September 2008

GENERAL PRACTICE UPDATE

Hypertensive disorders and renal disease in pregnancy

Abstract

Around 10–15% of pregnant women are affected by hypertensive disorders, which can affect the outcome of current and subsequent pregnancies, and have long-lasting effects on the health of both mother and baby. Risk factor identification and pre-conception preventive measures can help reduce the incidence of such conditions, and a range of antihypertensive agents can be given. Ongoing monitoring allows any deterioration in the condition to be dealt with early. In particular, renal disease, both predating and induced by pregnancy, should be identified, monitored and treated, to ensure the best outcome for both mother and baby.

Keywords

chronic kidney disease – hypertension – pre-eclampsia – pregnancy – renal disease

Authors

Lucy Mackillop
Registrar in Obstetric Medicine, Queen Charlotte's and Chelsea Hospital, London

Liz Lightstone
PhD, FRCP, Senior Lecturer and Honorary Consultant Physician, Imperial College London, Hammersmith Hospital, London

Hypertensive disorders are the most common medical conditions encountered in the obstetric population, affecting 10–15% of pregnant women. Hypertension in pregnancy covers a wide spectrum of disorders, including those resulting from pre-existing hypertension, gestational hypertension and pre-eclampsia (Box 1).

While it can be difficult to define the exact aetiology, accurate diagnosis is important for the management and prognosis of mother and child in the index pregnancy and subsequent pregnancies. Details of blood pressure, urinalysis, past medical history and family history prior to or in early pregnancy are imperative to aid diagnosis. Therefore it is in primary care that identification and risk assessment may take place.

Pre-eclampsia

Pre-eclampsia is a major cause of poor pregnancy outcome, including maternal and fetal morbidity and

Box 1. Definitions of hypertensive disorders in pregnancy

Hypertension	Definition
Hypertension in pregnancy	Blood pressure ≥140/90 mmHg on two separate occasions, at least 4 hours apart
Chronic/essential hypertension	Hypertension prior to pregnancy or occurring before 20 weeks' gestation
Pregnancy-induced/ gestational hypertension	Hypertension occurring after 20 weeks' gestation without proteinuria
Pre-eclampsia	Hypertension occurring after 20 weeks' gestation with proteinuria (>300 mg/24 hours, or ++ on urine dipstick on two consecutive urine samples in the absence of a urinary tract infection)
Superimposed pre-eclampsia	Pre-eclampsia occurring in a patient with pre-existing chronic hypertension. This is a difficult diagnosis to make as the patient may also have pre-existing proteinuria

Box 2. Risk factors for developing pre-eclampsia

- Sociodemographic factors
  - Extremes of reproductive age
  - Socio-economic status
  - Ethnic group
- Genetic factors – family history in mother and/or sister
- Pregnancy factors
  - Multiple pregnancies
  - Primigravidae
  - Assisted reproduction techniques
  - Previous pre-eclampsia
- Personal medical history
  - Obesity
  - Chronic renal disease
  - Chronic hypertension
  - Diabetes mellitus
  - Thrombophilia

Box 3. Pre-eclampsia statistics

- Pre-eclampsia affects 2–8% of pregnant women
- Relative risk of developing pre-eclampsia for individual pre-pregnancy risk factors:

Risk factor	Relative risk of developing pre-eclampsia
Chronic renal disease	20
Chronic hypertension	10
First-degree relative with hypertension in pregnancy	5
Twin pregnancy	4
Nulliparity	3
Maternal age >40 years	3
Obesity (body mass index >25)	2.7
Diabetes mellitus	2

- Complications of pre-eclampsia

Complication	Statistics
Eclampsia	1 in 2000 deliveries, 1–2% of women with pre-eclampsia[3]
HELLP syndrome (haemolysis, elevated liver enzymes, low platelets)	4–20% of women with pre-eclampsia[4]
Renal failure	1.1% of women with pre-eclampsia[3]

