Renal disease in pregnancy

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Abstract

Pregnancy in women with chronic kidney disease (CKD) is complicated and associated with risks of accelerated decline in renal function in the mother and adverse outcomes for the infant, including prematurity and growth restriction. Managing these risks requires a multidisciplinary approach including the patient, nephrologist, neonatologist and obstetrician. This review will present approaches to managing pregnancy in women with CKD.

Keywords chronic kidney disease; pregnancy; transplant

Introduction

Renal physiology in normal pregnancy

During normal pregnancy, the maternal cardiovascular system undergoes important changes. Blood volume and red cell mass increase by up to 50%, systemic vascular resistance falls and cardiac output increases by up to 30%. These cardiovascular adaptations have profound effects on renal function:

- renal blood flow increases by 50%
- glomerular filtration rate (GFR) increases by 30%
- serum creatinine decreases by 20%

Blood pressure falls in the first two trimesters and gradually returns to baseline as the pregnancy approaches term. Increased GFR, changes in glomerular haemodynamics, and possibly alterations in renal tubular function lead to an increase in urine protein excretion in pregnancy from an upper limit of 150 mg/d to 260 mg/d.

Renal size increases by approximately 1cm in bipolar length during normal pregnancy. Smooth muscle relaxation and compression of the ureters by the gravid uterus commonly lead to pelvicalyceal dilatation, more prominently on the right than the left.

Chronic kidney disease (CKD) is defined as abnormalities in kidney function and/or structure that are present for more than 3 months. For some individuals, the only sign of CKD may be the presence of abnormal urinary constituents such as microscopic haematuria and/or proteinuria whereas, in others, progressive loss of renal excretory function may be observed. The Kidney Disease Improving Global Outcomes (KDIGO) classifies CKD into 5 stages of increasing severity dependent on the estimated glomerular filtration rate (eGFR, Table 1).

CKD although rare in pregnancy, affecting 0.15% of pregnancies, is encountered with increasing frequency. Most affected women have early CKD, stages 1 to 3a, with eGFR >45ml/min.

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The Kidney Disease Improving Global Outcomes (KDIGO) classification of chronic kidney disease. Equation based estimated GFR calculations are not valid during pregnancy

CKD stage	Estimated GFR	Comment
G1	≥90 ml/min	Only classified as CKD if associated with renal structural or urinary dipstick abnormalities
G2	60–89 ml/min	
G3a	45–59 ml/min	
G3b	30–44 ml/min	
G4	15–29 ml/min	
G5	<15 ml/min or on dialysis	

Table 1

In women with CKD normal renal and haemodynamic adaptations to pregnancy may not occur, leading to adverse pregnancy outcomes.

Routine pregnancy care may be the first occasion that blood pressure and urinalysis are performed for some women and hypertension, proteinuria or haematuria detected at booking may uncover previously undiagnosed CKD. The development of hypertension and urinary dipstick abnormalities later in pregnancy may be manifestations of CKD, but more commonly represent pre-eclampsia. Chronic pyelonephritis is the most common CKD diagnosis encountered in pregnant women.

Renal assessment in pregnancy

Measuring renal excretory function

The gold-standard measure of renal excretory function is the GFR, but this is difficult to measure in routine clinical practice. Creatinine, a metabolic by-product of muscle metabolism, is filtered and excreted in the urine and serum creatinine levels are inversely proportional to GFR. Whilst serum creatinine has been widely used as a surrogate marker of GFR, the relationship between these two parameters is complex. Serum creatinine may be affected by age, ethnicity, medications, diet, gender and body composition. Therefore, the serum creatinine concentration may correlate poorly with GFR between individuals and GFR may be significantly reduced before creatinine levels rise outside the laboratory reference range.

In the general adult population, formulaic estimations of GFR (eGFR) based on serum creatinine, have now superseded reliance on creatinine values alone as the standard measure of renal function. These equations are based not only serum creatinine, but also on patient age and gender with adjustments for some ethnicities and provide a measure of renal function closer to the gold-standard. However, these equations are not validated for use during pregnancy and should not be used, although preconception baseline values of eGFR are useful in predicting maternal and fetal outcomes (see below).

Alternatively, renal function during pregnancy can be estimated by creatinine clearance. The utility of calculated creatinine clearance is limited by the requirement for a 24-h urine collection which is inconvenient and frequently incomplete.

