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## **Renal disease in pregnancy**

Renal disease can affect the outcome of pregnancy, pregnancy can affect the progression of pre-existing renal disease, and pregnancy can itself cause renal impairment. The renal system undergoes significant physiological and anatomical changes during a normal pregnancy:

- Renal plasma flow increases by 50-70% in pregnancy (the change is most pronounced in the first two trimesters).
- There is an increased glomerular filtration rate (GFR), which peaks at about the 13th week of pregnancy and can reach levels up to 150% of normal.
- Therefore, both urea and creatinine levels are decreased.
- Increased levels of progesterone at the beginning of pregnancy increase relaxation of arterial smooth muscles and so decrease peripheral vascular resistance, causing a blood pressure fall of approximately 10 mm Hg in the first 24 weeks of pregnancy.
- A change in tubular function with increased glycosuria also occurs (see 'Renal function in pregnancy', below).
- The anatomical changes are mainly in the collecting system. A dilatation of the ureters and pelvis occurs, which can lead to urinary stasis and an increased risk of developing urinary tract infections (UTIs).
- There is also an increase in overall kidney size by about 1-1.5 cm.
- In general, the physiological changes peak by the end of the second trimester and then start to return to pre-pregnancy levels; anatomical changes generally take up to three months postpartum to subside.

## **Renal function in pregnancy**

- Values considered normal when not pregnant may reflect decreased renal function in pregnancy. Creatinine above 75 µmol/L and urea above 4.5 mmol/L are indications for further investigation.<sup>[1]</sup>
- The use of estimated glomerular filtration rate (eGFR) is not recommended in pregnancy.
- Glycosuria is common and does not usually indicate diabetes or impaired glucose tolerance.
- Urinary protein excretion increases during pregnancy, but never to more than 300 mg/day and, therefore, overt proteinuria is abnormal.
- Women are at increased risk of UTI because of renal tract dilatation leading to urinary stasis.

### Proteinuria and haematuria

- Women with +1 (or more) dipstick positive proteinuria in the absence of infection should have the level of proteinuria quantified once infection and pre-eclampsia have been excluded.
- Baseline quantification of proteinuria should be by 24-hour collection for urine protein and by protein/creatinine ratio (PCR). PCR alone may be used for follow-up.
- Pregnant women with persistent proteinuria above 500 mg/day diagnosed before 20 weeks of gestation should be referred promptly to a nephrologist.
- Women with <u>nephrotic syndrome</u> should be given thromboprophylaxis with heparin in pregnancy and the puerperium.
- Higher levels of proteinuria may increase the risk for venous thromboembolism and may also warrant thromboprophylaxis in pregnancy.
- Isolated microscopic haematuria with structurally normal kidneys does not need to be investigated during pregnancy but should be evaluated if persistent following delivery.

## Urinary tract infection<sup>[2] [3]</sup>

- Asymptomatic bacteriuria is found in 2% of sexually active women, and in 2-10% of pregnant women.
- Because of the dilatation of the calyces and ureters that occurs in pregnancy, 25% will go on to develop pyelonephritis, which can cause intrauterine growth restriction due to reduced levels of maternal plasma protein Z, fetal death, and premature labour.<sup>[4]</sup>
- Pyelonephritis is relatively common at around 20 weeks and in the puerperium.
- Asymptomatic bacteriuria and UTIs in pregnancy should be treated with antibiotics. Antibiotic prophylaxis should be given to women with recurrent bacteriuria or UTIs and kidney disease.
- Any pregnant women with suspected pyelonephritis and any signs or symptoms to suggest a more serious illness, should be admitted immediately to hospital. Such signs and symptoms include:
  - Significant tachycardia.
  - Hypotension.
  - Breathlessness.
  - Impaired level of consciousness.
  - Perfuse sweating, rigors.
  - Pallor.
  - Significantly reduced mobility or temperature greater than 38°C or less than 36°C.
- For pregnant women who do not require admission, cefalexin is the recommended first-choice antibiotic.