- Risk of recurrence for pre-eclampsia is highly variable depending on the population studied:
  - Up to 65% risk of recurrence in a US population after severe second-trimester onset of pre-eclampsia in the index pregnancy[5]
  - 7.5% risk of recurrence in a Scottish population after later onset pre-eclampsia[6]

mortality. In the most recent Confidential Inquiry into Maternal and Child Health (CEMACH 2007), 14% of all pregnancy-associated deaths (18 women) were attributable to pre-eclampsia and eclampsia, and it was the second most common direct cause of maternal death in the UK for the period 2003–2005.[1]

The first national guidelines, *The Pre-eclampsia Community Guideline*,[2] on management strategies for pre-eclampsia in primary care were developed after consideration and grading of evidence from a systematic literature review and consensus of a multiprofessional and lay working group representing parties involved in the provision or use of maternity services in the UK. Its recommendations include risk stratification in early pregnancy, when to refer for specialist input, and recommended monitoring content, method and thresholds for further action.

Box 2 lists the common risk factors for developing pre-eclampsia, and Box 3 describes the relative risks of some of these risk factors, together with other useful statistics about pre-eclampsia.

Prevention

In addition to accurate diagnosis, risk stratification, appropriate referral and increased surveillance, several management options should be considered before conception or in early pregnancy to reduce the risk of pre-eclampsia.

For women with pre-existing hypertension, antihypertensives should be changed (see below). The vascular adaptations associated with later pre-eclampsia, and particularly uteroplacental insufficiency leading to intrauterine growth restriction (IUGR), occur in the first and early second trimester[7] – hence, blood pressure should be optimised early in the pregnancy.

Calcium supplementation (at least 1 g per day) may reduce the risk of gestational hypertension or pre-eclampsia, especially in women with a low dietary intake or at high risk of developing pre-eclampsia.[8] Therefore, assessment of dietary calcium intake and dietary advice should be undertaken. There is no evidence that antioxidant therapy, for example vitamin C or E, is protective for pre-ecplampsia.[9]

Antiplatelet therapy with low-dose aspirin (75 mg) may reduce the risk of pre-eclampsia and of perinatal death by about 15%. Aspirin should be considered for women at high risk of developing pre-eclampsia.[10]

Box 4. Risk of vascular disease after pre-eclampsia[11]

Disease	Weighted mean follow-up (years)	Relative risk (95% confidence interval)	Absolute risk at time of follow-up (%)
Hypertension	14.1	3.7 (2.7–5.05)	21.9
Ischaemic heart disease	11.7	2.16(1.86–2.25)	0.2
Stroke	10.4	1.81 (1.45–2.27)	0.2
Venous thromboembolism	4.7	1.79 (1.37–2.33)	0.3

Implications for the future

A recent meta-analysis[11] confirms that pre-eclampsia is a predictor of future vascular disease (Box 4). To put this in context, the magnitude of the risk for cardiovascular disease in women with a history of pre-eclampsia is similar to that for dyslipidaemia. There appears to be a dose–response relationship, with women who have had more severe hypertension, early-onset pre-eclampsia or pre-eclampsia in more than one pregnancy being more likely to develop vascular disease in later life than those with milder or later-onset pre-eclampsia.

A Norwegian linkage study provides support for the hypothesis that cardiovascular disease and pre-eclampsia have a shared pathogenesis.[12] This study found significant associations between higher waist circumference, systolic blood pressure, diastolic blood pressure and non-fasting total cholesterol before pregnancy and the subsequent development of pre-eclampsia.

Therefore, a diagnosis of pre-eclampsia should also trigger an assessment (and treatment if required) of cardiovascular risk factors after the index pre-eclamptic pregnancy.

