NICE Guidelines on Pre-Eclampsia

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Aim of the session:

To give an overview of the latest NICE guidance in relation to hypertensive disorders in pregnancy.

- Classifications of hypertension
- Management recommendations
- Prediction models and PlGF
High blood pressure in pregnancy (HDP)

• Affects 1:10 women

• 140/90mmHg or more

• 20% pre-existing (chronic)

• 80% de novo (gestational/pre-eclampsia)
Chronic Hypertension

- Pre-pregnancy or diagnosed before 20 weeks of pregnancy
- Associated with adverse maternal and fetal outcomes (stroke, low birth weight, NNU admission)
- Aim for tight BP control, fetal growth monitoring and repeated assessment for the development of pre-eclampsia and maternal complications.
- Can be managed in an outpatient setting.
• Consultant led care
• Stop antihypertensive treatments for women taking ACE inhibitors or ARBs and offer alternatives
• Labetalol, nifedipine and methyldopa now specified as suitable
• New guidance on tighter BP target control 135/85mmHg (previously 150/100mmHg)
• Offer treatment if not already on antihypertensive and BP > 140/90mmHg
• Offer aspirin 75-150mg OD from 12 weeks
• Offer PIGF test between 20 week up to 35 weeks if suspected of developing pre-eclampsia
• Lifestyle advice (weight management/exercise/diet/reducing salt intake)
• Weekly appointments if BP poorly controlled, 2-4 weeks if controlled
• Timing of birth agreed in partnership if >37 weeks and BP is maintained below 160/110mmHg with or without treatment
Gestational Hypertension

- Hypertension arising after 20 weeks’ gestation in the absence of proteinuria and without biochemical or haematological abnormalities.
- 140/90mmHg-159/109mmHg
- Severe – 160/110mmHg or more
- Not usually accompanied by fetal growth restriction.
- Outcomes in pregnancy normally good, but approx 25% will go on to develop PET (particularly if < 34 weeks) and have poorer outcomes.
Risk factors:

• P0
• Age (>40)
• Pregnancy interval more than 10 years
• Family history or previous history of gestational hypertension/pre-eclampsia
• Multiple pregnancy
• Raised BMI (>35kg/m²)
• Pre-existing vascular disease
• Pre-existing kidney disease
Management:

- ‘Watch and wait’
- BP 140-159/90-109mmHg can be managed as an outpatient with once or twice weekly blood pressure measurement and urine dipstick, weekly bloods, PlGF testing and 2-4 weekly ultrasound for fetal assessment.
- Consider pharmacological treatment if BP remains above 140/90mmHg
- Labetalol or nifedipine if labetalol unsuitable and methyldopa if labetalol and methyldopa unsuitable
• Admit if severe (160/110mmHg), but manage as hypertension if falls below
• Offer treatment and record BP every 15-30minutes until 135/85mmHg.
• Offer continued pharmacological treatment
• Daily urine dipstick while inpatient.
• Measure FBC, U+Es, LFTs at presentation then weekly.
• Carry out PIGF testing
• Fetal assessment
Timing of birth

• Do not offer planned early birth before 37 weeks if blood pressure is lower than 160/110mmHg unless there are other medical indications

• If birth is necessary, offer steroids and Magnesium Sulphate in line with NICE guidance on preterm labour and birth.
Outcomes:

**Watch and Wait**

- 2/10 severe hypertension
- 47% admission to NNU

**Treatment**

- 1/10 severe hypertension
- 23% admission to NNU

*Not a uniformly benign condition and risk of complications depends on the gestational age at which it develops.*

Pre-eclampsia may develop in 25% of such women.

Associated with cardiovascular disease in the long-term.
Pre-eclampsia

• Pre-eclampsia is a complex medical disorder associated with over 500,000 fetal and neonatal deaths and over 70,000 maternal deaths globally each year.

• Can deteriorate rapidly and without warning

• Proteinuria is not mandatory for a diagnosis of pre-eclampsia. Rather, this is diagnosed by the presence of new hypertension after 20 weeks’ gestation accompanied by proteinuria and/or evidence of maternal acute kidney injury, liver dysfunction, neurological features, haemolysis or thrombocytopenia, and/or fetal growth restriction.

