HYPERTENSION IN PREGNANCY

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Introduction

- 2008-2012 -- ±5 000 maternal deaths in South Africa → more than in any of the previous years
- Hypertensive disorders of pregnancy → ±14%
- Deficiencies in providing emergency health care also play an important role
- Need to re-emphasize the seriousness of the symptoms and signs that various disorders elicit in pregnant women seeking emergency health care

How should blood pressure be measured in pregnancy?

- Woman should be rested and sitting at a 45° angle
- BP cuff - appropriate size, at the level of the heart
- 2 readings over a period of time
- Korotkoff phase 5 to measure diastolic BP
- Automated BP readings to be used with caution
- Hypertension = systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg → at least 2 occasions at least 6 hours apart

How should proteinuria be measured in pregnancy?

- Visual urinary dipstick measurement
  - ✓1+ is regarded as significant
- 24 hour quantitative urinary protein measurements are recommended – should be recognised method of evaluating completeness of the sample
  - ✓Significant if result shows ≥300 mg protein
- Spot urinary protein:creatinine ratio
  - ✓Significant if ≥30 mg/mmol

Classification of hypertensive disorders in pregnancy

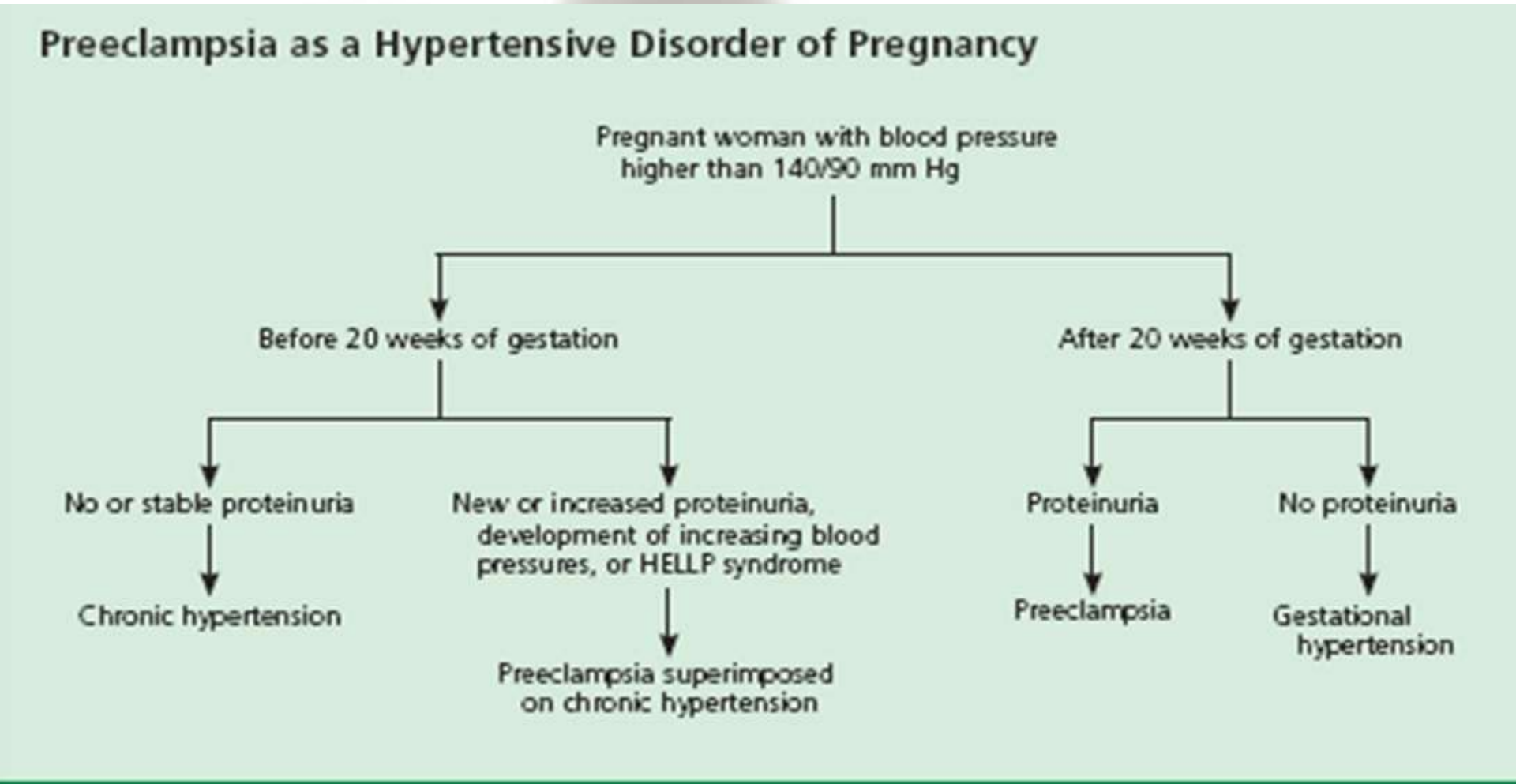


Figure 1. An algorithm for differentiating among hypertensive disorders in pregnant women (HELLP = *h*emolysis, *e*levated *l*iver enzymes, *l*ow *p*latelet count)

Management of chronic hypertension in pregnancy

- Patients should discuss antihypertensive treatment with the healthcare professional if they are planning pregnancy
- Stop ACE inhibitors, alpha- and beta-blockers, thiazides if they become pregnant (preferably within 2 working days of notification of pregnancy) - offer alternatives
- Encourage low dietary sodium intake
- Uncomplicated chronic hypertension aim to keep blood pressure lower than 150/100 mmHg
- Refer if secondary chronic hypertension or target-organ damage
- Schedule additional antenatal consultations based on the individual needs of the woman and her baby
- Do not offer birth to women with uncomplicated chronic hypertension before 37 weeks
- Post-partum measure blood pressure frequently - continue prenatal antihypertensive treatment

Management of gestational hypertension

