Hypertension in Pregnancy

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Significance

- Hypertension disorders of pregnancy (HDP) complicate 5-10% of pregnancies worldwide – up to 16% in SA

- The leading cause of direct/pregnancy related maternal deaths (almost similar with Obs Haem/ HIV = indirect cause) - HDP accounts for 14.8% maternal mortality in SA

- Deaths from Hypertensive disorders of pregnancy (HDP) not declining (some indication that it is climbing);
  - HDP are also associated with high numbers of stillbirths and neonatal deaths
Figure 1. Distribution of potential preventable deaths 2008-2017

NPRI – Non-pregnancy related infections; OH – Obstetric Haemorrhage; HDP – Hypertensive disorders of pregnancy; M&S – Pre-existing medical and surgical conditions
78.5% of maternal deaths due to HDP were at levels with specialist care

Almost 75% of the maternal deaths due to HDP - potentially preventable

Major problems: Lack of proper assessment, diagnosis at primary level of care, not adhering to standard protocols (regional, tertiary and national central hospitals), transport to higher tertiary hospitals for treatment
Figure 3. Proportion of potentially preventable deaths per disease category
Definitions
Hypertension

- **Normal blood pressure (BP):** systolic 120mmHg, diastolic 80mmHg
- **Hypertension** - systolic $\geq$ 140mmHg, diastolic $\geq$ 90mmHg taken 4-6 hrs apart, seated and upright, correct cuff size
Classification

- Gestational Hypertension
- Pre-eclampsia (PE)
- Chronic hypertension
- Chronic hypertension with superimposed PE

*International Society for the Study of Hypertension in Pregnancy (ISSHP) Classification*
Risk factors for hypertension

• Maternal factors
  • Primigravida
  • PMHx or FHx of Gestational hypertension
  • Diabetes Mellitus, Chronic hypertension, Renal insufficiency
  • Anti-phospholipid syndrome
  • Extremes of maternal age (< 18 or > 35)
  • Assisted reproductive therapies

• Fetal factors
  • Hydrops Fetalis
  • Previous stillbirth or intrauterine fetal demise
Pre-hypertension

- Low risk pregnant women
  - Pre-hypertension (135/85 - 139/89mmHg)
  - BP repeated within 30 mins – 2 hours: if still pre-hypertensive follow up within 3-7 days
  - Repeat BP is normal - low risk
Gestational Hypertension

- Pregnancy induced hypertension
- Systolic BP ≥ 140mmHg, diastolic BP ≥ 90mmHg
  - Occur after 20 weeks of gestation
  - High pressure on two or more consecutive occasions, 4 - 6 hours apart
  - No proteinuria
- In a previously normotensive woman
- BP returns to normal within 3 months postpartum
Chronic Hypertension

- Hypertension present before pregnancy
- Or first diagnosed before 20 weeks of gestation
- Not resolved by 12 weeks postpartum
Chronic Hypertension with Superimposed PE

- New-onset of hypertension
- Occurs after 20 weeks of gestation in women with pre-existing hypertension
- Worse proteinuria
- Sudden increase in blood pressure, thrombocytopenia
- Elevated liver enzymes
Pre-eclampsia

- New-onset of hypertension
  - Occur after 20 weeks of gestation
  - Proteinuria
  - In a previously normotensive woman
  - BP returns to normal within 3 months postpartum
Pre-eclampsia

- **Severe pre-eclampsia:**
  - BP $\geq 160/110$mmHg on two readings, 4 hours apart
  - Proteinuria $> 3\text{g}/24\text{ hours}$ or $3+/4+$ ($3\text{g/l}$ or $> 20\text{g/l}$ protein)
  - **Headache-blurred vision**
  - **Altered consciousness/irritability**
  - **Epigastric or right upper quadrant pain**
  - Pulmonary oedema
  - Thrombocytopenia
  - Impaired liver function
Pre-eclampsia: Pathophysiology

- Defective spiral artery remodeling
- Can't breathe
- Systemic vasoconstriction and endothelial dysfunction
- Hypertension and end-organ damage
- Hemolysis elevated liver enzymes low platelets
- Proteinuria

Placental hypoperfusion
- I want a belly button!
- Curative treatment is delivery
Pre-eclampsia: Pathophysiology

- Immune factors, genetic factors, dietary factors
  - Trophoblastic maladaptation
  - Reduced uteroplacental perfusion
  - Cellular anoxia
  - Release of angiogenic factors, apoptotic cells and trophoblastic debris
  - Vascular endothelial damage
- Organ system involvement
- Clinical signs and then increased BP, proteinuria and IUGR
Immunology of preeclampsia