• Pre-eclampsia may develop or be recognised for the first time intra-partum or early post-partum in some cases.
Risk Factors

**Moderate**
- first pregnancy
- age 40 years or older
- pregnancy interval of more than 10 years
- BMI of 35 kg/m² or more at first visit
- family history of pre-eclampsia
- multiple pregnancy.

**High**
- hypertensive disease during a previous pregnancy
- chronic kidney disease
- autoimmune disease such as systemic lupus erythematosus or antiphospholipid
- type 1 or type 2 diabetes
- chronic hypertension.
Aspirin

- Women with either 1 high risk factor, or more than 1 moderate risk factor for pre-eclampsia, are advised to take 75 mg of aspirin daily from 12 weeks' gestation until the birth of the baby (NICE, 2016).
- Women with established strong clinical risk factors for pre-eclampsia be treated, ideally before 16 weeks but definitely before 20 weeks, with 75–162 mg/day aspirin (ISSHP, 2018)
- They are also considered for more frequent blood pressure monitoring, and assessment for proteinuria.
- Women who have significant hypertension (diastolic pressure of 90–110 mmHg) or a proteinuria result of 1+ on urinalysis reagent strips need increased surveillance.
Assessment

- Performed by a HCP trained in the management of hypotensive disorders of pregnancy

- Concerns include:
  - Sustained systolic BP 160mmHg or higher
  - Abnormalities in biochemical or haematological investigations e.g. new and persistent increase in creatinine or fall in platelet count
  - Signs of impending eclampsia
  - Signs of pulmonary oedema
  - (other signs of severe pre-eclampsia)
  - Suspected fetal compromise
• Consider using fullPIERS or PREP-S validated risk prediction models to guide decision making surrounding appropriate place of care (need for in utero transfer) and thresholds for intervention.

• FullPIERS can be used any time in pregnancy

• PREP-S use only up to 34 weeks

• Neither predict neonatal outcomes
Management of Pre-eclampsia

<table>
<thead>
<tr>
<th>Degree of hypertension</th>
<th>Mild (140/90 mmHg to 149/99 mmHg)</th>
<th>Moderate (150/100 mmHg to 159/109 mmHg)</th>
<th>Severe (160/110 mmHg or higher)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admit to hospital</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Treat</td>
<td>No</td>
<td>With oral labetalol as first-line treatment</td>
<td>With oral labetalol as first-line treatment</td>
</tr>
<tr>
<td>Measure blood pressure</td>
<td>At least 4 times a day</td>
<td>At least 4 times a day</td>
<td>More than 4 times a day</td>
</tr>
<tr>
<td>Test for proteinuria</td>
<td>Do not repeat quantification of proteinuria</td>
<td>Do not repeat quantification of proteinuria</td>
<td>Do not repeat quantification of proteinuria</td>
</tr>
<tr>
<td>Blood tests</td>
<td>Monitor the following twice a week: kidney function, bilirubin, electrolytes, full blood count, transaminases</td>
<td>Monitor the following 3 times a week: kidney function, bilirubin, electrolytes, full blood count, transaminases</td>
<td>Monitor the following 3 times a week: kidney function, bilirubin, electrolytes, full blood count, transaminases</td>
</tr>
</tbody>
</table>
| **Fetal assessment** | Offer fetal heart auscultation at every antenatal appointment  
Carry out ultrasound assessment of the fetus at diagnosis and, if normal, repeat every 2 weeks  
Carry out a CTG at diagnosis and then only if clinically indicated  
(See section 1.6 for advice on fetal monitoring) | Offer fetal heart auscultation at every antenatal appointment  
Carry out ultrasound assessment of the fetus at diagnosis and, if normal, repeat every 2 weeks  
Carry out a CTG at diagnosis and then only if clinically indicated  
(See section 1.6 for advice on fetal monitoring) |

* Use an automated reagent-strip reading device for dipstick screening for proteinuria in a secondary care setting.

