Chapter 15

HYPERTENSIVE DISORDERS OF PREGNANCY
(Formerly GESTATIONAL HYPERTENSION) (Severe Pre-Eclampsia / Eclampsia)

Hypertension in pregnancy is a leading cause of maternal morbidity and mortality.

CLASSIFICATION OF HYPERTENSION:
“Hypertension is classified as pre-existing or gestational. Pre-existing hypertension pre-dates pregnancy or appears before 20 wks, and gestational hypertension appears at or after 20 wks. For both pre-existing and gestational hypertension, there are two subgroups: (1) with comorbid conditions and (2) with preeclampsia, defined by three criteria:

- Hypertension
- Proteinuria
- and adverse conditions.” (JOGC, March 2008, S12)

The term preeclampsia has been re-introduced for its brevity and international use. It is now used to replace previously used terms such as:

- Pre-existing hypertension with superimposed gestational hypertension, proteinuria and / or an adverse condition(s)
- Gestational hypertension with proteinuria
- Gestational hypertension (without proteinuria) with one or more of the adverse conditions. (JOGC, March 2008, S13)

DEFINITIONS:
Hypertension in pregnancy should be defined as a diastolic BP of ≥ 90 mmHg or systolic BP ≥ 140 mmHg, based on the average of at least 2 measurements, taken using the same arm. Mean arterial pressure (MAP) is no longer used as a criterion in the definition of hypertension as it is difficult to calculate. (JOGC, March 2008, S10)

Severe Hypertension should be defined as a systolic BP of ≥ 160 mmHg or a diastolic BP of ≥ 110 mmHg. A repeat measurement should be taken for confirmation in 15 minutes. (JOGC, March 2008, S10)

Preeclampsia in women with pre-existing hypertension is defined as resistant hypertension, new or worsening proteinuria, or one or more adverse conditions noted below. Resistant hypertension is elevation in blood pressure after 20 weeks gestation that requires three antihypertensive medications to control it. In women with gestational hypertension, preeclampsia is defined as new-onset proteinuria or one or more adverse conditions. Edema and weight gain have been excluded from the definition of preeclampsia. (JOGC, March 2008, S1-13)
“Severe preeclampsia is defined as preeclampsia with an onset before 34 weeks’ gestation, with heavy proteinuria or with one or more adverse conditions.” (JOGC, March 2008, S12)

“Proteinuria is defined as ≥ 0.3g/d in a 24 hr urine collection or ≥ 30 mg/mmol urinary creatinine in a spot (random) urine sample. Proteinuria should be strongly suspected when urinary dipstick protein is ≥ 2+.” (JOGC, March 2008, S11)

Heavy proteinuria is defined as 3 – 5 g/d. Proteinuria indicates glomerular dysfunction. (JOGC, March 2008, S12)

Women with certain comorbid conditions, such as cardiovascular disease, type I or II diabetes mellitus, renal disease or cerebrovascular disease are at increased risk of hypertensive problems during pregnancy. They also often warrant antihypertensive therapy over the short term, outside pregnancy. "With comorbid conditions" refers to conditions that are strong indicators for aggressive antihypertensive therapy outside of pregnancy.” They warrant special BP treatment thresholds and goals in pregnancy. (JOGC, March 2008, S12)

ADVERSE CONDITIONS OF GESTATIONAL HYPERTENSION: (JOGC, March 2008, S12) Adverse conditions include both end organ complications of the mother and direct fetal complications. (JOGC, March 2008, S13) These include:

1. Vascular/Pulmonary
   - Systolic BP > 160 mmHg or diastolic BP > 110mmHg
   - Pulmonary edema
   - Chest pain
   - Dyspnea

2. Renal
   - ↑ serum creatinine
   - ↓ serum albumin (< 20g/L)
   - Proteinuria

3. Hepatic
   - Elevated AST, ALT, LDH
   - Severe nausea / vomiting
   - Persistent abdominal or right upper quadrant pain
   - Jaundice

4. Hematologic
   - Platelets <100,000
   - Disseminated intravascular coagulopathy (DIC)
5. **CNS**
   - Persistent new or unusual headache
   - Visual disturbances
   - Hyperreflexia
   - Seizures
   - Stroke (may occur with a systolic BP $\geq 160$ mmHg)

6. **HELLP Syndrome**
   - Hemolysis
   - Low Platelets
   - Elevated Liver Enzymes

7. **Fetal Effects**
   - Intrauterine growth restriction
   - Oligohydramnios
   - Absent or reversed end-diastolic umbilical artery flow as indicted by Doppler flow studies
   - Atypical / abnormal fetal heart rate
   - Placental abruption
   - Prematurity
   - Intrauterine death

“The appearance of any of these manifestations of multi-organ involvement or the development of hypertension in pregnancy remote from term constitutes an obstetrical emergency. This emergency may need to be managed in conjunction with other professionals (including hematological, neonatal, nursing, obstetrical experts), locally or regionally. There must be access to laboratory, blood bank, pharmacy, and essential hospital facilities. Caregivers who lack ready access to many of these resources should develop protocols for their institutions for the rare emergency case that cannot be transferred to a tertiary care centre.” (SOGC, 2009-2010, p3-4)
ASSESSMENT:
The initial and ongoing evaluation of the woman with gestational hypertension involves assessment of symptoms associated with adverse conditions (see above), laboratory findings and assessment of the fetal / placental unit.

