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PRACTICE

EASILY MISSED?

Pre-eclampsia

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This is one of a series of occasional articles highlighting conditions that may be more common than many doctors realise or may be missed at first presentation. The series advisers are Anthony Harnden, university lecturer in general practice, Department of Primary Health Care, University of Oxford, and Richard Lehman, general practitioner, Banbury. To suggest a topic for this series, please email us at easilymissed@bmj.com.

A 36 year old primigravida woman attended for antenatal care at 10 weeks' gestation with a blood pressure 120/80 mm Hg and no proteinuria. At 28 weeks, she presented to her general practitioner with urinary frequency and mild dysuria. Urine analysis showed 3+ proteinuria, and her blood pressure was 144/90 mm Hg. The fundal height measured 3 cm less than expected for this gestation. A midstream urine sample was sent for culture and a review arranged for a week later. At 29 weeks, her blood pressure was 175/115 mm Hg, proteinuria was 3+, and no urinary infection had been isolated. She was urgently admitted to hospital, but on arrival no fetal heartbeat could be detected. Labour was induced and a growth restricted, stillborn infant was delivered. Maternal hypertension persisted postpartum.

What is pre-eclampsia?

Pre-eclampsia is defined by the gestational onset of hypertension and proteinuria.[1] It is, however, a multisystem disorder that can affect all maternal organs.[1 2] Delivery of the fetus and placenta remains the only cure, but preterm delivery may adversely affect neonatal outcome, with complications resulting from prematurity and low birth weight.[3] Pre-eclampsia evolves into eclampsia when maternal seizures develop. Eclampsia is rare in well resourced countries—just 1% of all women with pre-eclampsia develop eclampsia.[4] A severe form of pre-eclampsia characterised by microangiopathic haemolytic anaemia is often termed the HELLP (Haemolysis, Elevated Liver enzymes, and Low Platelets) syndrome.[2]

How common is pre-eclampsia?

Pre-eclampsia predominantly affects women in their first pregnancy (2-8% of first pregnancies)[5] and has a variable incidence across nations, being most common in Latin America and the Caribbean.[6] In the United Kingdom, about one in 200 pregnancies is affected by severe pre-eclampsia (about 3500 cases a year).[7]

Why is pre-eclampsia missed?

Pre-eclampsia is usually asymptomatic until it is in an advanced state,[2 8-10] and so it can evolve unchecked until the maternal condition has deteriorated to the point of severe organ failure and/or in utero death of the fetus.

In our case study, a urinary tract infection was suspected at 28 weeks, but a urinary tract infection rarely causes >1+ proteinuria. The significance of new onset proteinuria, hypertension, and reduced fetal growth was not understood. This woman should have been referred to hospital at 28 weeks' gestation for further assessment of suspected pre-eclampsia and fetal wellbeing.[9 10]

Why does it matter?

The last triennial audit of maternal deaths in the UK reported 22 deaths from pre-eclampsia, of which 20 were associated with substandard care and 14 were thought to be avoidable.[11] The most common cause of maternal death was cerebral haemorrhage secondary to uncontrolled systolic hypertension. Four maternal deaths were attributed to general practitioners' errors, including inappropriate urological referral for proteinuria, outpatient treatment of hypertension alone, and referral to a midwife for follow-up of jaundice that evolved into the HELLP syndrome.[11]

Life threatening maternal complications include uncontrolled hypertension and cerebrovascular accident; eclampsia; placental abruption; hepatic infarction and rupture; disseminated intravascular coagulation; pulmonary oedema; and renal failure.[7]

How is pre-eclampsia diagnosed?

Clinical

Guideline bodies advise a diagnosis of pre-eclampsia when blood pressure is >140/90 mm Hg in the second half of pregnancy, with ≥1+ proteinuria on reagent stick testing, which is confirmed by a protein:creatinine ratio of >30 mg/mmol.[1 9]

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New onset hypertension without proteinuria but with other maternal organ dysfunction, such as thrombocytopenia or raised liver enzyme values, may also indicate pre-eclampsia.[1] Some women have an isolated rise in blood pressure without proteinuria or other evidence of multisystem disorder of pre-eclampsia, and this is known as gestational hypertension. About 20% of women with gestational hypertension will go on to develop pre-eclampsia, especially if hypertension develops before 34 weeks.[12]

In the second half of pregnancy, the following symptoms should alert the clinician to check for hypertension and proteinuria: severe headache, with or without visual aura; epigastric pain, with or without nausea and vomiting; and sudden facial, hand, and feet oedema.[8-10]

Women with pre-existing cardiovascular risk factors such as chronic hypertension, diabetes mellitus, obesity (body mass index (kg/m^2) >35 at presentation), renal impairment, older mothers (>40 years old), and those who had pre-eclampsia in a previous pregnancy or who have a family history of pre-eclampsia (mother or sister) are at high risk of developing pre-eclampsia themselves.[2 9 10] Underlying chronic hypertension can be masked during the first half of pregnancy by gestational vasodilatation.