Abbreviations: BP, blood pressure; CTG, cardiotocography.
<table>
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<tr>
<th>Weeks of pregnancy</th>
<th>Timing of birth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before 34 weeks</td>
<td>Continue surveillance unless there are indications (see recommendation 1.5.7) for planned early birth. Offer intravenous magnesium sulfate and a course of antenatal corticosteroids in line with the NICE guideline on preterm labour and birth.</td>
</tr>
<tr>
<td>From 34 to 36+6 weeks</td>
<td>Continue surveillance unless there are indications (see recommendation 1.5.7) for planned early birth. When considering the option of planned early birth, take into account the woman's and baby's condition, risk factors (such as maternal comorbidities, multi-fetal pregnancy) and availability of neonatal unit beds. Consider a course of antenatal corticosteroids in line with the NICE guideline on preterm labour and birth.</td>
</tr>
<tr>
<td>37 weeks onwards</td>
<td>Initiate birth within 24–48 hours.</td>
</tr>
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Timing of birth

• Record maternal and fetal thresholds for planned early birth before 37 weeks in women with pre-eclampsia.

•Thresholds for considering planned early birth could include (but are not limited to) any of the following known features of severe pre-eclampsia:
  • inability to control maternal blood pressure despite using 3 or more classes of antihypertensives in appropriate doses
  • maternal pulse oximetry less than 90%
  • progressive deterioration in liver function, renal function, haemolysis, or platelet count
  • ongoing neurological features, such as severe intractable headache, repeated visual disturbances, eclampsia, placental abruption, reversed end-diastolic flow, abnormal CTG or stillbirth.
• Involve a senior obstetrician in any decisions on timing of birth for women with pre-eclampsia.
• Discuss with the anaesthetic team if birth is planned in a woman with pre-eclampsia.
• Discuss with the neonatal team if birth is planned in a woman with pre-eclampsia, and neonatal complications are anticipated.
• Offer intravenous magnesium sulphate and a course of antenatal corticosteroids if indicated, if early birth is planned for women with preterm pre-eclampsia, in line with the NICE guideline on preterm labour and birth.
Post birth.

- In the early post-partum period, women with pre-eclampsia should be considered at high risk for pre-eclamptic complications for at least 3 days and should have their clinical condition monitored at least every four hours while awake.

- AN antihypertensives should be continued, and consideration should be given to treating any hypertension before D6 postpartum with antihypertensive therapy. Thereafter, antihypertensives may be withdrawn slowly over days, but not ceased abruptly.

- It is important to note that eclamptic seizures may develop for the first time in the early post-partum period.

- Avoid Non-steroidal anti-inflammatory drugs (NSAIDs) for postpartum analgesia in pre-eclampsia and AKI.
Prediction Models

- FullPIERS
- PREP-S
- PIGF
FullPIERS: Pre-eclampsia Integrated Estimate of Risk

- Recently designed tool which assesses maternal signs, symptoms, and laboratory findings to generate a valid and reliable algorithm for predicting adverse maternal and perinatal outcome in patients with preeclampsia.
- Identifies women at increased risk of adverse outcome up to 7 days before complications arise.
- Helps to plan timing of delivery and place of care.
- Developed and internally validated in prospective, multi-centre study across Canada, New Zealand, Australia and UK using data from a cohort of 2023 women with pre-eclampsia admitted to tertiary perinatal units.
FullPIERS model

Factors included in model:

- Gestational age
- Presence or absence of chest pain or dyspnea
- Oxygen saturation
- Platelets
- Creatinine
- AST/ALT
FullPIERS calculator.
https://preempt.bcchr.ca/evidence/fullpiers
PREP-S Prediction model

Aims to predict the risk time of adverse outcomes at a number of time periods

- Can be used in women up to 34+6 days
- Factors in the model include
  - Maternal age
  - Gestational age at diagnosis
  - Presence or absence of tendon reflexes
  - Presence or absence of pre-existing conditions (hypertension, renal disease, diabetes mellitus, autoimmune disease, previous pre-eclampsia)
  - Systolic blood pressure
• Oxygen saturations
• Platelets
• Urea
• Creatinine
• PCR
• Whether woman receive antihypertensive or MgSo4 at diagnosis or 24hr

https://www.evidencio.com/models/show/1038
Placental Growth Factor

- PIGF-based tests measure the amount of PIGF in blood plasma or serum. PIGF is a protein involved in placental angiogenesis (the development of new blood vessels).