Immunological investigation of suspected intrinsic renal disease

Test	Comments
Antinuclear antibodies (ANA)	Associated with connective tissue diseases and SLE. Antibodies against double-stranded DNA (anti-dsDNA) and extractable nuclear antigens (ENA) should be performed if positive.
Anti-neutrophil cytoplasmic antibodies (ANCA)	Associated with small vessel vasculitis (Churg Strauss disease, granulomatosis with polyangiitis and microscopic polyangiitis).
Complement components C3 and C4	Decreased levels are found in active SLE, post-infectious glomerulonephritis, mesangiocapilliary glomerulonephritis, subacute bacterial endocarditis, cryoglobulinaemia and heavy chain-deposition disease
Other tests	Rheumatoid factor, cryoglobulins and C3 nephritic factor measurement may be indicated.

Table 2

Since eGFR equations are invalid during pregnancy and creatinine clearance is inconvenient, most centres continue to rely on changes in serum creatinine concentration to identify potential renal dysfunction during pregnancy, mindful that relative changes in creatinine have greater clinical utility than absolute values, and that the reference range for serum creatinine differs between pregnant and non-pregnant females.

Measuring urine protein excretion

Although urine dipstick analysis provides a rough guide, the most accurate method for measuring urine protein excretion is in a 24-h urine collection, but these are inconvenient for patients to perform and are often incomplete. In contemporary nephrology practice and obstetric medicine, the urine protein:creatinine ratio (PCR) or albumin:creatinine ratio (ACR) are accepted as surrogates for 24-h urine collections for measuring urine protein excretion. The units are mg/mmol (mg protein:mmol creatinine). This method corrects for variations in urine concentration and correlates closely with complete 24-h urine collection data, including in pregnant patients with CKD. Therefore, urine PCR or ACR can be reliably used for quantitative monitoring of proteinuria during pregnancy.

Chronic kidney disease with proteinuria in pregnancy

Case 1

A 29 year old lady was noted to have proteinuria throughout her first pregnancy. At 37 weeks she developed pre-eclampsia with worsening proteinuria and rising blood pressure with a serum creatinine of 56 μmol/L. She had an induced vaginal delivery, giving birth to a male baby that was small for gestational age. She was subsequently lost to follow up.

Three years later she booked at 8 weeks gestation in her second pregnancy. She was again found to have +++ proteinuria and + microscopic haematuria on urine dipstick analysis. Blood pressure is 112/72 and she was taking no medications.

How do you interpret these findings and what next steps would you take?

The finding of urinary abnormalities at such an early stage of pregnancy strongly suggests that there is underlying kidney disease rather than the abnormalities being pregnancy related. This notion is reinforced by the history of proteinuria throughout her previous pregnancy with the development of pre-eclampsia at 37 weeks. The combination of blood and protein in her urine is suggestive of glomerular disease.

At this stage, the key issues are to take a full history including any family history of renal disease, assess her level of renal function including any historic measures, quantify her proteinuria and endeavour to establish the diagnosis of her underlying renal disease. Therefore, it is necessary for her to have bloods to check serum creatinine and albumin, urine for protein creatinine ratio, an MSU, and a renal ultrasound scan (USS). She should have a renal immunology screen to exclude a connective tissue disorder such as lupus nephritis (Table 2).

The results reveal that her serum creatinine currently is 91 μmol/L, serum albumin is 31 g/L and the urine PCR is 650 mg/mmol creatinine. The urine is sterile, a renal USS scan is normal and the renal immunology screen is also normal.

The key abnormalities in the current patient are nephrotic range proteinuria (urine PCR >300 mg/mmol) and a low serum albumin, even taking account of her pregnancy. In the absence of oedema she does not fulfil the criteria for a diagnosis of nephrotic syndrome. Even though her serum creatinine is within the reference range it is higher than that measured 3 years previously, and is certainly high for pregnancy. Taken together these results suggest progressive underlying renal disease due to some type of glomerulonephritis.

What should be done next?

Given that glomerular proteinuria often worsens as pregnancy proceeds, it is very likely that she will become nephrotic in pregnancy, and nephrotic syndrome symptoms may be severe in pregnancy. It is therefore important if possible to establish a precise diagnosis at this stage. Nephrotic syndrome is not a single disorder but rather a collection of symptoms that may be result from multiple kidney diseases. To make a histological diagnosis a renal biopsy is required which, in addition to its diagnostic yield, will guide any potential immunosuppressive therapy that may directed at the underlying glomerular disease.

