Kidney disease and pregnancy

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Abstract

Women with kidney disease should be counselled about the risks pregnancy may pose to mother and fetus before they conceive. Although impaired baseline function and hypertension are associated with worse outcome, all women with renal disease should be advised that they may suffer irreversible kidney damage, may well need to change their medications in advance of pregnancy and face a higher risk of preeclampsia with its attendant risks to the fetus. They need to consider the implications of having a premature baby. Compared with the probability that pregnancy will exacerbate existing kidney disease, pregnancyinduced kidney disease in women with previously normal renal function is less common and kidney failure rare. The commonest causes are those associated with severe pre-eclampsia and are usually managed by early delivery. Proteinuria can persist for months after pre-eclampsia. Women with kidney disease who present in pregnancy should be assessed and a diagnosis made where possible. If their disease is relatively mild, they can be managed expectantly and monitored post partum. Arrangements for appropriate renal follow-up should be made for all women who present in pregnancy, to ensure that a diagnosis is secured and a proper management plan is in place. Women with kidney disease must generally be considered as having high-risk pregnancies; they need to be aware of this and to be managed in a centre with appropriate obstetric and kidney expertise.

Keywords hypertension; kidney function; post-partum management; pre-eclampsia; preconception advice; pregnancy; systemic lupus erythematosus

Physicians must be able to advise women with kidney disease about the possible effects of pregnancy upon their longterm health and kidney function, and of the disease and its treatment upon the fetus. Advice should include information on the effects of kidney disease and its treatment upon fertility, and the benefits of adjusting treatment before conception wherever possible. Occasionally, this is impossible because kidney disease can manifest for the first time during pregnancy.

Ultimately, physicians can only advise women on the risks of becoming pregnant, and some women will risk losing kidney function in exchange for what may be their only chance of pregnancy. It is well recognized that the presence of kidney disease is associated with adverse outcomes for both mother (pre-eclampsia, eclampsia and abruption) and fetus (prematurity, low birth weight or neonatal death).¹ However, meticulous

pre-pregnancy planning and antenatal care can reduce the risks for both mother and baby, and because these women are usually highly motivated it is possible to counsel them about problems while expecting a successful outcome.

Preconception advice for women with kidney disease

When to become pregnant

The main influence on the course of pregnancy in a woman with kidney disease is the degree of kidney impairment (Figure 1a and b) and whether this is associated with hypertension. All published data suggest that, in general, obstetric, fetal and kidney prognoses are excellent in women with serum creatinine lower than 120 micromol/litre and no hypertension.¹ The current renal approach in non-pregnant patients is always to consider kidney function in terms of estimated glomerular filtration rate (eGFR), using the Modification of Diet in Renal Disease (MDRD) equation.² This is because serum creatinine is hugely influenced by body 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, in pregnancy, the MDRD formula does not work well and published data suggest that serum creatinine remains the best marker of kidney function.³ Obstetric and kidney outlook are poorer in women with moderate kidney impairment (creatinine >125-250 micromol/litre), with or without hypertension, and severe kidney impairment is associated with a poor prognosis for both mother and fetus. Pregnancy in patients having dialysis is usually unexpected (and therefore identified late) and commonly associated with major problems for mother and baby, although recent work has demonstrated that intensive haemodialysis can markedly improve prognosis.⁴ Nevertheless, such pregnancies should always be managed in tertiary centres specializing in difficult dialysis and high-risk pregnancies. Kidney 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.⁵⁻⁷ Patients with kidney disease that is likely to progress should be advised to consider pregnancy early in the course of their disease. Circumstances in which a delay may be necessary are listed in Table 1.

Conventional advice to switch from angiotensin-converting enzyme inhibitors (ACEI) use before pregnancy was based on evidence from a survey of children exposed to ACEI only in the first trimester, who demonstrated an excess incidence of congenital (especially cardiac and neurological) malformations. However, a more recent (also retrospective) study found a lower incidence, related to the use of antihypertensives as a whole and not to ACEI in particular.^{8,9} The risk to the fetus must be balanced against the risk of reduced maternal kidney protection. For example, it is reasonable to advise a woman with mild kidney impairment, minimal proteinuria and easily manageable blood pressure to avoid ACEI before pregnancy, whereas in a woman with diabetic nephropathy, the risk of kidney progression would be significant if treatment with ACEI were stopped for a significant period. As a compromise, it might be reasonable to suggest that women at higher risk continue their ACEI until no later than 5-6 weeks of pregnancy, once they have been apprised of the balance of benefit and harm.

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Estimates of percentage of infants affected by fetal growth retardation (FGR), preterm delivery (Preterm) or perinatal death according to maternal serum creatinine pre pregnancy

b. Risk to the mother of >25% decline in renal function during and after pregnancy and/or developing pre-eclampsia (PET) according to pre-pregnancy serum creatinine



Creatinine pre-pregnancy (micromol/litre)

<125 125–180 >180 On dialysis
Based on data from Williams, D. and J. Davison, *Chronic kidney disease in pregnancy*. Br Med J 2008; 336: 211–5.

Figure 1

Risks associated with pregnancy in women with pre-existing kidney disease

Women with heavy proteinuria are likely to become overtly nephrotic early in pregnancy, with an increased risk of intravascular volume depletion and thromboses. Women with reflux nephropathy are likely to develop significant urinary tract infections during pregnancy and should be advised to take prophylactic antibiotics throughout. A single dose of an oral cephalosporin at night is often suitable. Trimethoprim and quinolones, such as ciprofloxacin, should be avoided during pregnancy.

Influence of treatment for kidney disease on future fertility

Patients commencing therapy with cytotoxic agents must be warned of the risk of infertility. Cyclophosphamide causes infertility in a dose-dependent and age-related manner; a total dose of 10 g seldom causes prolonged amenorrhoea in women under 20 years old, but the risk is high in women aged over 32 years.

Influence of progression of kidney disease on future fertility

Many kidney diseases have an indolent, protracted course, and once end-stage kidney failure occurs it may be several years before a kidney transplant becomes available. A young woman who does not become pregnant early in her disease may have to try to conceive later in life, when her natural fertility is failing.

Preconception investigations and management

Preconception counselling in women with kidney disease contemplating pregnancy requires assessment of kidney function and any accompanying anaemia, and effective management of hypertension and any associated systemic disease. The key areas to address are summarized in Table 2 and reviewed elsewhere.^{10,11}

Kidney disease presenting in pregnancy

Commonly, women are found to have proteinuria at their first clinic visit or early in pregnancy. It is important to make a diagnosis, and kidney biopsy is safe during early pregnancy. In later pregnancy, it is vital to differentiate primary kidney causes of proteinuria and pregnancy-induced kidney disease. Recurrent urinary tract infections (UTIs) are also 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.

Kidney disease caused by pregnancy

The most common cause of pregnancy-induced kidney disease is acute tubular necrosis associated with acute volume depletion

Indications for delay in conception

- Patients with relapsing/remitting diseases (e.g. kidney lupus, systemic vasculitis) are advised to wait until the disease has been in remission for at least 6 months and they are taking medications 'safe' for use in pregnancy
- Patients taking cytotoxic or teratogenic agents such as cyclophosphamide or mycophenolate mofetil must avoid becoming pregnant
- Patients with severe hypertension (even those with ostensibly normal function) should be made aware that drugs contraindicated in pregnancy (e.g. angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers) may need to be discontinued before pregnancy and definitely in the first trimester
- Kidney transplant patients are advised to delay pregnancy until 1 year after transplantation when they have more stable renal function

Table 1

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