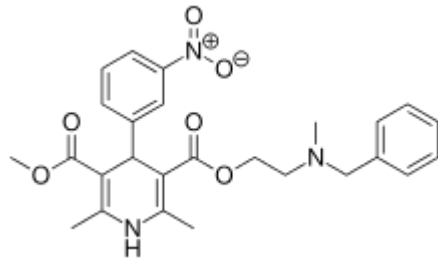


Image: "Chemical structure of nicardipine - a dihydropyridine L-type calcium channel blocker." by Autor/Fotograf, MD. License: Public Domain

Treatment of hypertension in pre-eclampsia is only indicated when systolic blood pressure is  $> 160$  or diastolic blood pressure is  $> 110$  mmHg. **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 of gestation, **betamethasone** 12 mg in two separate doses that are 24 hours apart is indicated to induce pulmonary maturation in the fetus if delivery is planned.

Patients with severe pre-eclampsia might benefit from **magnesium sulfate** which is also used in **eclampsia-related convulsions**. Additionally, magnesium sulfate in pre-eclampsia has been shown to prevent eclampsia. If magnesium sulfate is indicated, the patient should be admitted to the **intensive care unit** due to the high risk of end-organ failure associated with the administration of  $MgSO_4$ .

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, laboratory monitoring in the first 72 hours after delivery is indicated where most patients show a dramatic improvement. A further follow-up with **blood pressure measurement** and **urine assessment for proteinuria** is indicated too.

## Complications

Complications include :

- Chronic hypertension
- Proteinuria and other renal pathologies resulting from damage to renal tubules
- Bleeding disorders
- Neurological events like seizures, stroke, and hemorrhages.

## Prognosis

- Preeclampsia is responsible for 14% of total maternal deaths.
- A fetus born to mother having preeclampsia has the risk of developing autism and delayed developmental milestones.
- There are 10% chances of the recurrence of preeclampsia in further 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

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