Renal biopsy is not-contraindicated in early pregnancy and is considered safe if blood pressure is adequately controlled. After 28 weeks gestation renal biopsy becomes progressively more technically challenging with a growing gravid uterus, and the balance of risk starts to shift. Therefore, in women with serious renal disease before 28 weeks a biopsy should be performed to establish a diagnosis. After 32 weeks delivery should be expedited to facilitate renal investigations in the post-partum period

may be more appropriate. Between 28 and 32 weeks the decision is more difficult and needs to be assessed on a case-by-case basis.

A renal biopsy is performed and reveals a diagnosis of IgA nephropathy with some segmental glomerulosclerosis and mild tubulointerstitial scarring, but little other evidence of disease activity. If she were not pregnant the mainstay of management for this patient would be the maintenance of good blood pressure control and treatment with blockers of the renin angiotensin system, either an angiotensin converting enzyme inhibitor (ACEi) or an angiotensin receptor blocker (ARB). These agents reduce proteinuria and have been shown in multiple studies to protect against loss of renal function in proteinuric patients with various glomerular diseases, including IgA nephropathy, and their use is the standard of care in the non-pregnant proteinuric patient. Immunosuppression is not indicated at this stage in IgA nephropathy. Both ACEi and ARB are contraindicated in pregnancy (Table 3).

Nephrotic syndrome (proteinuria >3 g/24h, hypoalbuminaemia and oedema) occurs rarely in pregnancy, and usually in the third trimester as a manifestation of pre-eclampsia. Nephrotic syndrome in the first trimester generally reflects intrinsic renal disease and previous case series reported perinatal mortality of greater than 40%. More recent series suggest that outcomes are much more favourable, with mortality less than 5% in the UK. Proteinuria is also a significant risk factor for maternal thromboembolic disease.

Elevated urine protein excretion is associated with intrauterine growth restriction and preterm delivery. In women without CKD this effect can be almost wholly accounted for by concurrent comorbidity (predominantly hypertension, diabetes mellitus or pre-eclampsia). In women with CKD, however, increased proteinuria (greater than 1g/d) at baseline is associated with early delivery and small infants in the absence of pre-eclampsia, although it remains unclear whether this reflects early induction of labour or spontaneous premature labour.

How would you advise and manage her at this stage?

At this stage she requires counselling focusing on two main issues:

1. Will the kidney disease affect the fetal outcomes of pregnancy?
2. Will pregnancy affect the kidney disease?

Reports of pregnancy outcomes in women with CKD from the 1950s and 1960s painted a very bleak outlook for mothers and infants. However, in subsequent decades, as more experience has accrued, a much more positive view of CKD in pregnancy has developed which allows a more detailed assessment of individual risk and individualisation of care to optimize outcomes. It is now possible to offer advice as outlined below.

Fetal outcomes

Adverse fetal outcomes (preterm delivery, SGA, neonatal intensive care admission, persistent congenital disability or death) occur in approximately 20% of pregnancies in mothers with CKD, compared to 9% in those without CKD. Risks can be stratified according to baseline maternal renal function, blood pressure control, proteinuria and, to a lesser extent, aetiology of renal disease.

Renal function

The risks of adverse fetal outcomes increase with the severity of baseline renal dysfunction. Even early Stage G1 and G2 CKD, with pre-conception eGFR >60 ml/min, is associated with increased risk of prematurity and intrauterine growth restriction as compared to the general population, predominantly associated with an increased risk of pre-eclampsia. The effect of renal function is likely to be continuous, but mothers with more severe renal dysfunction (baseline serum creatinine greater than 180 μmol/l) are faced with risks of intrauterine growth restriction (65%), preterm delivery (90%) and perinatal mortality (10%).

Aetiology of CKD

The aetiology of CKD has minimal impact on fetal outcome, with a few exceptions. Asymptomatic bacteriuria and recurrent urinary tract infection, secondary to vesicoureteric reflux or structural abnormalities, are associated with an increased risk of preterm delivery and should be promptly treated. There is no clear difference in outcomes for women with different types of glomerulonephritis.