Degree of hypertension	Mild hypertension (140/90 to 149/99 mmHg)	Moderate hypertension (150/100 to 159/109 mmHg)	Severe hypertension (160/110 mmHg or higher)
Admit to hospital	No	No	Yes (until blood pressure is 159/109 mmHg or lower)
Treat	No	With oral α-methyl-dopa as first-line treatment to keep: • diastolic blood pressure between 80–100 mmHg • systolic blood pressure less than 150 mmHg	With oral α-methyl-dopa as first-line treatment to keep: • diastolic blood pressure between 80–100 mmHg • systolic blood pressure less than 150 mmHg
Measure BP	Not more than once a week	At least twice a week	At least four times a day
Test for proteinuria	At each visit using automated reagent-strip reading device or urinary protein:creatinine ratio	At each visit using automated reagent-strip reading device or urinary protein:creatinine ratio	Daily using automated reagent-strip reading device or urinary protein:creatinine ratio
Blood tests	Only those for routine antenatal care	Test kidney function, electrolytes, full blood count, transaminases, bilirubin Do not carry out further blood tests if no proteinuria at subsequent visits	Test at presentation and then monitor weekly: • kidney function, electrolytes, full blood count, transaminases, bilirubin

PRE-ECLAMPSIA

- New onset hypertension with proteinuria after 20 weeks gestation
- Resolves by 6 weeks postpartum
- Characterized as mild or severe based on the degree of hypertension and proteinuria, and the presence of symptoms resulting from involvement of the kidneys, brain, liver, and cardiovascular system
- The minimum post-diagnostic laboratory/imaging evaluation should include:
  - ✓ Platelet count
  - ✓ Serum creatinine
  - ✓ Serum aspartate aminotransferase (AST) or alanine aminotransferase (ALT)
  - ✓ Obstetrical ultrasound (fetal weight, amniotic fluid volume, umbilical artery Doppler)
  - ✓ Fetal assessment (biophysical profile or non-stress test)

Diagnosing severe pre-eclampsia

The presence of one or more of the following criteria upstages preeclampsia from mild to severe

Symptoms of central nervous system dysfunction:

- Visual disturbance (photopsia, scotomata, cortical blindness, retinal vasospasm)
- Severe headache (ie, incapacitating, "the worst headache I've ever had") or headache that persists and progresses despite analgesic therapy
- Altered mental status