Treatment of hypertension in pregnancy

Antenatal management

The aims of treating hypertension in pregnancy are to reduce the complications of severe hypertension such as cerebral hemorrhage while not causing underperfusion of the placenta. There is no consensus on the optimal level of blood pressure control but some evidence that being too aggressive may lead to a reduction in fetal weight.[13]

Antihypertensive agents should be commenced once the blood pressure is greater than 150/100 mmHg, with the aim of maintaining a blood pressure of no more than 140/90 mmHg. For women with pre-existing renal disease, it is reasonable to commence antihypertensives at a blood pressure of 140/90 mmHg.

Box 5 lists the antihypertensives that are most commonly used in pregnancy. No single agent is more effective than another, so clinicians should use the one they are most familiar with. Since the mode of action of these drugs is different, they may be used in combination.

Atenolol has been associated with IUGR and is only used occasionally in the management of cardiac conditions in pregnancy. Diuretics are generally avoided in pregnancy, and particularly in pre-eclampsia, as they further reduce the intravascular volume in the pre-eclamptic patient. Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) are contraindicated in pregnancy and should be stopped before conception as they have been associated with congenital abnormalities[15] and fetotoxic effects on the kidney.[16] Amlodipine and doxazosin have been used successfully in pregnancy, but, due to lack of data, they should be reserved for fourth-line therapy and should be commenced in conjunction with specialist input.

Postnatal management

Hypertension classically improves immediately postpartum but then rises again around day 3–5. Therefore, most women who required antihypertensives antenatally will be discharged on medication.

Due to its side-effects on mood, methyldopa should be avoided postnatally. Atenolol and enalapril are most commonly used postnatally in the UK. Of the ACEIs, enalapril has the most data in breast-feeding mothers and should be used until cessation of breast-feeding, at which time a longer acting ACEI or the woman's previous ACEI should be substituted. Nifedipine or amlodipine may also be used. All these antihypertensives appear to be safe for breast-feeding mothers.

Pregnancy-induced hypertension may take up to 6 months to resolve, and therefore regular follow-up and reassessment of blood pressure is required. All women discharged on antihypertensives should have their vascular risk factors assessed postnatally as discussed above.

Renal disease in pregnancy

Renal disease may be pre-existing or pregnancy induced, or may present coincidentally during pregnancy.

Box 5. Most commonly used antihypertensives in pregnancy[14]

Agent	Receptor	Dose range	Side-effects	Contraindications
Methyldopa	Central action	250 mg – 3 g three times a day	Gastrointestinal disturbance, dry mouth, headache, dizziness, low mood, sedation, stomatitis, bradycardia	Liver disease, depression, phaeochromocytoma
Nifedipine	Calcium channel antagonist	• 20–90 mg once daily slow release • 10–40 mg twice daily modified release	Headache, flushing, dizziness, lethargy, tachycardia, palpitations, ankle oedema, rash, nausea, visual disturbance	Aortic stenosis, aortic coarctation, liver disease
Labetalol	Alpha- and beta-adrenoreceptors	200–1600 mg three times a day	Bradycardia, bronchospasm, gastrointestinal disturbance, fatigue, tingling scalp	Asthma, phaeochromocytoma

Chronic kidney disease

With the introduction of the Quality and Outcomes Framework and the availability of estimated glomerular filtration rate (eGFR) in general practice, the diagnosis of chronic kidney disease (CKD) has increased.

There are important implications for women of childbearing age with CKD that should be discussed, ideally before conception. These include the risks of pregnancy on the woman's long-term well-being and renal function, the risks of the disease and its treatment to the fetus, and the limitations on fertility imposed by renal disease and its treatment (Box 6).