Medications use in CKD and pregnancy

Antihypertensives

Commonly Used	Comments	Contraindicated
1st Line:	Pure α- and β-blockers not usually used (needs to be level with labetolol)	ACE inhibitors
Labetalol (combined α- and β-blocker)		Angiotensin receptor blockers
Methyldopa		Aliskiren
Nifedipine	Little experience with other dihydropyridine Ca^{2+} antagonists (level with nifedipine)	Spironolactone
2nd Line:		Moxonidine
Hydralazine		Minoxidil (3rd trimester)
Diuretics:		Thiazide diuretics
Furosemide	Safe in second and third trimesters; used to treat oedema rather than hypertension (level with furosemide)	Diltiazem

Immunosuppressants

Commonly used	Comments	Contraindicated
Prednisolone	No evidence of teratogenicity. Extensive evidence to support use	Mycophenolate
Azathioprine		Sirolimus
Tacrolimus		Rituximab (some recent reports of safe use in pregnancy in selected cases)
Cyclosporin	No evidence of teratogenicity. Extensive evidence to support use	Methotrexate

Table 3

Hypertension

Uncontrolled hypertension in patients with CKD prior to conception, or in early pregnancy, is a key independent predictor of adverse fetal outcome. Blood pressure increases in the second half of pregnancy may be exaggerated in women with CKD due to limitations in vascular relaxation and increasing circulating volume as a result of relative over-activity of the renin-angiotensin system. Elevated blood pressure at baseline predicts the occurrence of prematurity, intrauterine growth restriction and neonatal mortality.

Blood pressure treatment targets for pregnant women with CKD are controversial. Fetal outcomes are similar in those with mild to moderate high blood pressure (<160/100 mmHg) and in patients treated for hypertension. Aggressive treatment of maternal hypertension during pregnancy (less than 120/80 mmHg) may lead to intrauterine growth restriction. In the absence of high quality evidence, the Royal College of Obstetricians and Gynaecologists (RCOG) in consensus guidelines, recommend that for pregnant women with CKD targets for blood pressure should be <120–139/70-85 mmHg.

Proteinuria

Increased urinary protein excretion is associated with intrauterine growth restriction and preterm delivery. Proteinuria > 1g/24hr (approximates to PCR 100 mg/mmol) at baseline is associated with early delivery and small infants in the absence of pre-eclampsia, although it remains unclear whether this reflects spontaneous premature labour or early induction of labour in the face of medical uncertainty.

Nephrotic syndrome occurs rarely in pregnancy and is usually, but not always, a result of pre-eclampsia. This is a serious complication in pregnancy, symptoms may be severe, and Case series indicate that nephrotic syndrome in the first trimester due to intrinsic renal disease is accompanied by a perinatal mortality rate of ~5% in the UK.

Maternal outcomes

Adverse maternal outcomes for women with CKD may include pre-eclampsia, transient or persistent loss of renal function, requirement for dialysis and death. As with fetal outcomes, maternal risks can be stratified according to baseline maternal renal function, blood pressure control, proteinuria and aetiology of renal disease.

Pre-eclampsia

Compared to the general population, the risk of developing pre-eclampsia for women with CKD is greatly elevated, and increases with worsening renal function; 20% for patients with mild renal impairment (serum creatinine <125 μmol/l) and 60–80% with severe impairment (serum creatinine >180 μmol/l), compared to approximately 5% in the general population. Because CKD is commonly associated with proteinuria and hypertension in the non-pregnant state, the diagnosis of 'superimposed pre-eclampsia' in pregnancy may be difficult and relies on arbitrary increases in these parameters with or without additional clinical features of pre-eclampsia (Box 1).

In high risk patients, aspirin (75 mg/day) reduces the incidence of pre-eclampsia by approximately 25%. Although not licensed for this indication, it is recommended that aspirin prophylaxis is offered to all women with CKD during pregnancy.

Criteria for the diagnosis of pre-eclampsia superimposed on CKD in pregnancy

- Blood pressure >160/110 mmHg
- Blood control suddenly worsening after a period of good control
- Development of proteinuria >2000 mg/d or abrupt worsening of proteinuria
- Serum creatinine increasing to >110 μmol/l

Box 1

Renal function

Decline in renal function during pregnancy is rare in women with mild renal impairment at baseline (serum creatinine <125 μmol/l). In contrast, women with moderate CKD (serum creatinine >125 μmol/l) have a 25% risk of permanently losing 25% of their kidney function as a result of pregnancy, increasing to a 50% risk in those with baseline creatinine >180 μmol/l. Furthermore, women with a preconception serum creatinine >180 μmol/l have a one in three chance of requiring dialysis during pregnancy or within 6 months of delivery.