- In normal pregnancy, PIGF levels rise and peak at 26–30 weeks, so when PIGF levels do not rise during pregnancy there may be placental dysfunction.

- In pre-eclampsia, levels of PIGF can be abnormally low.

- Placental growth factor (PIGF)-based tests are intended to be used with clinical judgement and other diagnostic tests, to help diagnose suspected pre-eclampsia in the second and third trimesters of pregnancy.

www.nice.org.uk/guidance/dg23
• Using PlGF-based tests in addition to standard clinical assessment could result in a faster and more accurate diagnosis of pre-eclampsia, and better risk assessment for adverse outcomes in women with suspected pre-eclampsia.

• It could also allow women in whom pre-eclampsia has been ruled out with a PlGF-based test to return to community care instead of being admitted to hospital for observation.

• Offers the ability to predict which pregnancies complicated by HDPs will go on to develop adverse outcomes and would help to improve disease management, including timing of delivery, and prevent adverse outcomes (Hypertension, 2017).
• Reduced circulating maternal free placental growth factor (PlGF) aids in the prediction or confirmation of a diagnosis of preeclampsia, fetal growth restriction, stillbirth, preterm birth, and delivery within 14 days of testing when pre-eclampsia is suspected.

• Low PlGF was associated with younger maternal age, higher blood pressure, earlier delivery, more therapeutic interventions, preterm birth, lower birth weight, and perinatal loss.

• Low PlGF (<100pg/ml) was associated with increased maternal and perinatal risks.

• PlGF <50pg/ml is particularly associated with stillbirth in women with suspected preeclampsia.
The availability of PlGF test results substantially reduced the time to clinical confirmation of pre-eclampsia.

Where PlGF was implemented, there was a lower incidence of maternal adverse outcomes, consistent with adoption of targeted, enhanced surveillance, as recommended in the clinical management algorithm for clinicians.

(The Lancet, 2019)
Resources:

- Early diagnosis of preeclampsia using placental growth factor: an operational pilot study in Maputo, Mozambique. Pregnancy Hypertension 2018; 11:26-31
- ISSHP classification, diagnosis and management recommendation for international practice (2018)
- NICE Guideline (NG 133) Hypertension in pregnancy: diagnosis and management. Published June 2019 (Updating CG107 published 2010) www.nice.org.uk/guidance/ng133
- Placental growth factor testing to assess women with suspected pre-eclampsia: a multicentre, pragmatic, stepped-wedge cluster-randomised controlled trial. Lancet 2019; 393: 1807–18
High blood pressure in pregnancy decision aid

This information booklet aims to support pregnant women with high blood pressure, their families, carers and to aid healthcare professionals to discuss treatment options versus 'watch and wait'.

NICE National Institute for Health and Care Excellence
What are the treatment options for ALL pregnant women with high blood pressure?

- No treatment (i.e. ‘watch and wait’ to see if your blood pressure becomes severely high before taking the blood pressure medicine)
- Treatment (taking medicines when your blood pressure is first high to stop severely high blood pressure developing)
  - Treatment choices in pregnancy are usually:
    - Labetalol
    - Nifedipine
    - Methyldopa
    - These medicines are known as antihypertensives.

What do the national NICE guidelines recommend the doctor and pregnant woman do?

For pregnant women with PRE-EXISTING high blood pressure:

- Stop taking angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) once pregnant because there is a higher chance of development problems in unborn babies if these medicines are taken during pregnancy.
  - ACE inhibitor examples: enalapril, lisinopril and ramipril
  - ARB examples: candesartan, losartan and valsartan

For ALL pregnant women with high blood pressure:

- Act to reduce the blood pressure if it is severely high (160/110mmHg)
- Offer treatment if the blood pressure is sustained above 140/90mmHg
  - Labetalol
  - Nifedipine
  - Methyldopa
- If on medication for high blood pressure, aim for a blood pressure of 135/85mmHg
- Review the medication if the blood pressure stays below 110/70mmHg

National guideline:

- Can my blood pressure be too high?
  - Severely high blood pressure - seek medical help straight away if your blood pressure is above 160/110mmHg
- When is it recommended that treatment is started?
  - When your blood pressure is sustained above 140/90mmHg
- What blood pressure should I be aiming for?
  - If on medication aim for a blood pressure of 135/85mmHg
- Can my blood pressure be too low?
  - A doctor should check your blood pressure tablets if your blood pressure is commonly below 110/70mmHg
High blood pressure in pregnancy: Treatment vs no treatment

