Hypertensive disorder of pregnancy

Hypertensive disease complicates 5-7 per cent of all pregnancies. It can be categorized generally into pre-existing hypertension, pregnancy-induced hypertension and pre-eclampsia.

To distinguish between these is clinically useful as management and likely prognosis are differing.

Hypertension during pregnancy is common, and even in the developed countries, women still die from pre-eclampsia and eclampsia.

**Pregnancy-induced hypertension (PIH):**

The term pregnancy-induced hypertension usually implies hypertension caused by pregnancy (but unrelated to other pathology associated with the pregnancy), a diagnosis that is difficult to make until after the pregnancy has ended. In other term PIH occurs when new onset hypertension develops in the second half of pregnancy (usually defined as after 20th week), and disappear after end of pregnancy.

**Classification and definition:**

The International Society for the Study of Hypertension in Pregnancy (ISSHP), used the term gestational hypertension to include all women with pregnancy-induced hypertension as long as they had been previously normotensive. They classified hypertensive disorder of pregnancy as follow:

A. *Gestational hypertension and/or proteinuria* developing during pregnancy, labour or the puerperium in a previously normotensive non-proteinuric women:
   1. Gestational hypertension (without proteinuria).
   2. Gestational proteinuria (without hypertension).
   3. Gestational proteinuric hypertension (pre-eclampsia).

B. *Chronic hypertension and chronic renal disease (proteinuria)* before 20 weeks of pregnancy.

C. *Unclassified hypertension* and/or proteinuria.

D. *Eclampsia.*
**Definitions:**

**Hypertension** in pregnancy is diagnosed as:
- Diastolic blood pressure (BP) more than 110 mmHg on any one occasion or
- Diastolic blood pressure (BP) than 90 mmHg on two or more consecutive occasions more than 4 hours apart.

**Proteinuria** in pregnancy is defined as:
- One 24-hour collection with total protein excretion more than 300 mg/24 hours or
- Two ‘clean-catch-midstream’ or catheter specimens of urine collected more than 4 hours apart with 2+ or greater on reagent strip.

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.

Chronic hypertension (with or without renal disease) existing prior to pregnancy can lead to development of superimposed pre-eclampsia.

Pre-eclampsia hypertension of at least two separate occasions and at least 4 hours apart and in the presence of at least 300 mg protein in 24 hour collection of urine, arising denovo after the 20th week of pregnancy in a previously normotensive woman and resolving completely by the sixth postpartum week.

**Incidence:**

Hypertension in pregnancy occurs in approximately one in five women after 20 weeks’ gestation.

Pre-eclampsia complicates approximately 2-3% of pregnancies. And it’s the second most common cause of direct death in pregnancy and puerperium in the UK.

**Risk factors:**

There are a number of general medical conditions and pregnancy-specific factors that predispose to the development of pre-eclampsia

- First pregnancy: pre-eclampsia is more common in primigravid women.
- Multiparous with pre-eclampsia in any previous pregnancy.
- Age 40 years or more.
- Body mass index of 35 or more.
- Family history of pre-eclampsia (in the mother or in the sister).
- Booking diastolic blood pressure of 80 mmHg or more.
• Booking proteinuria of 1+ or greater on more than one occasion or quantified at 0.3g or more/24 hours.
• Multiple pregnancies.
• Certain underlying medical conditions (pre-existing HT, pre-existing renal disease, pre-existing diabetes, antiphospholipid antibodies)

**Etiology and pathophysiology**

Pre-eclampsia only occurs in pregnancy, but has been described in pregnancies lacking a fetus (molar pregnancies), suggesting that is the presence of trophoblast tissue that provides the stimulus for the disorder. It is widely believed that defective trophoblast invasion results in relative under-perfusion of the placenta and that this result in release of factors into the maternal circulation that targets the vascular endothelium and pre-eclampsia is a multisystem disease it affects multiple organs concurrently like cardiovascular system resulting hypertension and edema, renal system resulting leading to proteinuria, hematological disorder resulting thrombocytopenia, the liver resulting elevated liver enzyme and HELLP syndrome, and CNS resulting hypertensive encephalopathy.