Blood pressure should be determined using:
- Sitting position with arm at heart level
- Appropriate size cuff
- Accurate mercury or aneroid sphygmomanometer, or an automated BP monitor that has been calibrated against a mercury or aneroid sphygmomanometer (automated BP machines may underestimate the BP if not appropriately calibrated)
- Korotkoff sounds V (disappearance of pulse sound) recorded
Repeat BP in 4 hours unless very high (diastolic 110 mmHg). If the BP is consistently higher in one arm, the arm with the higher values should always be used. (JOGC, March 2008, S9)

Laboratory assessments include:
Hematologic
- Hemoglobin
- WBC & differential
- platelet count
- blood film
- INR and aPTT, Fibrinogen

Hepatic
- ALT, AST, LDH, bilirubin
- Albumin (if very low then increased risk of pulmonary edema)
- Glucose (low in acute fatty liver of pregnancy)

Renal
- Serum creatinine
- Serum uric acid
- Urinalysis (routine & microscopy)
- Proteinuria

Assessment of Fetus
- Fetal movement count
- NST
- Fetal heart rate (intermittent or continuous electronic fetal monitoring depending on severity)
- Biophysical Profile
- Ultrasound for growth (gestational age dependant)
- Doppler flow studies (umbilical artery Doppler resistive index) (JOGC, March 2008, S15)
MANAGEMENT:
In general, the management of pregnancy related hypertension includes:

- Evaluation of the mother and fetus
- Prevention of adverse maternal and fetal outcomes
- Symptomatic support (SOGC, 2009-2010, p11)

Care can be managed through hospital day units or home care for women with non-severe preeclampsia or non-severe (pre-existing or gestational) hypertension. In-patient care is required for women with severe hypertension or severe preeclampsia. (JOGC, March 2008, S24) “Obstetric consultation is mandatory for women with severe preeclampsia.” (JOGC, March 2008, S31)

“Delivery is the definitive treatment for preeclampsia” … Consider delivery when:

a) the hypertensive disorder is associated with progressively worsening adverse maternal and fetal conditions, regardless of gestational age.

b) the patient is at or near term. (i.e. >34 weeks gestation)

When the fetus is immature and there are no adverse conditions, expectant management is recommended. Women should be closely observed for the development of adverse conditions and their progression. Antihypertensive treatment should be considered.” (SOGC, 2009-2010, p11-12)

Immediate treatment should include managing symptoms such as nausea and vomiting with an antiemetic to minimize maternal discomfort. Maternal pain (right upper quadrant pain, headache, etc.) should be managed appropriately. A component of maternal hypertension is adrenergic and may be modified by stress reduction. Some bed rest may be helpful but there is limited evidence to support the use of strict bed rest to reduce the effects of pre-eclampsia. (JOGC, March 2008, S24)

Antihypertensive Therapy:
Antihypertensive medications are used to reduce the risk of developing severe hypertension and its potential sequelae, such as cerebral vascular accidents, in the mother. They do not necessarily reduce the risk of seizures (eclampsia) or prevent adverse fetal outcomes such as IUGR. Whenever antihypertensive agents are used is it important to be mindful of avoiding a rapid drop in BP as this can reduce utero-placental perfusion resulting in fetal compromise. (SOGC, 2009-2010, p12)

The following recommendations apply to women with either pre-existing or gestational hypertension. It is recommended that all perinatal units have a management protocol for the treatment of severe hypertension.
For Severe Hypertension (systolic BP ≥ 160 mmHg or diastolic BP ≥ 110) (JOGC, March 2008, S25-26):
- BP should be lowered to <160 mm Hg systolic and <110 mm Hg.
- Initial antihypertensive therapy should be with
  - Labetalol
    - Start with 20 mg IV, repeat 20 – 80 mg IV q 30 min, or 1 – 2 mg/min, max 300 gm (then switch to oral)
  - Nifedipine capsules
    - 5–10g capsule to be bitten and swallowed, or just swallowed q30 min.
  - Nifedipine PA tablets
    - 10 mg PA tablet q 45 in to a max. of 80 mg/d
  - Hydralazine
    - Start with 5 mg IV: repeat 5 – 10 mg IV q 30 min. or 0.5 – 10 mg/hr IV, to a max. of 20 mg IV (or 30 mg IM)
- Continuous FHR monitoring is advised until BP is stable.
- Consider appropriateness of environment, potential need for patient transfer.