# Pregnancy in patients with pre-existing renal disease

Women with renal disease who are considering pregnancy should be offered pre-pregnancy assessment and counselling by a multidisciplinary team (which should include an obstetrician, a renal/obstetric physician and a specialist midwife). Chronic kidney disease (CKD) affects up to 6% of women of childbearing age in high-income countries, and is estimated to affect 3% of pregnant women. Advanced renal dysfunction, proteinuria, hypertension, and poorly controlled underlying primary renal disease are all significant risks for adverse maternal, fetal, and renal outcomes.<sup>[5]</sup>

Pregnancy is uncommon in women with end-stage renal disease (ESRD). Fertility rates are low in women on dialysis. However, advancements in the delivery of dialysis and obstetric care have led to improved live birth rates in women on dialysis but these pregnancies remain high-risk for both maternal and fetal complications.<sup>[7]</sup> <sup>[8]</sup>

- For women with normal or only mildly decreased pre-pregnancy renal function (serum creatinine below 125 µmol/L), obstetric outcome is usually successful without adverse effects on the long-term course of their disease; however, there is an increased risk of antenatal complications such as hypertension and pre-eclampsia (see the separate article Hypertension in Pregnancy).
- Women with more severe renal impairment are more likely to suffer hypertension, pre-eclampsia or premature labour, and to have a small baby, miscarriage or irreversible decline in renal function in the long term.<sup>[1]</sup>
- Pregnancy is extremely uncommon in women with end-stage kidney disease on dialysis, for a variety of reasons; most such women are infertile. Fertility often returns rapidly after a successful renal transplant.
- If women on dialysis do become pregnant, the outcome is usually poor with a very high risk of miscarriage, severe hypertension, small babies and prematurity.<sup>[9]</sup> A 50% increase in dialysis is needed. Live birth outcome is only about 50%. Outcome is better for those with renal transplants.<sup>[10]</sup>
- Medications, especially antihypertensive agents, must be reviewed in women with renal disease who wish to get pregnant. Prednisolone, azathioprine, ciclosporin and tacrolimus do not appear to be associated with fetal abnormality and should not be discontinued in pregnancy.

• In pregnant women with renal disease, the target blood pressure should be below 140/90 mm Hg. Women with kidney disease should be offered low-dose aspirin as prophylaxis against pre-eclampsia, with treatment starting within the first trimester.<sup>[11]</sup>

### Pregnancy-induced renal disease

Women found, or suspected to have, renal disease in pregnancy should be referred to a nephrologist.

- Pregnancy itself can cause acute kidney injury and renal disease can present for the first time during pregnancy.
- Acute kidney injury in pregnancy may be due to various causes, including:
  - Sepsis eg, septic abortion, pyelonephritis.
  - Haemolysis eg, sickling crisis, malaria.
  - Hypovolaemia eg, pre-eclampsia, antepartum haemorrhage, intrapartum or postpartum haemorrhage, disseminated intravascular coagulation (DIC).

General measures to treat pregnancy-related acute kidney injury include identification of the underlying cause of kidney injury, intravenous fluid resuscitation, timely initiation of dialysis if needed, and prompt fetal delivery, if necessary.<sup>[12]</sup>

# Problems related to specific kidney diseases in pregnancy

- Reflux nephropathy:
  - Prophylactic antibiotics are required.
  - Potential for inheritance.

- Systemic lupus erythematosus:
  - High risk of spontaneous abortion.
  - May need immunosuppressant therapy.
  - Problems for the fetus (eg, neonatal lupus, heart block).
- Diabetic nephropathy:
  - Deterioration of hypertension.
  - Increased risk of pre-eclampsia.
  - Accelerated decline in renal function.
- Kidney transplant recipient:
  - Increased risk of miscarriage in the first trimester.
  - Risk from some immunosuppressants (eg, mycophenolate mofetil).
  - Increased risk of hypertension.
  - Premature delivery.

#### **Further reading**

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