Symptoms of liver capsule distention:

- Right upper quadrant or epigastric pain
- Nausea, vomiting

Hepatocellular injury:

- Serum transaminase concentration ≥ twice normal

Severe blood pressure elevation:

- Systolic blood pressure ≥160 mm Hg or diastolic blood pressure ≥110 mm Hg on two occasions at least six hours apart

Thrombocytopenia:

- <100,000 platelets/microL

Proteinuria:

- ≥5 grams in 24 hours

Oliguria <500 mL in 24 hours

Fetal growth restriction

Pulmonary edema or cyanosis

Aetiology and risk factors

Table 1. Preeclampsia: Etiology and Risk Factors

Theories of pathogenesis	Risk factors[7,12]
Abnormal placental implantation (defects in trophoblasts and spiral arterioles)[13,14]	Antiphospholipid antibody syndrome
Angiogenic factors (increased sFlt-1, decreased placental growth factor levels)[15,16]	Chronic hypertension
Cardiovascular maladaptation and vasoconstriction	Chronic renal disease
Genetic predisposition (maternal, paternal, thrombophilias)[17-20]	Elevated body mass index
Immunologic intolerance between fetoplacental and maternal tissue[7]	Maternal age older than 40 years
Platelet activation	Multiple gestation
Vascular endothelial damage or dysfunction[7]	Nulliparity
	Preeclampsia in a previous pregnancy (particularly if severe or before 32 weeks of gestation)
	Pregestational diabetes mellitus

NOTE: *Previously, young maternal age was considered a risk factor, but this was not supported by a systematic review.*[21]

sFlt-1 = soluble fms-like tyrosine kinase 1.

Information from references 7, and 12 through 21.

Symptoms of pre-eclampsia

- Pregnant women should be made aware of the need to seek immediate advice from a healthcare professional if they experience symptoms of pre-eclampsia
- ***Symptoms include:***
  - ✓ severe headache
  - ✓ problems with vision, such as blurring or flashing before the eyes
  - ✓ severe pain just below the ribs
  - ✓ vomiting
  - ✓ sudden swelling of the face, hands or feet

Prevention of pre-eclampsia

- Common cause of maternal and perinatal morbidity and mortality
- Early delivery is the only effective treatment
- An intervention that could prevent preeclampsia would have a significant impact on maternal and infant health
- Many different strategies to prevent preeclampsia have been investigated - none are effective
- ***Low-dose aspirin*** - some evidence of benefit
  - ✓ Low-risk for preeclampsia - no proven benefit
  - ✓ Moderate to high risk of preeclampsia recommended
  - ✓ No consensus to define women at moderate to high risk
  - ✓ Optimum low dose of aspirin is unclear - suggest 75- 81 mg per day beginning at the end of the first trimester. Aspirin is discontinued 5 to 10 days before expected delivery
- ***Routine calcium supplementation*** is not recommended - may be a benefit in high-risk populations or in those consuming a low calcium diet
- ***Vitamin C and E and fish oil*** supplementation is not recommended
- No drug prevents progression to more severe disease
- Early diagnosis + appropriate management may prevent some of the dangerous sequelae of the disease

Management of pre-eclampsia

Degree of hypertension	Mild hypertension (140/90 to 149/99 mmHg)	Moderate hypertension (150/100 to 159/109 mmHg)	Severe hypertension (160/110 mmHg or higher)
Admit to hospital	Yes	Yes	Yes
Treat	With oral α-methyl dopa as first-line treatment to keep: diastolic blood pressure between 80–100 mmHg Systolic blood pressure less than 150 mmHg	With oral α-methyl dopa as first-line treatment to keep: diastolic blood pressure between 80–100 mmHg Systolic blood pressure less than 150 mmHg	With oral α-methyl dopa as first-line treatment to keep: diastolic blood pressure between 80–100 mmHg systolic blood pressure less than 150 mmHg
Measure BP	At least 4 times a day	At least 4 times a day	More than 4 times a day, depending on clinical circumstances
Test for proteinuria	Do not repeat quantification of proteinuria	Do not repeat quantification of proteinuria	Do not repeat quantification of proteinuria
Blood tests	Monitor using the following tests twice a week: kidney function, electrolytes, full blood count, transaminases, bilirubin	Monitor using the following tests three times a week: kidney function, electrolytes, full blood count, transaminases, bilirubin	Monitor using the following tests three times a week: kidney function, electrolytes, full blood count, transaminases, bilirubin