Preconception advice

The main influences on the course of a pregnancy are the degree of renal impairment (Box 7) and hypertension – indeed, the evidence suggests that hypertension is the most important prognostic factor. All published data suggest that, in general, obstetric, fetal and renal prognoses are excellent in women with a serum creatinine level less than 120 µmol/l and no hypertension.[19]

The current renal approach is always to consider renal function in terms of eGFR using the MDRD equation.[20] This is because serum creatinine is hugely influenced by size, muscle mass, diet, ethnicity, age and gender, and does not tend to rise above the normal range until about 70% of the GFR has been lost. However, the MDRD formula has not been validated in pregnancy.[21] There is only one small published prospective study relating obstetric outcomes to preconception eGFR rather than serum creatinine level.[22]

Using the MDRD equation, Imbasciati and colleagues prospectively studied 49 non-diabetic white women with an eGFR of less than 60 ml/min/1.73 m^2. Interestingly only the combination of an eGFR of less than 40 ml/min/1.73 m^2 and proteinuria greater than 1 g per 24 hours before conception were predictors of shorter renal survival (hazard ratio 5.2; 95% confidence interval 1.7–15.9).

Obstetric and renal outlook are poorer in women

Box 6. Adverse outcomes associated with renal disease in pregnancy

Maternal

- Reduced fertility (generally only if prior exposure to cytotoxics)
- Hypertension
- Pre-eclampsia
- Deteriorating renal function
- Increase in complications. e.g. placental abruption
- Increased risk of caesarean section or operative delivery

Fetal

- Prematurity (spontaneous and iatrogenic)
- Small for gestational age
- Low birth weight
- Increased neonatal mortality

Box 7. Obstetric and renal outcome and renal function

Creatinine (µmol/l)	Problems during pregnancy (%)	Successful obstetric outcome (%)	Long-term renal problems (%)
<120	26	96 (85)	<3 (8)
125–250	47	90 (69)	25 (70)
>250	86	75 (61)	53 (92)

Based on data collected in 1973–97 from 2477 women with 3602 pregnancies; does not include collagen diseases.

Numbers in parentheses refer to complications developing before 28 weeks' gestation.

Source: Professor John Davison, Directorate of Women's Services, Royal Victoria Infirmary and Associated Hospitals NHS Trust, Newcastle upon Tyne, UK.

September 2008

Box 8. Indications for delay in conception

- Patients with relapsing/remitting diseases (e.g. renal lupus erythematosus or systemic vasculitis) are advised to wait until the disease has been in remission for at least 6 months
- Patients taking cytotoxic agents such as cyclophosphamide must avoid becoming pregnant for at least 3 months after stopping the medication
- Patients with hypertension should be made aware of the antihypertensives that are contraindicated in pregnancy, and these should be changed before conception

with moderate renal impairment (creatinine over 125 but less than 250 µmol/l), with or without hypertension, and severe renal impairment is associated with a poor prognosis for both mother and fetus. Pregnancy in dialysis patients is usually unexpected and therefore diagnosed late, and is associated with major problems for mother and baby. Such pregnancies should always be managed in tertiary centres specialising in high-risk pregnancies. Renal transplant patients are advised to postpone pregnancy for at least 1 year until graft function is stable and immunosuppression is at a relatively low level.[23,24]

Patients with renal disease that is likely to progress should be advised to become pregnant early in the course of their disease. Circumstances in which a delay may be necessary are listed in Box 8.

The advice to discontinue ACEIs or ARBs prior to pregnancy must, however, be tempered with the risk of renal progression in heavily proteinuric patients, for example those with diabetic nephropathy. Although all women should be counselled of the risks, it might be reasonable to suggest that such patients, if they accept the risks, continue their ACEI until pregnancy has been confirmed.[25,26]

Management of CKD in pregnancy

Pregnant women with underlying renal disease must be referred to a centre with combined expertise and facilities for regular monitoring of maternal and fetal well-being. The management of CKD in pregnancy is summarised in Box 9.

Postnatal follow-up

It is extremely important to follow up women with CKD postnatally. Medications stopped during pregnancy (e.g. statins) should be recommenced as indicated. Blood pressure control should be optimised, and renal function should be monitored closely.

