Pre-eclampsia

Lec: NO. 8
Abnormal placentation

In pregnancies destined to be complicated by preeclampsia, FGR and/or abruptio placentae, there is a complete or partial failure of trophoblast invasion of the myometrial segments of the spiral arteries. Hence, spiral arteries retain some of their pre-pregnancy characteristics being relatively narrow bore and of low capacitance and high resistance and resulting in impaired perfusion of the fetoplacental unit. The mechanism underlying decreased trophoblast invasion in complicated pregnancies is poorly understood but it may reflect an ‘immune intolerance’ of the mother to the invading trophoblast. Affected placentae have gross morphological changes, which include infarcts and basal haematomas. An infarct represents an area of ischaemic necrosis of a cotyledon resulting from a spiral artery occlusion usually by thrombosis.
**Definition**

**pre-eclampsia** as hypertension of at least 140/90 mmHg recorded on at least two separate occasions and at least 4 hours apart and in the presence of at least 300 mg protein in a 24 hour collection of urine, arising de novo after the 20th week of pregnancy in a previously normotensive woman and resolving completely by the sixth postpartum week.

**Chronic hypertension** (with or without renal disease) existing prior to pregnancy can predispose to the later development of superimposed pre-eclampsia. Even in the absence of superimposed pre-eclampsia
Non-proteinuric gestational hypertension, i.e. hypertension arising for the first time in the second half of pregnancy and in the absence of proteinuria, is not associated with adverse pregnancy outcome.
Incidence

Pre-eclampsia complicates approximately 2–3 per cent of pregnancies, but the incidence varies depending on the exact definition used and the population studied.
Epidemiology

• Pre-eclampsia is more common in primigravid women.
• Overall the recurrence risk in a subsequent pregnancy is 20 per cent, but is much higher if severe pre-eclampsia developed at an extremely early gestation in the first pregnancy.
• There also appears to be a maternal genetic predisposition to pre-eclampsia as there is a three- to four-fold increase in the incidence of pre-eclampsia in the first degree relatives of affected women.
• There are a number of general medical conditions and pregnancy-specific factors that predispose to the development of pre-eclampsia.
Risk factors for pre-eclampsia

• First pregnancy
• Multiparous with:
  • pre-eclampsia in any previous pregnancy
  • ten years or more since last baby
• Age 40 years or more
• Body mass index of 35 or more
• Family history of pre-eclampsia (in mother or sister)
• Booking diastolic blood pressure of 80 mmHg or more
• Booking proteinuria (of 1 on more than one occasion or quantified at 0.3 g/24 hour)
• Multiple pregnancy
• Certain underlying medical conditions:
  • pre-existing hypertension
  • pre-existing renal disease
  • pre-existing diabetes
  • antiphospholipid antibodies
Aetiology and pathophysiology

Pre-eclampsia only occurs in pregnancy, but has been described in pregnancies lacking a fetus (molar pregnancies) and in the absence of a uterus (abdominal pregnancies) suggesting that it is the presence of trophoblast tissue that provides the stimulus for the disorder. Placental bed biopsies have demonstrated that trophoblast invasion is patchy in pre-eclampsia and the spiral arteries retain their muscular walls. This is thought to prevent the development of a high flow, low impedance uteroplacental circulation. The reason why trophoblast invades less effectively in these pregnancies is not known but may reflect an abnormal adaptation of the maternal immune system.

Growth factors, cytokines and products of oxidative stress caused by hypoxic-reperfusion injury in the placenta.
Cardiovascular system
Pre-eclampsia is characterized by marked peripheral vasoconstriction, resulting in hypertension. The intravascular high pressure and loss of endothelial cell integrity results in greater vascular permeability and contributes to the formation of generalized oedema.

Renal system
In the kidney, a highly characteristic lesion called ‘glomeruloendotheliosis’ is seen. This is relatively specific for pre-eclampsia (it is not seen with other hypertensive disorders) and is associated with impaired glomerular filtration and selective loss of intermediate weight proteins, such as albumin and transferrin, leading to proteinuria.
The liver

HELLP syndrome (haemolysis, elevation of liver enzymes and low platelets). HELLP syndrome is a particularly severe form of pre-eclampsia, occurring in just 2–4 per cent of women with the disease. It is associated with a high fetal loss rate (of up to 60 per cent).