Selecting anti-hypertensive drug treatment in pregnancy

Drug	Dose	Action	Contra-indications	Practice points
A-Methyldopa	250-750mg tds	Central	Depression	Slow onset of action over 24-hours. Dry mouth, sedation, depression, blurred vision
Clonidine	75-300µg tds			Withdrawal effect
Labetalol	100-400mg tds	β-blocker with mild α-vasodilator effect	Asthma, chronic airways limitation	Bradycardia, bronchospasm, headache, nausea, scalp tingling (usually resolves in 24-48hr)
Oxprenolol	20-160mg tds	β-blocker with ISA	Heart block	
Nifedipine	20mg bd – 60mg SR bd	Ca channel antagonist	Aortic stenosis	Severe headache associated with flushing, tachycardia, peripheral oedema, constipation
Prazosin	0.5-5mg tds	α-blocker		First-dose effect- orthostatic hypotension
Hydralazine	25-50mg tds	Vasodilator		Flushing, headache, nausea, lupus-like syndrome

Management of pre-eclampsia

- Manage conservatively - do not plan same-day delivery of the baby until 34 weeks
- Offer birth to women with pre-eclampsia before 34 weeks if:
  - ✓ severe hypertension develops refractory to treatment
  - ✓ maternal or fetal indications develop
- Recommend birth for women who have pre-eclampsia with severe hypertension after 34 weeks when their BP has been controlled
- Post-natally:
  - ✓ start antihypertensive treatment if BP is ≥150/100 mmHg
  - ✓ ask women with pre-eclampsia who have given birth about severe headache and epigastric pain each time BP is measured
  - ✓ Consider reducing treatment if their BP falls <140/90 mmHg. Reduce antihypertensive treatment if their BP falls <130/80 mmHg

Management of hypertensive emergencies

- Refer to the appropriate level of care
- ***Anticonvulsants***
  - ✓ Severe hypertension or severe pre-eclampsia has or previously had an eclamptic fit - give intravenous magnesium sulphate
  - ✓ If considering magnesium sulphate treatment, use the following as features of severe pre-eclampsia:
  - ✓ severe hypertension and proteinuria or
  - ✓ mild or moderate hypertension and proteinuria with one or more of the following:
    - symptoms of severe headache
    - problems with vision, such as blurring or flashing before the eyes
    - severe pain just below the ribs or vomiting
    - papilloedema
    - signs of clonus (≥3 beats)
    - liver tenderness
    - HELLP syndrome
    - platelet count falling to below 100 x 109 per litre
    - abnormal liver enzymes (ALT or AST rising to above 70 iu/litre).
  - ✓ Do not use diazepam, phenytoin or lytic cocktail as an alternative to magnesium sulphate in women with eclampsia.

- ***Fluid balance and volume expansion***
  - ✓ Do not use volume expansion in women with severe pre-eclampsia - limit fluids to 80ml/hour

$MgSO_4$

- ***2 regimes:***
  - ✓ Loading dose of 4g in 200mL of normal saline, IV over 20min + 5g IM in each buttock, followed by 5g IM in alternate buttocks every 4hours for 24hours i.e. 6doses
  - ✓ Loading dose of 4 to 6g diluted in 200mL of normal saline, IV over 15-20min, followed by a continuous infusion of 1-2g/hour for 24hours
- Monitor urine output, respiratory rate, deep tendon reflexes
- With renal dysfunction, may require a lower dose
- Is NOT a hypotensive agent
- Works as a centrally acting anticonvulsant
- ***Toxicity:***
  - ✓ Respiratory rate < 12
  - ✓ Deep tendon reflexes not detectable
  - ✓ Altered sensorium
  - ✓ Urine output < 25-30 cc/hour
- ***Antidote:***
  - ✓ 10 ml of 10% solution of calcium gluconate 1 g IV over 2 minutes