- First time pregnancies
- Number of immune markers
- ??HIV as immune deficient condition – reduces the risk

<table>
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<tbody>
<tr>
<td>HDP (661)</td>
<td>85</td>
<td>409</td>
<td>167</td>
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<tr>
<td>PET (181)</td>
<td>13</td>
<td>122</td>
<td>46</td>
</tr>
<tr>
<td>Eclampsia(347)</td>
<td>54</td>
<td>206</td>
<td>87</td>
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</tbody>
</table>
HIV and HDP

Associations between HIV, highly active anti-retroviral therapy, and hypertensive disorders of pregnancy among maternal deaths in South Africa 2011–2013

Hannah M. Sebitloane1* | Jagidesa Moodley2 | Benn Sartorius3
FIGURE 2  Comparison of relative risks of maternal death being due to hypertensive disorders of pregnancy from the Saving Mothers report with estimated relative risks from Browne et al. 6 and Calvert et al. 7 Abbreviations: HAART, highly active anti-retroviral therapy; AIDS with HAART, individuals with CD4 counts below 200 cells/mm³ or WHO clinical stage 4 HIV/AIDS infection who were receiving HAART; AIDS no HAART, individuals with CD4 counts below 200 cells/mm³ or WHO clinical stage 4 HIV/AIDS infection who were not receiving HAART; HIV positive but not requiring HAART, individuals with CD4 count of at least 200 cells/mm³; HIV uninfected, individuals without HIV infections.
Complications of Pre-eclampsia

- **Maternal**
  - Renal failure
  - Cardiac failure
  - Liver failure
  - Eclamptic fits
  - Abruptio placentae
  - Stroke
  - HELLP Syndrome
  - Thrombocytopenia

- **Fetal**
  - Placental Insufficiency
  - Placental infarctions
  - IUGR
  - Fetal distress
  - Fetal death
Approach to Management
Approach and Management
BP measurement technique

- Seated position with legs uncrossed - in a relaxed position
- Arm at level of heart, free of clothing, supported
- Appropriate size cuff
- Length of cuff 2.5 x MUAC
- If MUAC > 33cm - larger cuff size should be used
- Machines should be regularly calibrated
- Slight elevations in BP/ BP between 140 – 150mmHg: BP should be repeated in 15 minutes
Approach and Management
Pre-eclampsia

- Prevention
- Calcium
- Vitamin C, Vitamin E
- Prostaglandin precursors (omega fatty acid)
- Anti-platelets: low dose aspirin
- Heparin
- Sodium, Magnesium, Selenium, Zinc
- Lycopene, mitochondrial antioxidants, Co-enzyme Q, melatonin
- Diuretics
- Isocaloric balanced protein / protein and energy restriction (obese)
Ca supplementation

- **Given to all pregnant women.**
  - 500mg of elemental calcium daily with 2-hour gap between iron and calcium intake.
  - Start at any gestation but start as early as possible.

- WHO recommendation 1.5g of elemental calcium daily based on 1 systematic review. Repeat review done on low dose calcium – similar results to high dose trials. 1.5g is a high dose.
- SA studies – women are very calcium deficient; 500mg/day of elemental calcium is a reasonable dosage.
  - Should it be taken after certain gestational age?
  - Should it be prescribed to women who already have pre-eclampsia?
    - **Calcium reduces BP in women with hypertension therefore should not be restricted to women for prevention of hypertension. No harm described to date.**
  - (More women with HELLP syndrome in calcium group in trials but significantly less serious outcomes in calcium group.)
Approach and Management

Pre-eclampsia

- Pre-eclampsia associated with vasospasm and activation of the coagulation-haemostasis systems
- Caused partly by an imbalance in the thromboxane A2-prostacyclin ratio

**Low-dose aspirin:**
- Inhibits biosynthesis of platelet thromboxane A2
- Little effect on vascular prostacyclin production

**Low-dose aspirin and heparin:**
- Higher systemic inflammatory response in PE
- Higher prevalence of placental thrombotic lesions in PE
Criteria for initiating low dose aspirin

Guidelines suggest 75-162mg/day from 12-14/40

High Risk
- Hypertension in previous pregnancy
- Renal disease
- Autoimmune disease
- Diabetes (Type 1, 2)
- Chronic hypertension

Moderate Risk (Should have more than 1 risk factor)
- Age > 40 years
- Nulliparity
- Pregnancy interval < 2 years or > 10 years
- BMI > 35
- Family history of PE
- Multiple gestation
Drugs suitable for use in pregnancy

• **Alpha-receptor antagonists: Methyldopa**
  Loading dose: 1-2g po daily
  Continuation: 500mg 3 times daily to maximum of 2g daily
  Decrease systemic vascular resistance

• **Alpha and beta-receptor antagonists: Labetalol**
  Can be used as a short acting agent
  Induces vasodilation

• **Calcium channel blockers: Nifedipine**
  Long acting used both ante- and post-partum
  Or short acting agent: 10 mg, oral
  Decrease systemic vascular resistance, increase
  Cardiac output

• **Arteriolar Vasodilators: Hydralazine**
  Adjunct to methyldopa
  Decrease systemic vascular resistance
  Can be used as a rapid agent
  *Bethamethasone - 12mg, 12 hourly (two doses) to stimulate fetal maturity if urgent
delivery is required.*
Approach and Management
Severe Pre-eclampsia

- Systolic BP ≥ 160mmHg, diastolic ≥ 110mmHg on two occasions at least 4-6 hours apart
- Proteinuria ≥ 5g in a 24 hour urine specimen, ≥ +++ on two random urine samples collected at least 4 hours apart

- Features
  - Oliguria of less than 500mL in 24 hours
  - Cerebral or visual disturbances
  - Pulmonary oedema or cyanosis
  - Epigastric or RUQ pain
  - Impaired liver function
  - Thrombocytopenia (<100 × 10⁹/L)
  - Fetal growth restriction
Approach and Management
Severe Pre-eclampsia

- Admission to high care (regional or tertiary hospitals)
- Stabilisation:
  - One IV line slowly with 200ml ringers lactate or 200ml normal saline
  - Magnesium sulphate (4g IV in 200ml normal Saline/Ringers lactate over 20 minutes, 10g IMI (5g in each buttock))
  - To lower high BP: 10mg Nifedipine orally. Repeated every 30 minutes if the BP does not drop below 160/110mmHg
  - 1g Alpha Methyldopa orally, thereafter 750mg, 8 hourly
  - Insert a urinary catheter and monitor the urine output every hour
  - If urine output drops to < 25 ml/hour, one additional bolus of 200ml can be given
  - Blood investigations
Approach and Management
Severe Pre-eclampsia

- Exclude pulmonary oedema, Congestive Cardiac Failure, Imminent Eclampsia, abruptio placentae
- Assess viability and fetal condition
- Plan for delivery – time and mode
Approach and Management
Severe Pre-eclampsia

• HELLP syndrome criteria for diagnosis
  • Haemolysis
    • Peripheral smear
    • LDH > 600
    • Raised unconjugated bilirubin
    • Raised haptoglobin levels
  • Elevated Liver enzymes
    • AST > 70
    • Enzymes 2x upper limit of normal
  • Low Platelets
    • Sibai criteria < 100
    • Tennessee criteria < 150
    • Mississippi criteria
      • Mild 100-150
      • Moderate 50-99
      • Severe < 50
Approach and Management
Severe Pre-eclampsia

- MgSO$_4$

**Sibai regime:**
- 6g: 200ml over 30min IV
- 8g: 200ml at 2g/hour in IVAC pump (54ml/hour)
  - 24 hours post delivery of placenta in eclampsia, imminent eclampsia

**Pritchard regime:**
- 4g IV over 4 minutes + 5g imi in each buttock (14g in total)
- 5g imi every 4 hours in alternate buttocks

**Monitor:**
- **Hourly** – BP, Pulse, RR, Urine output (at least 0.5ml/kg/hour)
- **4 hourly** - Patellar reflexes
Approach and Management
Severe Pre-eclampsia

• Assess gestational age and fetal condition

• Corticosteroids from 28-34/40
  Maximum effect if delivery occurs between 24 hours and 7 days from commencing treatment

• CTG monitoring if > 34/40, Completion of steroids
Approach and Management
Severe Pre-eclampsia

- Delivery mode
- Maternal condition
- Cervical score
- Fetal viability
- Obstetric indication for c/s

- Normal delivery
  - No need for elective assisted delivery
  - If BP not controlled before pushing – shorten the second stage with forceps or vacuum
Approach and Management
Severe Pre-eclampsia – immediate delivery

- Term reached (38/40)
- Uncontrolled hypertension

**Maternal factors**
- Worsening renal function, renal failure
- Hepatic dysfunction
- Progressive TCP
- HELLP
- DIC
- CCF, CVA
- Eclampsia, Imminent Eclampsia
Approach and Management
Severe Pre-eclampsia – immediate delivery

- Fetal factors
- IUGR
- Oligohydramnios
- Abnormal dopplers
- Abruptio placentae
- Non-reactive CTG
Approach and Management

Eclampsia

Antenatal complications

- Abruptio placenta
- HELLP syndrome
- Pulmonary oedema

Post-delivery complications

- Anaemia
- Coagulopathy
- Admission to intensive care unit
- Maternal deaths
Approach and Management
Eclampsia

- Stabilize patient
- Airway management
- IV access
- Control convulsions: MgSO\textsubscript{4}
- Maintain Diastolic BP of 95-105mmHg. Short acting agents: Hydralazine, Nifedipine, Labetalol
- Investigations – Haemoglobin, renal function, platelet count, central venous pressure, Urea, creatinine, Coagulation screen and LFT if thrombocytopenia, fetal surveillance

*To reverse MgSO\textsubscript{4} toxicity: Calcium Gluconate (10%) - 10 ml slowly intravenously over 10 minutes
Approach and Management
Eclampsia

- Delivery – C/S
  - Low GCS
  - Associated abruptio placentae
  - Obstetric indications

- Pain relief during labour and delivery:
  - Systemic opioids
  - Epidural anaesthesia

- Post-delivery - High care for at least 24 hours, MgSO₄ therapy, tapering off antihypertensives, BP control, contraception
Hypertensive Disorders of Pregnancy Guidelines: 2019

- **New Guidelines**
  - Improve management of women with HDP
  - Reduce mortality rates

- **Implementation**
  - Increase access to contraceptives
  - Improve access to quality antenatal care
  - Strengthen information, diagnosis and treatment of HDP
SAVING MOTHERS REPORT 2017
REPORT ON KEY DECISIONS TAKEN BY THE NATIONAL HEALTH COUNCIL, 6-7 DECEMBER 2018

- **Strengthen information, diagnosis and treatment of Hypertensive Disorders of Pregnancy** Ensure that all clinics have protocols and guidelines (including referral)
  - DCSTs to ensure that protocols are available and are used (and provide training in the use of protocols were necessary)
  - Train nurses to manage / initiate treatment for HDP immediately especially that of severe hypertension ) and refer pregnant women with hypertension timeously
  - Ensure that functional BP machines are available at all clinics
  - Provide calcium carbonate as part of antenatal care to prevent HDP and provide low dose aspirin for those at risk of HDP
  - Speak to DBE about providing information to all learners about reproductive health matters and to ensure pregnant learners get their BP measured regularly
  - Minister to issue a circular to clinical managers on the management of staff especially sessional doctors and the availability and use of clinical protocols on management of hypertension
Implications of Hypertension in Pregnancy

- Maternal morbidity and mortality
  - Renal impairment - failure
  - Hepatic impairment
  - Blood dyscrasias (TCP, haemolysis - anaemia)
  - Eclampsia
  - Pulmonary oedema
  - APH - PPH (abruptio)
  - Increased operative delivery
  - CCF
  - Cerebral oedema
  - CVA
  - Development of chronic hypertension, IHD in later life
Implications of hypertension in Pregnancy

- Neonatal morbidity and mortality
  - Abruptio
  - IUGR
  - Congenital anomalies (antihypertensive use)
  - IUD
  - SGA
  - Prolonged NICU stays
  - Risk of chronic disease in adulthood
• The ISSHP high risk factors list be used during history taking for identifying patients at risk at all levels of health care and aspirin should be started for those at risk but only if the woman books early enough to start aspirin (ideally 12-14 weeks) but can be up to 20 weeks’ gestation (with 75–162 mg/day aspirin – a quarter or half an aspirin tablet) (9,10,11)
• Prior pre-eclampsia
• Chronic hypertension
• Multiple gestation
• Pre-gestational diabetes
• Maternal BMI>35
• Anti-phospholipid syndrome/SLE
• Assisted reproduction therapies
Causes of Maternal mortality

- Severe PE, Eclampsia
- Cerebral haemorrhage: 30–40%
- Pulmonary oedema: 30–38%
- Cerebral oedema: 19%
- Renal failure: 10%
- Coagulopathy: 9%
- Airway obstruction: 6%
Approach and Management
Chronic Hypertension

- Pre-pregnancy counselling
- ACE inhibitor
- Angiotensin Receptor Blocker
- Hydrochlorothiazide
- Convert to pregnancy safe drugs if possible
Approach and Management
Chronic Hypertension

A) low-normal BP
- Physiological BP drop in pregnancy
- Antihypertensives can be stopped
- Monitor BP
- Re-institute treatment as required

B) Continue antihypertensives - if safe in pregnancy

C) Change from current medication to pregnancy - friendly medication
Approach and Management

Antenatal care

- Assess for secondary causes of hypertension
- Exclude target organ damage:
  - Fundoscopy
  - ECG
  - Urine dipstick to test for proteinuria
  - Protein/Creatinine Ratio or 24 hour urine protein - assess amount protein
- Renal US
Approach and Management Postpartum Care

- Do not discharge before 24 hours
- Daily BP for the first 2 days
- 1 BP test between day 3-5 \textit{NICE guidelines}

- BP goal: 140/90mmHg

- Continue with magnesium sulphate to 24 hours after delivery or 24 hours after last fit
- Antihypertensive drug – calcium channel blockers, diuretic (> 48 hours), ACE Inhibitors and diuretics can be used in combination

- Contraception - choice based on breastfeeding, BP control and underlying co-morbidity
Approach and Management
Pre-eclampsia

- Screening: Establish aetiology of hypertension, plan treatment, evaluate prognosis
- History-taking with ISSHP high risk factors list
  - Previous history of hypertension
  - Family history of hypertension
- Evidence of other organ involvement
  - Cardiac
  - Renal
  - Peripheral vasculature
- Continuing Assessment
  - 4 hourly BP recording
  - Maternal investigations
  - Fetal surveillance
Approach and Management
Pre-eclampsia

• **Mother** - Haemoglobin, Platelets, Urea, creatinine, uric acid, 24 hour proteinuria, if thrombocytopenia present: peripheral blood smear, coagulation: platelet, LFT: AST and LDH, ALT **optional**: ECG, Echo, chest x-ray

• **Fetus** - Gestational age, Fetal activity (kick count), Non-stress test, Ultrasound - Biometry, Amniotic Fluid volume, Doppler velocimetry
Approach (cont)

• Calcium supplementation - all pregnant women

• 500mg of calcium daily with a 2 hour gap between iron and calcium intake

• Start at any time in gestation but as early as possible
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<tr>
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<th>Chronic hypertension</th>
<th>Pre-eclampsia</th>
<th>Superimposed pre-eclampsia</th>
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</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>Usually &gt; 30 years</td>
<td>Young or &gt; 35 years</td>
<td>Usually &gt; 30 years</td>
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<tr>
<td><strong>Gravidity</strong></td>
<td>Multigravida</td>
<td>Primigravida</td>
<td>Multigravida</td>
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<tr>
<td><strong>Order of signs</strong></td>
<td>Fall pregnant while hypertensive</td>
<td>Weight gain Hypertension Oedema Proteinuria</td>
<td>Already hypertensive Develops severe hypertension and proteinuria Eclampsia</td>
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<tr>
<td><strong>Risk: Maternal and fetal</strong></td>
<td>Low to mild</td>
<td>Mild to high</td>
<td>High</td>
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<tr>
<td><strong>Risk of recurring in subsequent pregnancies</strong></td>
<td>High</td>
<td>Small</td>
<td>High</td>
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<tr>
<td><strong>Renal function</strong></td>
<td>Relatively unaffected</td>
<td>Early increase in urea, creatinine, urates</td>
<td>Increased urea and creatinine but urate can rise disproportionally pre-eclampsia</td>
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<tr>
<td><strong>Retina</strong></td>
<td>Hypertensive changes</td>
<td>Segmental spasm</td>
<td>Hypertensive changes</td>
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Approach and Management
Chronic Hypertension

Patients with a risk for PE

- Low dose aspirin from 12/40

- Calcium supplementation (if deficient) from initial visit
Approach and Management

- Hypertension with no risk factors, no proteinuria, no symptoms
- Alpha Methyldopa (500mg, 8 hourly)
- Follow-up 3-7 days

- Investigation: haemoglobin, platelets, creatinine, sonar for fetal evaluation
Approach and Management

- Hypertension with risk factors but no proteinuria
- Refer to District hospital
- Low dose aspirin

- Investigations: haemoglobin, platelets, creatinine, sonar for fetal evaluation
Basic Antenatal Care Plus - BANC Plus

- Implementation of BANC Plus in 4 catchment areas in SA (Gauteng: Pholosong, Northern Cape: Upington, North West: Mafikeng, Limpopo: Vhembe)
- More clinic visits, BP taken, increase in detection of hypertension and appropriate treatment
- However, there was no change in stillbirth rate
- Decrease in the number of stillbirths classified as unexplained
- Increase in the number of stillbirths classified as result of hypertension
- Avoidable factor - not responding to antenatal hypertension management
- Perinatal deaths - poor management
- Targeting primary health care clinics - improve antenatal care and improve referral system to the next level of expertise