For Non-severe Hypertension (BP 140-159/90-109) (JOGC, March 2008, S26-27)
- For women who do not have co-morbid conditions, antihypertensive agents should be used to keep the systolic BP at 130 – 155 mm Hg and the diastolic BP at 80 – 105 mm Hg.
- For women with co-morbid conditions, antihypertensive drug therapy should be used to keep the systolic BP at 130 – 139 mm Hg and the diastolic BP at 80 – 89 mm Hg.
- Initial therapy can be with either
  - Metyldopa (Aldomet)
    - 250 – 500 mg po BID – QID (max. 2 g/d)
  - Labetalol
    - 100 – 400 mg. po BID – TID, (max. 1200 mg/d) or
  - Nifedipine PA tablets (10 – 20 mg po BiD – TiD (max. 180 mg/d) or
  - Nifedipine XL preparation (20 – 60 mg po OD (max. 120 mg/d)

Remember that Angiotensin Converting Enzyme (ACE) inhibitors and Angiotensin Receptor Blockers (ARBs) are contraindicated in pregnancy! Atenolol ® is not recommended due to increased rates of IUGR, hypotension and bradycardia. (SOGC, 2009-2010. P15)
Magnesium Sulphate
Magnesium Sulphate is not an antihypertensive. Its use is recommended only for seizure prophylaxis and seizure treatment in women who have severe preeclampsia. Blood pressure is not always a reliable predictor for the risk of seizures. Phenytoin and benzodiazepines should not be used for seizure prophylaxis unless there is a contraindication to MgSO₄ or it is not effective. (JOGC, March 2008, S32)

Magnesium sulphate should ideally be administered intravenously. The MgSO₄ solution should be piggy-backed to a mainline infusion and administered through an infusion pump.

Prophylaxis for Seizure Prevention (SOGC, 2009-10, p17)

Dosage:
- 4 g IV over 20-30 minutes, followed by 1-2 g/hour IV

Side effects:
- Weakness
- Paralysis
- Cardiac toxicity
- Reduced respiratory rate or cessation of breathing

Monitor:
- Reflexes
- Respiration
- Level of consciousness
- Hourly urine output

*Caution should be exercised when combined with calcium channel blockers (i.e.: Nifedipine) and in women with renal failure, although the risk of complications is low (<1%).

THE ANTIDOTE TO MAGNESIUM IS:
10cc OF 10% CALCIUM GLUCONATE, IV OVER 3 MINUTES
(Avoiding magnesium overdose is preferable!)
(SOGC, 2009-2010, p17)

Seizure Treatment:
If seizures (eclampsia) occur, the woman must be stabilized following which birth can be planned. MgSO₄, 4gm. IV over 20 – 30 minutes may be given to stop the seizure activity, followed by a maintenance dose of 1g/hour IV. In the event of a recurrent seizure while on MgSO₄, re-bolus with 2g IV over 20-30 minutes. Women at risk of seizure activity should be treated with MgSO₄ during labour and for the first 24 hours following delivery. (SOGC, 2009-2010, p18)
Fluid Management:
Careful attention should be given to minimize intravenous and oral intake in women with preeclampsia to avoid pulmonary edema. The standard bolus of intravenous fluid usually given to women prior to epidural anesthesia should not be administered. It is common to use 0.9 NaCl in case the patient is in heart failure. In the third stage of labour lesser degrees of postpartum hemorrhage may result in hypotension and shock as a result of vascular space contraction. Plasma volume expansion is not recommended for women with preeclampsia.
(SOGC, 2009-2010, p15)

REMEMBER THAT HYPOTENSION AND SHOCK MAY DEVELOP AT A LESSER DEGREE OF HEMORRHAGE IN THE THIRD STAGE OF LABOUR BECAUSE OF VASCULAR SPACE CONTRACTION (SOGC, 2009-2010, p15)

Urine output <15 ml/hr is not unusual in pre-eclampsia, particularly postpartum. Urine output is best monitored with an indwelling urinary catheter, connected to a urometer in cases of severe preeclampsia. In the presence of oliguria consider:
- Clinical assessment of volume status
- Measure renal function (creatinine)
- Heightened awareness of magnesium toxicity
- Consider a small fluid bolus (500 mL normal saline)
- Monitor O₂ saturation, keep it >95%
- Consider appropriate consultation

BEWARE OF PULMONARY EDEMA
(SOGC, 2009-2010, p16)
THERAPIES FOR HELLP SYNDROME:
Recommendations (JOGC, March 2008, S33)

HELLP syndrome consists of:

- **H** Hemolysis
- **EL** Elevated Liver Enzymes
- **LP** Low Platelets

  - Prophylactic transfusion of platelets is not recommended, even prior to Caesarean section, when platelet count is $>50 \times 10^9/L$ and there is no excessive bleeding or platelet dysfunction.