Jones and Hayslett studied 82 pregnancies in 67 women with moderate-to-severe renal impairment and found that 43% had deterioration in their renal function

Box 9. The management of CKD in pregnancy

Assess level of renal function

- Baseline and monthly urea, electrolytes, creatinine, bone profile, uric acid and bicarbonate. Prepregnancy eGFR if available
- Baseline ultrasound scans (renal size, scars, obstruction)

Assess proteinuria

- In pregnancy, pathological proteinuria is >300 mg per 24 hours (equivalent to a protein:creatinine ratio [PCR] of approximately 30)
- Women with nephrotic-range proteinuria should receive thromboprophylaxis antenatally and for 6 weeks postnatally. (Weight- and renal function-dependent dose: 40 mg low molecular weight heparin daily for a women with normal renal function and weighing 50–90 kg at booking)
- Thromboprophylaxis should be considered in women with intermediate proteinuria
- Proteinuria may be expected to double in pregnancy
- Pre-eclampsia should always be excluded

Assess bacteriuria

- Patients with reflux nephropathy are likely to develop significant urinary tract infections during pregnancy and should be advised to take prophylactic antibiotics throughout. A single cephalosporin at night is often suitable. Trimethoprim, ciprofloxacin and nitrofurantoin should be avoided
- Patients with reflux nephropathy may need monitoring for renal obstruction with regular renal ultrasonography.

Assess anaemia

- Correct iron or other deficiencies
- Assess whether likely to need erythropoietin during pregnancy (aim to avoid transfusions)

Assess activity of renal disease or underlying systemic disease

- Urinary sediment and urine PCR
- Patients with systemic lupus erythematosus – clinical assessment to include screening for pulmonary hypertension and lupus serology

Treat hypertension effectively

- Switch antihypertensives as per advice above

Seek advice from a renal specialist regarding adjustment of immunosuppressant drugs

- Alternative therapies may be advocated
- Dose adjustment may be necessary
- More intensive drug level monitoring may be required

Low-dose aspirin should be considered

- For pre-eclampsia prophylaxis
- For women with antiphospholipid syndrome

antenatally or immediately postnatally. Although 8% of these women recovered their pregnancy-induced loss in function, a further 10% had accelerated decline between 6 weeks and 6 months postpartum.[27]

Renal disease presenting in pregnancy

GFR rises by 50% in pregnant women with normal renal function causing serum creatinine to fall – the normal mean serum creatinine for a pregnant woman being 51µmol/l (0.5mg/dl) vs 73µmol/l (0.82mg/dl) in non-pregnant women. Therefore, a creatinine of greater than 75 µmol/l after 6 weeks' gestation should raise the suspicion of renal impairment. Commonly, women may also present with proteinuria at their first clinic visit or early in pregnancy. It is important to make a diagnosis, and renal biopsy is safe during early pregnancy. In later pregnancy, it is vital to differentiate primary renal causes of proteinuria and pregnancy-induced renal disease. In general nephrotic syndrome presenting after 24/40 gestation is due to pre-eclampsia unless proved otherwise. Recurrent urinary tract infections (UTIs) are common in those with underlying structural abnormalities (e.g. chronic pyelonephritis, reflux nephropathy). The presence of haematuria and proteinuria almost always suggests the presence of glomerular disease. Isolated haematuria is not uncommon in the general population. If underlying renal disease is suspected, urgent referral to a centre with renal and high-risk obstetric expertise is indicated.

Pregnancy-induced renal disease

The most common cause of pregnancy-induced renal disease is acute tubular necrosis associated with acute volume depletion (Box 10). However, pre-eclampsia (particularly the HELLP variant) can cause specific renal lesions that may mimic primary renal disease.[28] Pregnant patients appear to be particularly at risk from the devastating complication of cortical necrosis, which results in irreversible renal failure. Less commonly, patients present early postpartum with haemolytic–uraemic syndrome (HUS).