Investigations

For pregnant women with new onset hypertension (>140/90 mm Hg) and new onset proteinuria (≥1+ proteinuria on reagent stick testing) after 20 weeks' gestation, conduct the following investigations[1 9 10]:

Full blood count—To look for platelet consumption (platelets <100×10^9/L) and haemolysis (anaemia with fragmented red cells). In pre-eclampsia the haemoglobin concentration is generally mildly raised (>120 g/L) owing to haemoconcentration

Urea and electrolytes—To look for renal dysfunction (raised serum creatinine concentration >90 µmol/L)

Liver enzymes—To look for transaminitis (alanine aminotransferase >32 IU/L; aspartate aminotransferase >30 IU/L)

Urine sample or 24 h urine collection—To quantify clinically significant proteinuria (ratio of protein to creatinine (>30 mg/mmol) or 24 hour urine collection >300 mg)

Assessment of fetus—Ultrasound assessment of fetal growth and the volume of amniotic fluid; and Doppler velocimetry of umbilical arteries.

The results of these blood and urine tests are needed within hours. As it can take several days for blood test results to be received in primary care, general practitioners should send patients to their local maternity hospital for these investigations, as well as for fetal assessment.

Pre-eclampsia can be difficult to diagnose in women with pre-existing hypertension, especially if there is pre-existing renal disease with proteinuria. Under these circumstances, pre-eclampsia can evolve in the second half of pregnancy with a surge in blood pressure or proteinuria, but more usually other elements of this multiorgan syndrome are apparent, such as thrombocytopenia, raised level of liver transaminases, and reduced fetal growth. The uric acid level is often raised in women with pre-eclampsia, but in isolation it is of poor predictive and diagnostic value and should not be tested.[9 10]

How is pre-eclampsia managed?

Pre-eclampsia may progress unpredictably, within hours or over weeks. NICE guidelines therefore recommend immediate hospital referral for assessment of mother and fetus, with conservative management in a hospital that has facilities for emergency delivery and resuscitation of pre-term infants.[9]

Delivery of the placenta remains the only cure for pre-eclampsia. Childbirth should be considered if pre-eclampsia is identified after 37 weeks' gestation.[13] At 34-37 weeks' gestation, the decision to deliver is a clinical judgment that must weigh the risks to the mother of prolonging the pregnancy against the benefits for the preterm fetus.

Before 34 weeks, clinicians should try to prolong the pregnancy for the benefit of fetal maturity. This involves antihypertensive treatment with nifedipine slow release, labetolol, or methyldopa to keep the blood pressure between 130/80 mm Hg and 150/100 mm Hg.[9] There is little evidence to support choosing any one of these antihypertensive agents over another.[9 10] Magnesium sulphate will reduce the risk of eclamptic seizures,[4] and monitoring the fetal condition will guide the decision for timing of delivery.[9] Antenatal administration of corticosteroids will improve fetal lung maturity in anticipation of preterm delivery.[14]

Maternal hypertension usually recovers within two to three weeks of delivery but can take up to three months.[15] Pre-eclampsia will recur in about 15% of women who had pre-eclampsia in their first pregnancy, although this risk may be as high as 25% if the pre-eclampsia led to birth before 34 weeks and as high as 50% if birth was before 28 weeks.[16] Daily low dose aspirin (75-100 mg) from before 16 weeks' gestation in future pregnancies reduces the risk of recurrent, severe pre-eclampsia.[17]

Some women will continue to have hypertension three months after childbirth. This is presumed to be the result of previously unidentified chronic hypertension or secondary causes of hypertension.[18] Even those who have made a full recovery from pre-eclampsia are nevertheless at risk of hypertension and heart disease in later life.[19] Although the optimal follow-up regimen to minimise the risk of future cardiovascular disease is currently unclear,[9 10] pragmatic steps in primary care include encouraging optimal weight range through diet and exercise, and regular screening for hypertension, hyperlipidaemia, and diabetes.

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Key points

- For pregnant women with new onset hypertension (>140/90 mm Hg) and ≥1+ proteinuria, or other features of the multisystem disorder that might suggest pre-eclampsia in the second half of pregnancy, referral to their hospital maternity unit for immediate assessment is needed
- Pre-eclampsia can be life threatening to the mother (with complications such as cerebral haemorrhage resulting from uncontrolled hypertension) and to the fetus (with complications of prematurity and low birth weight)
- Pre-eclampsia is unpredictable and usually asymptomatic until the condition is advanced. It can evolve rapidly, requiring urgent delivery within hours of diagnosis, or progress slowly over weeks with conservative management
- Women who have had pre-eclampsia are at increased risk of chronic hypertension and cardiovascular disease in later life

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