Proteinuria

In general nephrology persistent increases in urine PCR suggest progressive renal disease, and chronic proteinuria is nephrotoxic *per se*. During normal pregnancy, where urinary protein excretion can double, the impact of proteinuria on kidney function in the short term is less clear.

In patients with pre-conception eGFR <40 ml/min, proteinuria >1g/24h is associated with an increased rate of post-partum renal decline compared with than those with less proteinuria. No similar effect was seen in patients with preserved renal function.

Mothers with nephrotic syndrome during pregnancy are at increased risk of venous thromboembolism. Loss of antithrombotic serum components in the urine leads to increased thrombotic tendency and strong consideration should be given to the use of prophylactic anticoagulation with low molecular weight heparin (LMWH).

Lower levels of proteinuria in women with normal renal function do not have a prominent independent effect on maternal outcomes during pregnancy, but baseline proteinuria may predict the risk of loss of renal function or dialysis post-partum.

Aetiology of CKD

The underlying aetiology of CKD has little impact on maternal outcome independent of renal function and blood pressure control. There is no clear difference in outcomes for women with different types of glomerulonephritis, including IgA nephropathy.

Lupus nephritis often becomes quiescent during pregnancy as a result of increased endogenous corticosteroid production. Consequently, flares can often occur in the puerperium when increased vigilance is recommended. If lupus flares do occur during pregnancy they can be difficult to distinguish from pre-eclampsia and need careful assessment by a multidisciplinary team.

Patients with structural abnormalities of the urinary tract (eg reflux nephropathy) who may be at particular risk of recurrent urinary tract infection should be screened regularly. Asymptomatic bacteriuria should be actively treated to reduce the risk of potentially serious sepsis and reduce the incidence of preterm delivery.

Hypertension

There are contradictory reports of the impact of blood pressure during pregnancy on progression of maternal renal disease. Contemporary prospective data suggest that baseline diastolic blood pressure >75mmHg, or the need for antihypertensive agents, is predictive of accelerated decline in renal function postpartum. Severe hypertension (>160/100 mmHg) in the third trimester requires treatment to reduce the risk of intracerebral haemorrhage in labour.

Venous thromboembolism prophylaxis

Pregnancy is a pro-thrombotic state and this is exacerbated by heavy proteinuria. Consensus opinion recommends that patients with nephrotic syndrome should receive prophylactic low molecular weight heparin (LMWH) during pregnancy and until 6 weeks post-partum. There is less evidence to support LMWH prophylaxis for women with heavy proteinuria but without nephrotic syndrome, or more modest proteinuria. Nevertheless, many practitioners encourage the use of LMWH throughout pregnancy for women with a PCR >100 mg/mmol, particularly if women are obese or have other risk factors for venous thromboembolism. Advice on thromboprophylaxis in pregnancy is published by the RCOG. LMWH should be continued for at least 6 weeks following delivery.

Immediate management

The woman in our Case study would seem to have normal renal function and normal blood pressure, and these are favourable observations at this stage. Whilst her IgA nephropathy does not itself require specific treatment, she cannot receive the ACEi or ARB that would be standard of care in the non-pregnant patient. The major risk is her proteinuria and the potential for this to worsen in pregnancy. Appropriate counselling at this stage is crucial to prepare her for possible developments later in pregnancy.

In addition to this counselling she should:

- be commenced on aspirin, no later than 12 weeks of gestation, as this has been shown to reduce the risk of severe pre-eclampsia
- receive prophylactic LMWH throughout pregnancy due to the combined thromboembolic risks of pregnancy and heavy proteinuria. After a short break around the time of delivery, this should continue until 6 weeks post-partum. In patients with impaired renal function dose adjustments for LMWH may be required and monitoring of factor Xa levels can sometimes be helpful.
- be placed under close follow-up throughout pregnancy with multidisciplinary team clinic visits at least every 4−6 weeks, focusing particularly on changes in renal function, blood pressure and proteinuria and fetal growth.