The proposed etiology is summarized as follow

- Genetic predisposition
- Abnormal immunogenic response
- Deficient trophoblast invasion
- Hypoperfused placenta
- Circulating factors and endothelial cell activation
- Clinical manifestations of disease

**Clinical presentation**

The classic symptoms of pre-eclampsia include a frontal head ache, visual disturbance and epigastric pain. However, the majority of women with pre-eclampsia is asymptomatic or merely complains of general vague ‘flu-like’ symptoms. During history
taking enquiry about above mentioned risk factors should be done as risk factors are found in one third of the patient.

Clinical examination should include a complete obstetric and neurological examination. HT is usually the first sign, but occasionally is absent or normal or transient until the late stage of disease.

How to check the blood pressure?

For correct measurement the patient should be rest for more than 10 minutes or hospitalized, be in either sitting or left lateral position and the arm should be at the level of heart, mercury sphygmomanometer is preferred and it should be with appropriate cuff size that fit the upper arm of pregnant women (that is the bladder encircle more than 80% of arm).

Korotkoff phase is preferred over phase 4.

Dependent edema of the feet is very common in healthy pregnancy. However, rapidly progressive edema of the face and hand may suggest pre-eclampsia. Epigastric tenderness is a worrying sign and suggests liver involvement. Neurological examination may reveal hperreflexia and clonus in severe cases. Urine testing for protein should be considered part of the clinical examination. BMI should be calculated.

**Testing for proteinuria:**

Dipstick analysis: Its quantitatively in accurate, the results may be as follow:
- Trace: seldom significant.
- 1+: possible significant protienuria, warrants quantifying.
- 2+ or more: probable significant protienuria, warrants quantifying.

Protein: creatinin ratio:
- If more than 30 mg/mol means probable significant protienuria
- 24 hour collection:
  - If more than 0.3g/24 hour represents confirmed significant protienuria.

**Complications:**

**Maternal complications:**
- CNS involvement(seizure& stroke)
- Disseminated intravascular coagulopathy.
- Renal failure.
- Hepatic failure.
- HELLP syndrome.
- High rate of C/S.
- Ante partum and postpartum hemorrhage.
- Death.
- Future risk of chronic hypertension.

**Fetal complications:**
- Intrauterine growth restriction.
- Placental infarct and IUD.
- Placental abruption.
- Prematurity.
- Perinatal death.
- Future cardiovascular disease.

**Management and treatment:**

There is no cure for pre-eclampsia other than to end the pregnancy by delivering the baby and the placenta. This can be significant problem if it occurs early in pregnancy, particularly at gestations below 34 week. In such cases and when the disease is sever, steroid should be administered to enhance lung maturity and delivery should be prompted. Other indications for premature delivery are uncontrolled BP, deteriorating liver and renal functions, hematological and neurological complications and deteriorating fetal conditions. Therefore, management strategies are aimed at minimizing risk to the mother in order to continued fetal growth so if the pregnancy is at term, termination of pregnancy should be decided immediately after stabilizing the mother.

**The principles of management are:**
- Early recognition of the symptomless syndrome;
- Awareness of the seriousness of the condition;
- Use of agreed guidelines for managements and use of antihypertensive and anticonvulsant drugs;
- Well-timed delivery to avoid maternal and fetal complication;
- Post-natal follow up and counseling for future pregnancy.