The later renal impairment occurs, the more likely it is to reflect pregnancy-induced renal disease. Pre-eclampsia and HELLP syndrome usually occur antepartum (although renal function may decline postpartum), whereas HUS classically occurs unexpectedly within days to weeks postpartum. Pre-eclampsia and acute fatty liver of pregnancy (AFLP) are more common in nulliparous women. HELLP syndrome is more common in multiparous women – the group most likely to develop acute renal failure (13.5%).[29]

Acute renal dysfunction associated with pre-eclampsia or HELLP syndrome has an excellent prognosis. However, a significant proportion of patients with pre-existing renal disease or hypertension suffer irreversible decline or even loss of renal function; HUS generally has a much worse prognosis.

Box 10. Acute renal failure in pregnancy

- Hyperemesis
- Sepsis
- Haemorrhage
- Pre-eclampsia/HELLP/AFLP/HUS
- Obstruction

Much rarer than it used to be: <1/20,000 pregnancies.

Early diagnosis and appropriate resuscitation (e.g. fluids, clotting) often prevents the onset of acute tubular necrosis.

Further information

For an overview of the impact of renal disease on pregnancy, consult the recently published consensus statement from the RCOG 54th Study Group on *Renal Disease in Pregnancy*, edited by John Davison, Catherine Nelson-Piercy, Sean Kehoe and Philip Baker 2008, and published by the Royal College of Obstetricians and Gynaecologists, London. ■

REFERENCES

1. Royal College of Obstetricians and Gynaecologists. *Confidential enquiry into maternal and child health, 2007. Saving mothers' lives 2002–2005.* London: RCOG.
2. Milne F, Redman C, Walker J *et al.* The Pre-eclampsia Community Guideline (PRCOG): how to screen for and detect onset of pre-eclampsia in the community. *BMJ* 2005; **330**: 576–80.
3. Altman D, Carroli G, Duley L *et al.* Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial. *Lancet* 2002; **359**: 1877–90.
4. Guntupalli SR, Steingrub J. Hepatic disease and pregnancy: an overview of diagnosis and management. *Crit Care Med* 2005; **33** (10 Suppl): S332–9.
5. Sibai BM, Mercer B, Sarinoglu C. Severe preeclampsia in the second trimester: recurrence risk and long-term prognosis. *Am J Obstet Gynecol* 1991; **165** (5 Pt 1): 1408–12.
6. Campbell DM, MacGillivray I, Carr-Hill R. Pre-eclampsia in second pregnancy. *Br J Obstet Gynaecol* 1985; **92**: 131–40.
7. Sibai BM. Chronic hypertension in pregnancy. *Clin Perinatol* 1991; **18**: 833–44.
8. Hofmeyr GJ, Duley L, Atallah A. Dietary calcium supplementation for prevention of pre-eclampsia and related problems: a systematic review and commentary. *Br J Obstetr Gynaecol* 2007; **114**: 933–43.
9. Rumbold A, Duley L, Crowther C, Haslam R. Antioxidants for preventing pre-eclampsia. *Cochrane Database Syst Rev* 2008; (1): CD004227.
10. Knight M, Duley L, Henderson-Smart DJ, King JF. Antiplatelet agents for preventing and treating pre-eclampsia. *Cochrane Database Syst Rev* 2000; (2): CD000492.
11. Bellamy L, Casas J-P, Hingorani AD, Williams DJ. Pre-eclampsia and risk of cardiovascular disease and cancer in later life: systematic review and meta-analysis. *BMJ* 2007; **335**: 974–7.
12. Magnussen EB, Vatten LJ, Lund-Nilsen TI *et al.* Prepregnancy cardiovascular risk factors as predictors of pre-eclampsia: population based cohort study. *BMJ* 2007; **335**: 978.