Acute BP lowering for severe hypertension (systolic ≥160mmHg; diastolic ≥110mmHg)

Drug	Dose	Route	Onset of Action
Labetalol	20-50mg	IV bolus over 2min	5min, repeat after 15-30min
Nifedipine	5-10mg capsule 10-20mg tablet	Oral Oral	10-20min, repeat after 30min 30-45min, repeat after 45min
Hydralazine	5-10mg	IV bolus	20min, repeat after 30min
Diazoxide	15-45mg Max. 300mg	IV rapid bolus	3-5min, repeat after 5min

Post-partum hypertension-preeclampsia

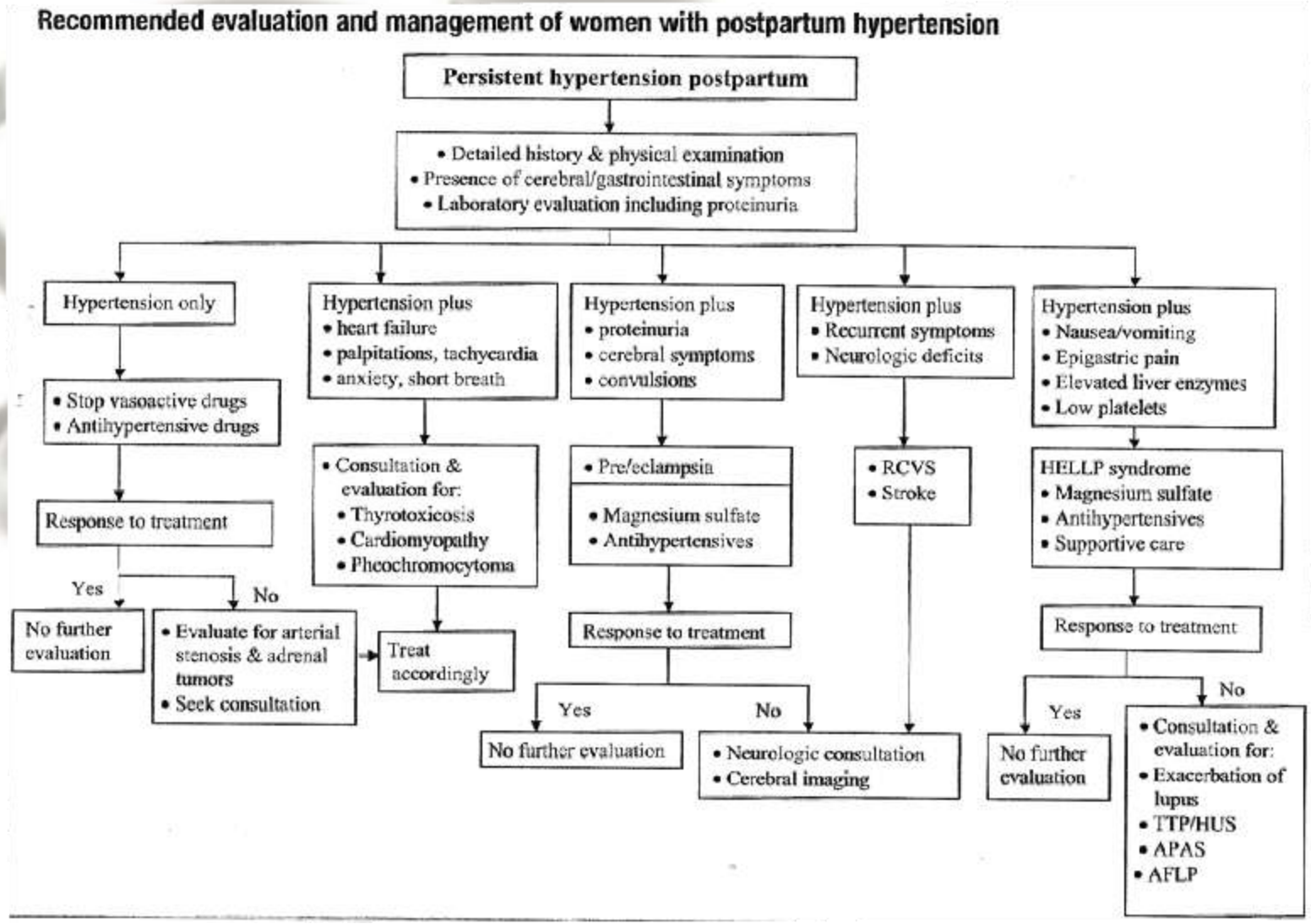
- Can be related to persistence of gestational hypertension, preeclampsia, or preexisting chronic hypertension, or it could develop de novo secondary to other causes
- Exact incidence of postpartum hypertension is unknown

