Renal disease in pregnancy

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Abstract

Pregnancy in women with chronic kidney disease (CKD) is 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 collaboration between patient, nephrologist, neonatologist and obstetrician. In this review we will discuss approaches to managing pregnancy in women with CKD.

Keywords chronic kidney disease; dialysis; pregnancy; transplant

Introduction

Chronic kidney disease (CKD) is defined as abnormalities in serum biochemistry, urinary constituents (blood and/or protein) or renal structure that are present for 3 months or more. The Kidney Disease Improving Global Outcomes (KDIGO) classification of CKD divides CKD into five stages dependent on the estimated glomerular filtration rate (eGFR, Table 1).

CKD whilst rare in pregnancy, affecting 0.15% of pregnancies, is encountered with increasing frequency. However, most affected women have early CKD, stages 1 to 3a, with eGFR >45 ml/minute. Pregnancy may be the first time 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 a manifestation of CKD, but more commonly represents pre-eclampsia. Chronic pyelonephritis is the commonest known aetiology of CKD in pregnant women (Figure 1).

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%.

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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 1 cm 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.

The magnitude of these changes makes it unsurprising that limitation to adaptation by CKD can lead to adverse pregnancy outcomes.

Pregnancy in women with chronic kidney disease

Advice for women with CKD embarking upon pregnancy tends to focus on two issues:

1. Will the kidney disease affect the 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 many women with CKD in pregnancy have been described who have few, if any, problems. Identification of women at higher risk can facilitate individualisation of care and optimise outcomes.

Measuring renal function in pregnancy

Glomerular filtration rate: creatinine is a metabolic by-product of muscle metabolism that is filtered and excreted through the renal tract, thus serum creatinine levels are inversely proportionate to GFR. Serum creatinine is also affected by age, ethnicity, medication, diet, gender and body composition, so absolute serum creatinine concentrations correlate poorly with GFR between individuals.

In the general population, serum creatinine has been superseded by eGFR as a marker of renal function. eGFR is calculated using equations, most commonly the MDRD or CKD-EPI formulae. These are based on serum creatinine, patient age, gender and ethnicity. Importantly, these calculations are not validated for use during pregnancy and should not be used. 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 hour urine collection. This is inconvenient and frequently incomplete.

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. Preconception baseline values of eGFR are useful in predicting maternal and fetal outcomes however (see below).

Proteinuria: proteinuria is an independent predictor of progressive renal failure in patients with CKD and a diagnostic marker of pre-eclampsia in pregnancy. Traditionally, protein excretion is quantified by measurement in a 24 hour collection of urine. This

The Kidney Disease Improving Global Outcomes (KDIGO) classification of chronic kidney disease

CKD stage	Estimated GFR	Comment
G1	≥90 ml/minute	Only classified as CKD if associated with renal structural or urinary dipstick abnormalities
G2	60–89 ml/minute	
G3	30–59 ml/minute	May be sub-classified into: G3a: 45–59 ml/minute G3b: 30–44 ml/minute
G4	15–29 ml/minute	
G5	<15 ml/minute or on dialysis	

GFR; glomerular filtration rate.
Equation based estimated GFR calculations are not valid during pregnancy.

Table 1

is inconvenient for the patient and collections are often incomplete. Nevertheless, if performed correctly, this remains the most accurate method available.

In contemporary nephrology practice and obstetric medicine, the urine protein:creatinine ratio (PCR) or albumin:creatinine ratio (ACR) are accepted as surrogates for 24 hour urine collections for protein estimation. Assuming steady production and excretion of creatinine, this method corrects for variations in urine concentration and correlates closely with complete 24 hour urine collection data, including in pregnant patients with CKD. Thus PCR or ACR can be used for quantitative monitoring of proteinuria during pregnancy.

Fetal outcomes

Adverse fetal outcomes (preterm delivery, SGA, neonatal intensive care admission, persistent congenital disability or death) occur in 18% 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.

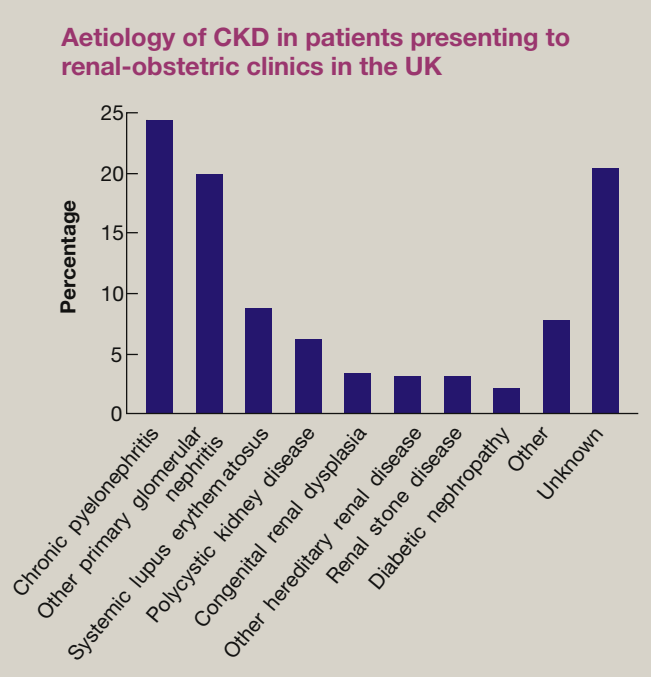

Figure 1

Renal function: the risks of adverse fetal outcomes increase with the severity of baseline renal dysfunction. Even early Stage G1 and G2 CKD, with preconception eGFR >60 ml/minute, is associated with increased risk of prematurity and intrauterine growth restriction as compared to the general population, predominantly, but not entirely, due to an increased risk of developing 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/litre) 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. Diabetes mellitus and SLE may cause CKD, but adverse fetal outcomes are also associated with non-renal manifestations of these conditions, such as hyperglycaemia, thrombophilia and antinuclear antibodies.

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.

In optimising fetal outcomes, blood pressure treatment targets for 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