13. Von Dadelszen P, Omstein MP, Bull SB, Kren G, Magee LA. Fall in mean arterial pressure and fetal growth restriction in pregnancy hypertension: a meta-analysis. *Lancet* 2000; **355**: 87–92.
14. Greer IA, Nelson-Piercy C, Walters B. *Maternal medicine: medical problems in pregnancy.* Edinburgh: Churchill Livingstone, 2007.
15. Cooper WO, Hernandez-Diaz S, Arbogast PG *et al.* Major congenital malformations after first-trimester exposure to ACE inhibitors. *N Engl J Med* 2006; **354**: 2443–51.
16. Shotan A, Widerhorn J, Hurst A, Elkayam U. Risks of angiotensin-converting enzyme inhibition during pregnancy: experimental and clinical evidence, potential mechanisms, and recommendations for use. *Am J Med* 1994; **96**: 451–6.
17. Fischer MJ. Chronic kidney disease and pregnancy: maternal and fetal outcomes. *Adv Chronic Kidney Dis* 2007; **14**: 132–45.
18. Fischer MJ, Lehnerz SD, Hebert JR, Parikh CR. Kidney disease is an independent risk factor for adverse fetal and maternal outcomes in pregnancy. *Am J Kidney Dis* 2004; **43**: 415–23.
19. Hou S. Historical perspective of pregnancy in chronic kidney disease. *Adv Chronic Kidney Dis* 2007; **14**: 116–18.
20. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. *Am J Kidney Dis* 2003; **41**: 1–12.
21. Smith MC, Moran P, Ward MK, Davison JM, Assessment of glomerular filtration rate during pregnancy using the MDRD formula. *Br J Obstet Gynaecol* 2008; **115**: 109–12.
22. Imbasciati E, Gregorini G, Cabiddu G *et al.* Pregnancy in CKD stages 3 to 5: fetal and maternal outcomes. *Am J Kidney Dis* 2007; **49**: 753–62.
23. McKay DB, Josephson MA, Armenti VT *et al.* Reproduction and transplantation: report on the AST Consensus Conference on Reproductive Issues and Transplantation. *Am J Transplant* 2005; **5**: 1592–9.
24. Transplantation EEGoR. European best practice guidelines for renal transplantation. Section IV: Long-term management of the transplant recipient. IV.10. Pregnancy in renal transplant recipients. *Nephrol Dial Transplant* 2002; **17** (Suppl. 4): 50–5.
25. Tabacova S, Little R, Tsong Y, Vega A, Kimmel CA. Adverse pregnancy outcomes associated with maternal enalapril antihypertensive treatment. *Pharmacoepidemiol Drug Saf* 2003; **12**: 633–46.
26. Alwan S, Polifka JE, Friedman JM. Angiotensin II receptor antagonist treatment during pregnancy. *Birth Defects Res A Clin Mol Teratol* 2005; **73**:123–30.

Practice points

- **Do not overlook the fact that a patient is a woman of childbearing age – discuss issues of fertility and pregnancy early in the course of her disease and modify treatment if she is planning a pregnancy.**
- **It is critical to control blood pressure well before conception as well as antenatally.**
- **The normal range for creatinine in pregnant women is significantly lower than in non-pregnant women – beware a creatinine level over 75 µmol/l.**
- **In pre-existing renal disease, the outlook for mother and baby is better in the presence of normal renal function and blood pressure; therefore, in chronic diseases recommend the patient becomes pregnant sooner rather than later.**
- **Renal disease caused by pregnancy may mimic underlying renal disease, may lead to irreversible renal decline and is more common in women with pre-existing renal disease and hypertension, in whom it has a worse prognosis.**

27. Jones DC, Hayslett JP. Outcome of pregnancy in women with moderate or severe renal insufficiency. *N Engl J Med* 1996; **335**: 226–32.
28. Sibai BM. Imitators of severe preeclampsia. *Obstet Gynecol* 2007; **109**: 956–66.
29. Romero Arauz JF, Lara González AL, Ramos León JC, Izquierdo Puente JC. Maternal morbidity and mortality in HELLP Syndrome. *Ginecol Obstet Mex* 2001; **69**: 189–93.