  - Along with appropriate consultations, consideration should be given to ordering blood products, including platelets, when platelet count is $<50 \times 10^9/L$, platelet count is falling rapidly, and/or there is coagulopathy.

  - Platelet transfusion should be strongly considered prior to vaginal and cesarean section delivery when platelet count is $<20 \times 10^9/L$.

  - Corticosteroids may be considered for women with a platelet count $<50 \times 10^9/L$.

  - There is insufficient evidence to make a recommendation regarding the usefulness of plasma exchange or plasmapheresis.

**Stress Reduction**

- Quiet environment
- Clear explanation of management plan to patient/family
- Minimization of negative stimuli
- Consistent, confident team approach (nursing, obstetrics, anaesthesia, hematology, paediatrics)

**Other Therapies for Treatment of Preeclampsia:**

- Thromboprophylaxis may be considered when bed rest is prescribed.

- Low dose aspirin is **not** recommended for treatment of preeclampsia.

**Transport:**

When local resources are limited and maternal and fetal conditions permit, the outcome may be improved by transporting the mother to an appropriate referral centre. Every unit should have a transport protocol available. Principles to be addressed prior to transport include:
Perinatal Outreach Program of Southwestern Ontario
PERINATAL MANUAL CHAPTER 15 - HYPERTENSIVE DISORDERS OF PREGNANCY
(Severe Pre-Eclampsia/Eclampsia)

Maternal blood pressure control
Is the fetus stable?
Seizure prophylaxis if appropriate
Intubation/ventilation
Ensure that calcium gluconate is available
Decisions regarding the mode of transport (road or air ambulance) and the need for accompanying personnel and the required skill set will be made by the referring centre with input from the receiving centre. (SOGC, October 2005, PS 165)

Delivery is the Cure:
- Gestational hypertension is a progressive disease
- Timely delivery minimizes maternal and neonatal morbidity and mortality
- Optimize maternal status before intervention to delivery
- Delay delivery to allow transfer only when maternal and fetal conditions permit
- Delay delivery to gain fetal maturity only in selected cases, <34 weeks and in a centre with sufficient resources.
- When delivery is considered prior to 34 weeks gestation, antenatal corticosteroids should be administered to accelerate fetal pulmonary maturity
- Expectant management is potentially harmful in the presence of gestational hypertension with adverse conditions, fetal maturity, or suspected fetal compromise. (SOGC, 2009-2010, p17-18)

KEY POINTS:

Peripartum Management (SOGC, 2009-2010, p18)
- Do not reduce blood pressure too rapidly
- Do not acutely reduce diastolic BP below 90 mm Hg
- Do not fluid overload
- Epidural analgesia may be used in the absence of low platelets or coagulopathy
- Avoid using ACE inhibitors or angiotensin receptor blockers
- Multispecialty approach:
  - Obstetrics care provider
  - Anaesthesiology
  - Paediatrics/Neonatology
  - Nursing
  - Internal medicine/haematology/nephrology/neurology, as needed

Postpartum Management
Gestational hypertension may present initially or worsen transiently following delivery. Proteinuria and other adverse conditions may also become worse in the early postpartum period.
All women must be followed carefully in the postpartum period with ongoing attention to blood pressure control, renal function, seizure risk and laboratory investigations, with particular attention to potential end-organ dysfunction. (SOGC, 2009-2010, p19)

Postpartum thromboprophylaxis may be considered for women who have had a Caesarean Section or who have been on bed rest for greater than four days. (JOGC, March 2008, S34)

“Non-steroidal anti-inflammatory drugs (NSAIDS) should not be given postpartum if hypertension is difficult to control or if there is oliguria, or an elevated creatinine level.” (JOGC, March 2008, S34)

Severe postpartum hypertension should be treated with antihypertensive agents to keep the BP < 160/110 mm Hg. Antihypertensive medications should also be considered to treat postpartum women with non-severe hypertension especially if they also have co-morbidities. (JOGC, March 2008, S34)

“Antihypertensives acceptable for use with breastfeeding include:
- Nifedipine XL
- Labetalol
- Methyldopa
- Captopril
- Enalapril” (JOGC, March 2008, S34)

These patients should only be discharged when there is clinical and laboratory evidence of improvement and evidence that end-organ failure has resolved. Arrangement for adequate outpatient surveillance should be made. Follow-up should be arranged for clinical and blood pressure assessment within one week of discharge. (SOGC, 2009-2010, p19)

It is reasonable to discharge a woman whose BP remains at < 160/110 mm Hg for at least 24 hours. (SOGC, 2009-2010, p19)

REFERENCES:

