Hypertension in Pregnancy

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University Hospital Birmingham
Hypertension in Pregnancy

http://www.nice.org.uk/guidance/CG107
# Definitions of Hypertension in Pregnancy

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Significant Proteinuria*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic Hypertension</td>
<td>&lt;20 weeks</td>
</tr>
<tr>
<td>Gestational Hypertension</td>
<td>&gt;20 weeks</td>
</tr>
<tr>
<td>Pre-Eclampsia (PET)</td>
<td>&gt;20 weeks</td>
</tr>
<tr>
<td>PET Superimposed on Chronic Hypertension</td>
<td>&gt;20 weeks</td>
</tr>
</tbody>
</table>

*Significant proteinuria* is > 300 mg protein in a 24-hour urine collection OR >30mg/ml in a spot urinary protein:creatinine sample
# Severity Of Hypertension

<table>
<thead>
<tr>
<th></th>
<th>Systolic BP*</th>
<th>Diastolic BP*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>140-149</td>
<td>90-99</td>
</tr>
<tr>
<td>Moderate</td>
<td>150-159</td>
<td>100-109</td>
</tr>
<tr>
<td>Severe</td>
<td>&gt;160</td>
<td>&gt;110</td>
</tr>
</tbody>
</table>

* Measurement of BP in Pregnancy

NICE clinical guideline 107: 2011
Proteinuria

Assessment

– Automated reagent strip reading device
– If > +1 (without UTI) further assess with
  • Protein/creatinine ratio (PCR):
  • 24h urine protein (validated):
    • Abnormal PCR > 30 mg/mmol
    • Abnormal 24h >300mg*

* Lab must use method to assess completeness of collection
Physiological Adaptation to Normal Pregnancy

Major Challenge for those with CKD
Physiology of Normal Pregnancy

GFR

Weeks

Sturgiss et al. 1994
Physiological changes to the kidney during healthy pregnancy.

Renal blood flow and glomerular filtration rate changes in pregnancy

- Effective renal plasma flow
- Glomerular filtration rate

Renal haemodynamics
- Renal blood flow (70%)
- Plethoric kidney swells
- Bipolar diameter (1 cm)
- Glomerular filtration rate (50%)
- Proteinuria (≤ 260 mg/24 h)

Tubular function
- Glycosuria
- Bicarbonaturia (metabolic acidosis)
- Calciuria
- Plasma osmolality (↑10 mosmol/kg)

Endocrine function
- Renin
- Erythropoietin
- Active vitamin D

Weeks’ gestation

Pelvicalyceal dimensions (right > left)

Williams D, Davison J BMJ 2008;336:211-215
Aspirin in Prevention of PET in High Risk Pregnancies


<table>
<thead>
<tr>
<th>Study (year)</th>
<th>Odds ratio (95% CI)</th>
<th>% Weight</th>
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</thead>
<tbody>
<tr>
<td>Beaufils (1985)</td>
<td>0.12 (0.02, 0.69)</td>
<td>1.2</td>
</tr>
<tr>
<td>Benigni (1989)</td>
<td>0.94 (0.06, 15.72)</td>
<td>0.5</td>
</tr>
<tr>
<td>Azar (1990)</td>
<td>0.98 (0.13, 7.18)</td>
<td>1.0</td>
</tr>
<tr>
<td>EPREDA (1991)</td>
<td>0.50 (0.15, 1.66)</td>
<td>2.7</td>
</tr>
<tr>
<td>Parazzini (1993)</td>
<td>0.79 (0.41, 1.53)</td>
<td>9.1</td>
</tr>
<tr>
<td>Rogov (1993)</td>
<td>0.14 (0.00, 7.26)</td>
<td>0.3</td>
</tr>
<tr>
<td>Viinikka (1993)</td>
<td>7.70 (0.48, 124.04)</td>
<td>0.5</td>
</tr>
<tr>
<td>August (1994)</td>
<td>1.04 (0.06, 17.17)</td>
<td>0.5</td>
</tr>
<tr>
<td>CLASP (1994)</td>
<td>0.75 (0.54, 1.03)</td>
<td>38.5</td>
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<tr>
<td>ECPPA (1996)</td>
<td>1.23 (0.75, 2.04)</td>
<td>15.5</td>
</tr>
<tr>
<td>Gallery (1997)</td>
<td>1.73 (0.33, 8.94)</td>
<td>1.5</td>
</tr>
<tr>
<td>Byaruhanga (1998)</td>
<td>0.41 (0.16, 1.08)</td>
<td>4.3</td>
</tr>
<tr>
<td>Caritis (1998)</td>
<td>0.74 (0.50, 1.11)</td>
<td>24.5</td>
</tr>
<tr>
<td>Overall (95% CI)</td>
<td>0.79 (0.64, 0.96)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Event</th>
<th>Odds Ratio</th>
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</thead>
<tbody>
<tr>
<td>PET</td>
<td>0.79</td>
</tr>
<tr>
<td>Perinatal death</td>
<td>0.79</td>
</tr>
<tr>
<td>Birth Wt</td>
<td>215g</td>
</tr>
<tr>
<td>Abruption</td>
<td>0.98</td>
</tr>
</tbody>
</table>

Risks of Pre-eclampsia: Aspirin 75mg

Moderate risk
- First pregnancy
- Age > 40
- Pregnancy interval > 10 years
- BMI > 35
- FH of PET
- Twins

High Risk
- Hypertension in previous pregnancy
- CKD
- SLE/APS
- Type 1 or 2 DM
- Chronic Hypertension

If 2 moderate of 1 Severe risk factors advise Aspirin 75mg from 12 weeks
Renal disease vs Pre-eclampsia; (systemic disease)

**Golden Rules**
- Proteinuria >20 weeks = PET
- BP control in PET does not stop illness
- Rx of severe PET = delivery
- Most conditions improve with delivery
What BP Treatment Target?

Chronic hypertension
- BP <150/100

End Organ Damage or Renal disease?
- BP <140/90

CHIPS study 2009

Maternal-Fetal Interface
Drug Transfer

IVC - Fetal liver - Placenta - Uterus
Management of Chronic Hypertension

Preconception Counselling

• Is BP Essential or secondary?
• Avoid conception on ACEi, ARB, Chlorthiazide
• Conversion and control to ‘pregnancy safe drugs’
  – Labetolol
  – Nifedipine LA
  – Methyl Dopa
• Discuss risks of worsening hypertension/PET
• Smoking/weight/Folic acid
• Aspirin from 12 weeks
ACE inhibitor: Safety in Early Pregnancy

0.5 million pregnancies

De-Kun Li, BMJ 2011:
Risk of Major Congenital Malformations; ACE during the First Trimester

- ACEi exposure in early pregnancy increasing
- Cardiac and CNS malformations in first trimester use
- Discontinue ACE/ARB pre-pregnancy and stabilise on alternative Treatment (Pre-conception counselling/contraception)

Cooper et al, NEJM 2006;8354:2443
Chronic Hypertension

Antenatal care

• Target BP < 150/100 or
• If end organ damage target <140/90
• Stop ACEi/ARB within 2 days and convert
• If secondary hypertension (Renal) refer to combined specialist clinic
• Add Aspirin 75mg at 12 weeks
• Plan additional ANC visits
• Timing of Birth: If refractory severe (>160/110) hypertension plan birth (after steroids)
Chronic Hypertension

Postnatal care

Antihypertensive treatment
- Aim to keep BP < 140/90 mmHg.
- Measure BP:
  - daily for first 2 days after birth
  - at least once 3–5 days after birth
  - as clinically indicated if antihypertensive treatment changed.
- If methyldopa was used during pregnancy, stop within 2 days of birth and restart pre-pregnancy antihypertensive treatment.
- Continue antenatal hypertensive treatment.

If woman breastfeeding
- Avoid diuretic treatment for hypertension.
- Assess clinical wellbeing of baby, especially adequacy of feeding, at least daily for first 2 days after birth.
- Offer woman information about safety of drugs for babies receiving breast milk (see page 18).

Follow-up care

- Review long-term treatment 2 weeks after birth.
- Offer medical review at 6–8 week postnatal review with pre-pregnancy care team.
Gestational hypertension

Antenatal care

Carry out full assessment in secondary care
- A healthcare professional trained in the management of hypertensive disorders should carry out the assessment.
- Take into account previous history of pre-eclampsia or gestational hypertension, pre-existing vascular or kidney disease, moderate risk factors for pre-eclampsia (see page 7) and gestational age at presentation.

Mild hypertension (BP 140/90–149/99 mmHg)
- Do not admit to hospital.
- Do not treat hypertension.
- Measure BP no more than weekly.
- Test for proteinuria (see page 6) at each visit using an automated reagent-strip reading device or urinary protein:creatinine ratio.
- Carry out routine antenatal blood tests.
- If presenting before 32 weeks or at high risk of pre-eclampsia (see page 7), test for proteinuria and measure BP 2 times a week.

Moderate hypertension (BP 150/100–159/109 mmHg)
- Do not admit to hospital.
- Treat with first-line oral labetalol to keep BP < 150/80–100 mmHg.
- Measure BP at least 2 times a week.
- Test for proteinuria (see page 6) at each visit using an automated reagent-strip reading device or urinary protein:creatinine ratio.
- Test kidney function, electrolytes, FBC, transaminases, bilirubin.
- No further blood tests if no subsequent proteinuria.

Severe hypertension (BP ≥ 160/110 mmHg)
- Admit to hospital until BP ≤ 159/109 mmHg.
- Do not offer bed rest in hospital.
- Treat with first-line oral labetalol to keep BP < 150/80–100 mmHg.
- Measure BP at least 4 times a day.
- Test for proteinuria (see page 6) daily using an automated reagent-strip reading device or urinary protein:creatinine ratio.
- Test kidney function, electrolytes, FBC, transaminases, bilirubin at presentation and then monitor weekly.

Timing of birth
- Do not offer birth before 37 weeks.
- After 37 weeks, timing of and maternal and fetal indications for birth should be agreed between woman and senior obstetrician.
- If refractory severe gestational hypertension, offer birth after course of corticosteroids (if required) is completed.

- In women receiving outpatient care after severe hypertension has been effectively controlled in hospital:
  - measure BP and test for proteinuria 2 times a week
  - carry out blood tests weekly.
Maternal Chronic Kidney Disease and Pregnancy
Causes of CKD in Pregnancy

- Hypertension/Sickle
- Reflux nephropathy
- Primary GN
- Lupus Nephritis
- Diabetic Nephropathy
- Polycystic kidney disease

Pregnancy-Screening Opportunity for CKD
Pregnancy identifies unrecognised Renal Disease
Pregnancy and Kidney Disease

- Pregnancy frequently unmask previously unrecognised renal disease
- Proteinuria <20 weeks in absence of infection indicates renal disease
- Hypertension < 20 weeks may indicate CKD
Pregnancy in Renal Disease

Frequency increasing
Often complicated
Care optimal in Obstetric Renal Clinic
Heavy Proteinuria is common in women with CKD in Pregnancy in 3rd Trimester

Proteinuria in Pregnancy

Categorised by proteinuria before 20 weeks (g/24 hours)

UK CORD 2006
## Effects of Pre-pregnancy Creatinine on Pregnancy Outcome

<table>
<thead>
<tr>
<th>Pre-Pregnancy Creatinine</th>
<th>Pre-term delivery (%)</th>
<th>Fetal growth restriction (%)</th>
<th>Pre-eclampsia (%)</th>
<th>Peri-natal death (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;125</td>
<td>30</td>
<td>25</td>
<td>22</td>
<td>1</td>
</tr>
<tr>
<td>125-180</td>
<td>60</td>
<td>40</td>
<td>40</td>
<td>5</td>
</tr>
<tr>
<td>&gt;180</td>
<td>&gt;90</td>
<td>65</td>
<td>60</td>
<td>10</td>
</tr>
<tr>
<td>On Dialysis</td>
<td>&gt;90</td>
<td>&gt;90</td>
<td>75</td>
<td>50 (25)</td>
</tr>
</tbody>
</table>

Williams, Davison BMJ 2008;336:211-5
Effect of Pregnancy on Maternal Renal function: Loss of >25% renal function

<table>
<thead>
<tr>
<th>Pre-Pregnancy Creatinine (umol/l)</th>
<th>During pregnancy</th>
<th>Persists postpartum</th>
<th>ESRF at 1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;125</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>125-180</td>
<td>40</td>
<td>20</td>
<td>2</td>
</tr>
<tr>
<td>&gt;180</td>
<td>70</td>
<td>50</td>
<td>35</td>
</tr>
</tbody>
</table>

Based on literature review 1985-2007

Williams, Davison BMJ 2008;336:211-5
Gestational Hypertension

Postnatal care

- Continue antenatal antihypertensive treatment.
- If no antenatal antihypertensive treatment, start antihypertensive treatment if BP ≥ 150/100 mmHg.
- Measure BP:
  - daily for first 2 days after birth
  - at least once 3–5 days after birth
  - as clinically indicated if antihypertensive treatment changed.
- If methyldopa was used during pregnancy, stop within 2 days of birth.
- If BP falls to < 130/80 mmHg, reduce antihypertensive treatment.
- If BP falls to < 140/90 mmHg, consider reducing antihypertensive treatment.

If woman breastfeeding

- Avoid diuretic treatment for hypertension.
- Assess clinical wellbeing of baby, especially adequacy of feeding, at least daily for first 2 days after birth.
- Offer woman information about safety of drugs for babies receiving breast milk (see page 18).

Follow-up care

- At transfer to community care, write a care plan that includes:
  - who will provide follow-up care, including medical review if needed
  - frequency of blood pressure monitoring
  - thresholds for reducing or stopping treatment
  - indications for referral to primary care for blood pressure review.
- If antihypertensive treatment is to be continued, offer medical review 2 weeks after transfer to community care.
- Offer medical review at 6–8 week postnatal review.
- If antihypertensive treatment is to be continued after 6–8 week postnatal review, offer specialist assessment of hypertension.
Pre-eclampsia

Antenatal care

- A healthcare professional trained in management of hypertensive disorders of pregnancy should assess the woman at each consultation.
- Admit the woman to hospital.
- Do not repeat quantification of proteinuria.
- Carry out fetal monitoring (see page 14).

Mild hypertension (BP 140/90–149/99 mmHg)
- Do not treat hypertension.
- Measure BP at least 4 times a day.
- Test kidney function, electrolytes, FBC, transaminases, bilirubin 2 times a week.

Moderate hypertension (BP 150/100–159/109 mmHg)
- Treat with first-line oral labetalol to keep BP < 150/80–100 mmHg.
- Measure BP at least 4 times a day.
- Test kidney function, electrolytes, FBC, transaminases, bilirubin 3 times a week.

Severe hypertension (BP ≥ 160/110 mmHg)
- Referral to level 2 critical care needed? (see page 16)
Pre-eclampsia

Follow-up care and postnatal review

**At transfer to community care**

- Write a care plan that includes:
  - who will provide follow-up care, including medical review if needed
  - frequency of blood pressure monitoring
  - thresholds for reducing or stopping treatment
  - indications for referral to primary care for blood pressure review
  - self-monitoring for symptoms.
- Measure BP every 1–2 days for up to 2 weeks after transfer to community care, until antihypertensive treatment stopped and no hypertension.
- Offer medical review if still taking antihypertensive treatment 2 weeks after transfer to community care.
- If biochemical and haematological indices improving but within abnormal range, or not improving relative to pregnancy ranges, repeat platelet count, transaminases and serum creatinine measurements as clinically indicated.

**At postnatal review (6–8 weeks after birth)**

- Offer medical review.
- Offer specialist referral if antihypertensive treatment still needed.
- Repeat platelet count, transaminases and serum creatinine measurements if indicated.
- Carry out a urinary reagent-strip test. If proteinuria ≥ 1+:
  - offer further review at 3 months to assess kidney function
  - consider offering referral for specialist kidney assessment.

1 See page 20 for contraindications and special warnings during pregnancy and lactation.
Bp Drug Choice and Breast Feeding

Breastfeeding

Tell women that the following drugs have no known adverse effects on babies receiving breast milk:
- labetalol
- nifedipine
- enalapril
- captopril
- atenolol
- metoprolol.

Tell women that there is insufficient evidence on the safety of the following drugs in babies receiving breast milk:
- ARBs
- amlodipine
- ACE inhibitors other than enalapril and captopril.
# Long Term Health Risks

| Future risk                      | Hypertensive disorder                      | Severe pre-eclampsia, HELLP syndrome or eclampsia |
|----------------------------------|--------------------------------------------|------------------------------------------------|--|
| **Gestational hypertension in future pregnancy** | Risk ranges from about 1 in 6 (16%) to about 1 in 2 (47%). | Risk ranges from about 1 in 8 (13%) to about 1 in 2 (53%). |
| **Pre-eclampsia in future pregnancy** | Risk ranges from 1 in 50 (2%) to about 1 in 14 (7%). | Risk up to about 1 in 6 (16%). No additional risk if interval before next pregnancy < 10 years. | If birth was needed before 34 weeks risk is about 1 in 4 (25%). If birth was needed before 28 weeks risk is about 1 in 2 (55%). |
| **Cardiovascular disease**       | Increased risk of hypertension and its complications. | Increased risk of hypertension and its complications. | Increased risk of hypertension and its complications. |
| **End-stage kidney disease**     | If no proteinuria and no hypertension at 6–8 week postnatal review, relative risk increased but absolute risk low. No follow-up needed. | Routine screening not needed. | |
| **Thrombophilia**               | Routine screening not needed.               |                                                    |
Reducing Risk of Hypertensive Disorders in Pregnancy

- Preconception Counselling
- Avoid ACEi/ARB and stabilise on preg-friendly
- Aspirin 75mg for pregnancy at high risk PET
- Target BP <150/100
- Assess proteinuria: automated strip reader
- If > +1-use Protein/creatinine ratio (>30)
- Proteinuria <20 weeks = Renal Disease (refer)
- Gestational Hypertension-plan care package
- PET-plan package of care
- Post Natal follow up-If hypertensive consider referral
## Risks in Future Pregnancy after PET

<table>
<thead>
<tr>
<th>Condition</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational Hypertension</td>
<td>1 in 8 to 1 in 2</td>
</tr>
<tr>
<td>Pre-eclampsia</td>
<td>1 in 6</td>
</tr>
<tr>
<td>Pre-eclampsia (if severe PET/HELLP delivery &lt;34 weeks)</td>
<td>1 in 4</td>
</tr>
<tr>
<td>Pre-eclampsia (If severe and birth &lt;28 weeks)</td>
<td>1 in 2</td>
</tr>
<tr>
<td>Mild CKD</td>
<td>1 in 4</td>
</tr>
</tbody>
</table>
Hypertension in Pregnancy

http://www.nice.org.uk/guidance/CG107
Baby joy for triple transplant patient

Brave Mary gives birth to baby she thought she’d never have after kidney transplant

Christmas will be double the fun this year for former transplant patient Mary Hibbs after giving birth to the baby she never thought she would have.

Five years ago this month (Dec), Mary was in theatre undergoing a third kidney transplant, thanks to her sister Donna who agreed to be a live donor.

Mary waited three years for her first kidney transplant after she was diagnosed with kidney reflux when she was just eight years old.

However, in 1996, the 33-year-old went into renal failure once again and this time was given a kidney from her nurse Elaine, becoming the first person in the West Midlands to receive a live kidney transplant.

Mary was told her chances of