An in-consultation aid to support discussions about blood pressure in pregnancy treatment options

National guideline:
- Can my blood pressure be too high?
  - Severe high blood pressure: work closely with your doctor.
  - If your blood pressure is above 160/110 mmHg.
- When is it recommended that treatment is started?
  - When your blood pressure is sustained above 140/90 mmHg.
- What blood pressure should I be aiming for?
  - If medication is used for a blood pressure of 130/80 mmHg.

Benefits of treatment:
- On average, in every 100 women with raised blood pressure who start treatment (compared to those who do not), 10 fewer developed severely high blood pressure.
- Severe high blood pressure:
  - No Treatment: 20:100
  - Treatment: 10:100

Side-effects of treatment:
- Women:
  - Up to 1:10 will get:
    - Dizziness
    - Tiredness
- Baby/Child:
  - Taking blood pressure medication may benefit your baby.
  - The long-term effect on your child’s health has been less well studied (currently no major concerns exist).

Setting targets: Reducing severely high blood pressure
- On average, in every 100 women who aim for a blood pressure of 135/85 mmHg (compared with 130/100 mmHg), 33 fewer will get severely high blood pressure.
- Severe high blood pressure:
  - BP >160/110 mmHg: 41:100
  - BP <150/100 mmHg: 28:100

Severely high blood pressure - Outcomes in women
- Very rarely, pregnant women can have a stroke. This happens to about 15 women in 1 million. On average, in every 100 women who do have a stroke, 96 women will have severely high blood pressure and 4 women will not.
  - Stroke: 96:100

Severely high blood pressure - Outcomes in babies
- On average, in every 100 women with severely high blood pressure (compared to high blood pressure only), 7 more babies will be born with low birth weight.
  - Low birth weight: 24:100

Admission to neonatal unit:
- On average, in every 100 women with severely high blood pressure (compared to raised blood pressure only), 24 more babies will need neonatal unit admission.
  - BP >160/110 mmHg: 47:100
  - BP <160/110 mmHg: 23:100

1:10 women have high blood pressure in pregnancy

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This report is published in full in a variety of formats at: www.engage.nhs.uk
High blood pressure in pregnancy  Medication choice

1. Labetalol
   - Type: Beta blocker
   - Total dose: 200-400mg
   - Usual freq: 3 times daily (inc. lunchtime)
   - Has a license
   - Common side-effects (about 1:10 women): headaches and shortness of breath. Not advised in women with Asthma.

2. Nifedipine
   - Type: Calcium channel blocker
   - Total dose: 20-40mg
   - Usual freq: 2 times daily
   - Has a license
   - Common side-effect (about 1:10 women): headaches

3. Methyldopa
   - Type: Central acting agent
   - Total dose: 500-2000mg
   - Usual freq: 3 times daily (inc. lunchtime)
   - Does not have a license for use in pregnancy (used for many years)
   - Frequency of side-effects unknown: low mood and extreme tiredness. Not advised in women with a history of depression or in the postnatal period.

All three medications lower BP in pregnancy. They are ranked by NICE guideline recommendations.

Side-effects

Women
- Common side-effects (about 1:10 women): headaches and shortness of breath. Not advised in women with Asthma.

Baby
- Possible temporary low blood sugars immediately after birth
- No known side-effects

Child
- The longer-term effect on your child’s health has not been well studied (currently no major concerns exist).
- The longer-term effect on your child’s health has not been well studied (currently no major concerns exist).
- The longer-term effect on your child’s health has not been well studied (currently no major concerns exist).

All three medications can commonly cause dizziness and tiredness (about 1:10 women).

When comparing the outcomes of babies born to women taking blood pressure lowering medication no differences in safety have been found between the three medications.

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ANY QUESTIONS?
Summary

• Three main types of hypertension in pregnancy.

• Management is similar in all cases, but needs to be individualised for each women using an MDT approach

• Prediction tools and PI GF may be useful

• Risk of complications continues after birth

• Implications for longterm cardiovascular and renal health