Case 2

A 27 year-old lady has end-stage renal disease due to reflux nephropathy as a consequence of vesicoureteric reflux (VUR) as a child, having received a living related donor renal transplant in the left iliac fossa 6 years earlier. She has treated hypertension and her current eGFR is 56 ml/min/1.73m^2 and the urine PCR is 20 mg/mmol. She is currently well on stable immunosuppression, with no episodes of rejection since the transplant procedure. Her current medications are ramipril, atorvastatin, prednisolone, tacrolimus, and mycophenolate mofetil. She has recently married and attends clinic for preconception counselling about the risks associated with pregnancy.

How would you advise her?

There are now thousands of reports of successful pregnancies in renal transplant recipients, and this is a common scenario in renal obstetric clinics. This lady is a stable renal transplant recipient with excellent transplant function on a typical combination of medications. She does, by definition, have CKD with chronic hypertension and therefore will be exposed to the associated risks in any pregnancy.

The major issues that impact on pregnancy outcomes for transplant patients are similar to those relevant to non-transplant CKD patients; baseline maternal renal function, adequacy of blood pressure control and degree of proteinuria (see above for discussion). In addition, there are specific pregnancy issues related to her transplant including the time since transplantation, the location of the transplanted organ, the proximity of any episodes of acute rejection, and the use of transplant immunosuppression.

It is advised that pregnancy should be delayed for 12 months after transplantation and for at least 6 months after any episode of rejection. Good transplant function is associated with good pregnancy outcomes and vice versa. From these perspectives with regard to the current patient, this is the optimum time for her to consider pregnancy planning.

She will need to adjust her medications. Statins cannot be used in pregnancy and this can be safely stopped without the need for an alternative. Ramipril, as an ACEi, is contraindicated in pregnancy and this patient is using this to treat hypertension. The ramipril will need to be discontinued and the patient converted to an alternative antihypertensive appropriate for pregnancy (Table 3). It is essential that her blood pressure remains well controlled before conception, and this transition process may take several weeks.

Similarly, mycophenolate mofetil is contraindicated in pregnancy (Table 3) and will need to be discontinued at least 6 weeks prior to conception. Liaison will be needed with her transplant physician who may decide to convert her on to an alternative immunosuppressant such as azathioprine, during her pregnancy. Ideally conception should be deferred for 3−6 months after the cessation of mycophenolate mofetil and any conversion, to ensure stable transplant function.

Calcineurin inhibitors such as tacrolimus are widely used in pregnancy although complex pharmacokinetic changes often result in reduced blood levels. Consequently, it is important to measure the trough levels of tacrolimus on a monthly basis during pregnancy and titrate the dose upwards to maintain therapeutic levels as necessary.

Her prednisolone can be safely continued. She will need to take aspirin as pre-eclampsia prophylaxis in pregnancy.

She will need monthly MSU to monitor for urine infection. Confirmed asymptomatic bacteriuria and symptomatic UTI during pregnancy should be treated with antibiotics to reduce the risk of ascending infection and preterm delivery. If more than one episode of bacteriuria is confirmed during pregnancy, prophylactic antibiotics should be prescribed. The choice of antibiotic is determined by stage of pregnancy, sensitivities of the cultured organisms and local practice. Cephalosporins and penicillins are safe and well-tolerated throughout pregnancy. Gentamicin may be used for severe pyelonephritis with appropriate monitoring. Trimethoprim is a folate antagonist and should be avoided in the first trimester. Nitrofurantoin is associated with neonatal haemolysis if used in the third trimester and should be avoided. Quinolones should be avoided.

Familial clustering of vesicoureteric reflux is well described, although the genetics is complex and not fully understood. Nonetheless she should be counselled about the possibility of any offspring having VUR, and therefore the baby should be referred for ultrasound scanning shortly after birth.

Vaginal delivery is not contraindicated following renal transplantation. If Caesarean section is necessary according to standard obstetric indications, then the course of the transplanted ureter must be considered during a lower segment approach, to avoid damage. ◆

FURTHER READING

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Practice points

- Maternal and fetal risks are related to prevailing renal function and blood pressure control prior to conception.
- Women with CKD, including transplant patients, should be offered aspirin prophylaxis during pregnancy to reduce the risk of pre-eclampsia
- Women with heavy proteinuria are at increased risk of thromboembolism and should be considered for prophylaxis during pregnancy
- Asymptomatic bacteriuria and urinary tract infection should be promptly treated during pregnancy.
- Optimizing timing of delivery requires multidisciplinary input