Neurological system

The development of convulsions in a woman with pre-eclampsia is defined as eclampsia.
Clinical presentation

The classic symptoms of pre-eclampsia include a frontal headache, visual disturbance and epigastric pain.

Clinical examination

- Complete obstetric and neurological examination
- Hypertension.
- Rapidly progressive oedema of the face and hands may suggest pre-eclampsia.
- Epigastric tenderness is a worrying sign and suggests liver involvement.
- Hyperreflexia and clonus in severe cases
- Urine testing for protein.
Testing for proteinuria
Dipstick urinalysis
• Instant result but quantitatively inaccurate
• Results: trace: seldom significant; 1: possible significant proteinuria, warrants quantifying; 2: probable significant proteinuria, warrants quantifying
Protein:creatinine ratio
• Fast (within an hour)
• Results semi-quantitative: 30 mg/mol – probable significant proteinuria
24 hour collection
• Slow
• Results: 0.3 g/24 hour represents confirmed significant proteinuria
Management and treatment

There is no cure for pre-eclampsia other than to end the pregnancy by delivering the baby (and placenta).

The principles of management of pre-eclampsia are:
• early recognition of the symptomless syndrome;
• awareness of the serious nature of the condition in its severest form;
• adherence to agreed guidelines for admission to hospital, investigation and the use of antihypertensive and anticonvulsant therapy;
• well-timed delivery to pre-empt serious maternal or fetal complications;
• post-natal follow up and counselling for future pregnancies.
mild hypertension, minimal protein and normal haematological and biochemical parameters may be monitored as outpatients.

moderate or severe hypertension, significant proteinuria or abnormal haematological or biochemical parameters require admission and inpatient management.
Investigations for pre-eclampsia
To monitor maternal complications:
- Full blood count (with particular emphasis on falling platelet count and rising haematocrit)
- If platelet values are normal, additional clotting studies are not indicated
- Serum renal profile (including serum uric acid levels)
- Serum liver profile
- Frequent repeat proteinuria quantification is probably unhelpful once a diagnosis of pre-eclampsia has been made
To monitor fetal complications
• Ultrasound assessment of:
  • fetal size
  • amniotic fluid volume
  • maternal and fetal Dopplers
• Antenatal cardiotocography used in conjunction with ultrasound surveillance, provides a useful but by no means infallible indication of fetal well-being. A loss of baseline variability or decelerations may indicate fetal hypoxia
### Antihypertensives Used in the Management of Pre-eclampsia

Methyldopa is a centrally acting antihypertensive agent. It has a long established safety record in pregnancy.

Labetalol is an alpha-blocking and betablocking agent. It too has a good safety record in pregnancy and can be given orally and intravenously.

Nifedipine is a calcium-channel blocker with a rapid onset of action. It can, however, cause severe headache that may mimic worsening disease.
In severe cases of fulminating disease, an intravenous infusion of hydralazine or labetalol can be titrated rapidly against changes in the blood pressure. The drug of choice for the treatment of eclampsia is magnesium sulphate. This is given intravenously and has been shown to reduce the incidence of further convulsions in women with eclampsia. Magnesium sulphate should also be used in women with severe pre-eclampsia to prevent the onset of convulsions.
Additional points in management

Iatrogenic premature delivery of the fetus is often required in severe pre-eclampsia.

< 34 weeks gestation steroids should be given.

Delivery before term is often by Caesarean section.

Prophylactic Subcutaneous heparin and issued with antithromboembolic stockings.

Epidural anaesthesia is indicated as it helps control blood pressure.

Ergometrine is avoided in the management of the third stage as it can significantly increase blood pressure.
Screening

• No single blood biomarker has emerged that either alone or in combination with other biomarkers or clinical data possesses sufficient sensitivity and specificity to be clinically useful.

• Doppler ultrasound uterine artery waveform analysis to identify women at risk of pre-eclampsia (and other adverse pregnancy outcomes).

Prevention

Low-dose aspirin (typically 75 mg daily).
Calcium supplementation.
Vitamins C and E do not lower the risk of pre-eclampsia.