Etiology/differential diagnosis of postpartum hypertension

- New-onset hypertension-preeclampsia, due to
  - ✓ Volume overload (Large volume of fluids, regional analgesia, delayed mobilization)
  - ✓ Medications/drugs (Non-steroidal analgesics, ergot derivatives, ibuprofen, indomethacin, phenylpropanolamine, ephedrine, ergotamine)
- Persistence of GH-preeclampsia
- Late-onset eclampsia
- HELLP syndrome
- Preexisting/undiagnosed hypertension (Hypertension prior to pregnancy, or <20 weeks)
  - ✓ Preexisting renal disease
  - ✓ Hyperthyroidism
  - ✓ Primary hyperaldosteronism
  - ✓ Pheochromocytoma
  - ✓ Renal artery stenosis
- Cerebral vasoconstriction syndrome
- Cerebral venous thrombosis/stroke
- TTP/hemolytic uremic syndrome

- Evaluation should be performed in a stepwise fashion
- May require a multidisciplinary approach
- Management requires a well-formulated plan that takes the following factors into consideration:
  - ✓ pre-delivery risk factors
  - ✓ time of onset in relation to delivery
  - ✓ presence of signs/symptoms
  - ✓ results of laboratory/imaging findings
  - ✓ response to initial therapy
- Most common cause is gestational hypertension, preeclampsia, or essential chronic hypertension
- Initial management will depend on their history, clinical findings, presence or absence of associated symptoms, results of laboratory findings, response to treatment of hypertension

Evaluation and management of women with post-partum hypertension



Advice and follow-up care at transfer to community care

- Tell women who had pre-eclampsia that their risk of developing:
  - ✓ gestational hypertension in a future pregnancy ranges from about 1 in 8 (13%) pregnancies to about 1 in 2 (53%) pregnancies
  - ✓ pre-eclampsia in a future pregnancy is up to about 1 in 6 (16%) pregnancies
  - ✓ pre-eclampsia in a future pregnancy is about 1 in 4 (25%) pregnancies if their pre-eclampsia was complicated by severe pre-eclampsia, HELLP syndrome or eclampsia and led to birth before 34 weeks, and about 1 in 2 (55%) pregnancies if it led to birth before 28 weeks

Predicting pre-eclampsia

- Major contributor to maternal mortality worldwide
- First cause of maternal admission to intensive care units
- Associated with an increased risk of perinatal mortality
- Accurate prediction of preeclampsia may allow more efficient allocation of resources
- No single test that predicts preeclampsia with sufficient accuracy to be clinically useful
- No consensus on the optimal timing of screening
- The following screening tools have been evaluated:
  - ✓ *Maternal history* – demographic characteristics, past medical, family or obstetric history
  - ✓ *Maternal haemodynamic and vascular studies* – blood pressure at early booking, maternal cardiac output
  - ✓ *Biochemical markers* – products of fetal and placental origin, markers of renal or endothelial damage, markers of oxidative stress and angiogenic factors
  - ✓ *Uterine artery Dopplers*
  - ✓ *Combined tests*

Conclusion

- Women with preeclampsia or gestational hypertension → increased risk of subsequent cardiovascular morbidity (hypertension and coronary heart disease)
- Counsel patients about the benefits of exercising regularly, avoiding smoking and maintaining a healthy diet
- Hypertensive disorders of pregnancy are a common - ±12% have some degree of hypertension
- GPs are likely to be faced with such patients -
  - ✓ be aware of the complications associated
  - ✓ inform patients of the dangers associated with hypertension
  - ✓ treat acute severe hypertension immediately
  - ✓ refer promptly to a level II or III hospital