A diagnosis of pre-eclampsia usually requires admission. Patient with mild hypertension, minimal proteinuria and normal hematological and biochemical test may be monitored as outpatients but will require frequent visit attendance for fetal and maternal assessment.
Women with moderate to severe HT, significant proteinuria or abnormal testes require admission and inpatient management. Investigation indicated in the ongoing management of pre-eclampsia are the following:

**To monitor maternal conditions:**
- Full blood count with particular attention on falling platelet count and rising haematocrit.
- Coagulation profile if platelet counts are abnormal.
- Serum renal function test like urea, creatinin and uric acid.
- Serum liver profile (SGPT, SGOT ...)
- Urine for albumin.

**To monitor fetal complication:**
- Ultrasounds for fetal size and amniotic fluid volume.
- Antenatal cardiotocography (CTG).
- Fetal and maternal Doppler.

**Antihypertensive drugs:** the aim of antihypertensive drugs is to lower the BP (aiming at diastolic blood pressure not less than 80mmHg) without reducing uterine blood flow and compromising the fetus. There are a variety of antihypertensive drugs.
- Methyldopa is a centrally acting antihypertensive agent with recorded long term safety during pregnancy. Its available in oral tablet of 250 mg. however, it can only be given orally, it takes upwards of 24 hours to take effect (not used for emergency) and has a range of unpleasant side effects, including sedation and depression.
- Labetalol is a combined alpha and beta blocking agent, it also has long term safety profile and can be given both orally and intravenously.
- Hydralazine is act by vasodilatation and also can be given orally and intravenously and is used also in emergency management of hypertension.

Both labetalol and hydralazine can be given by infusion in severe fulminating conditions.
- Nifedipine is a calcium-channel blocker with a rapid onset of action. It can, however, cause severe head ache that may mimic worsening disease.
- Magnesium sulphate (although used to control eclampsia) but can also be used in pre-eclampsia to prevent the onset of convulsion.

**Labour and delivery:**

The time and mode of delivery depends on many factors like gestational age, severity of the conditions, prior obstetric history, and fetal conditions. Iatrogenic premature delivery is often required in sever pre-eclampsia. If her condition allowed the mother should be transferred to a center with adequate facilities to care for
premature baby. Steroid should be given and the delivery in these cases is usually by caesarean section. Such patients are at particularly high risk for thromboembolism and should be given prophylactic subcutaneous heparin and to wear antithrombotic stocking. Epidural anesthesia can be used if platelet and clotting factors are normal. If the vaginal delivery is decided (weather spontaneous or by induction), BP should be measured frequently (every 15 minutes) and high reading during labour can be controlled by both intravenous labetalol and hydralazine.

Appropriate fluid management is necessary to avoid fluid overload as they are prone to pulmonary edema. Most protocol prefers crystalloid. A Foley’s catheter should be inserted to monitor input and output. Avoid use of ergometrine as in rise BP.

**Anesthesia:**
General anesthesia posses risk, as endotracheal intubation may cause severe HT. Regional blockade is the preferred method of analgesia for labour and of anesthesia for operative delivery provided that platelet counts are more than $80 \times 10^9/L$.

**Post partum care:**
The patient should be intensively monitored for at least 48 hours post partum as most of eclamptic fit occurs at this time. As blood pressure may remain high in few days post partum, antihypertensive may need to be continued.

All patients should be reviewed 6-12 weeks post partum and in addition of blood pressure checking, the renal and liver function tests should be reviewed.

Any predisposing factors should be investigated and implication on future pregnancy should be discussed.

Patient should be provided with appropriate safe contraception.

**Screening and prevention:**
Unfortunately there is currently no screening test for pre-eclampsia. However the ability of the Doppler ultrasound of uterine artery waveform analysis to identify women at risk of pre-eclampsia has been studied. In at risk pregnancies there will be characteristic "notch". Thos is of value only in high but not in low risk cases with predictive value of 20%.

Established preventive measures include:
- Low dose aspirin (75mg) daily, which modestly reduce the risk.
- In high risk cases, calcium supplementation may reduce the risk.
- Anti oxidant like vitamin C and E, zinc and other are controversial.
- Fish oil containing n-3fatty acid may inhibit thromboxane A2, need further study.