Stage 1 chronic kidney disease in pregnancy

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Summary: Stage 1 chronic kidney disease (CKD) is defined by normal renal function, an estimated glomerular filtration rate of >90 mL/minute and abnormalities on urinalysis or ultrasound. These patients when pregnant are commonly seen, and diagnoses include diabetic nephropathy, glomerulonephritis, nephrolithiasis, reflux nephropathy, polycystic kidney disease and lupus nephritis. Underlying renal disease may also first become apparent in pregnancy, posing a diagnostic challenge. Patients tend to do well, but all need to be closely monitored particularly for hypertension and pre-eclampsia, which are more common in patients with stage 1 CKD overall. Relevant pregnancy outcomes may be divided into maternal (e.g. renal deterioration, nephrolithiasis, lupus flare, urinary infection or pyelonephritis), fetal (e.g. growth restriction, fetal death or stillbirth) and obstetric (e.g. hypertension, pre-eclampsia, preterm delivery, thrombosis). Specific diagnoses, their clinical features, management strategies and prognosis are reviewed.

INTRODUCTION

Stage 1 chronic kidney disease (CKD) is defined by normal or near-normal renal function, an estimated glomerular filtration rate (eGFR) of >90 mL/minute and abnormalities on urinalysis or ultrasound. From 1–3% of women of child-bearing age are affected,¹ including those with diabetic nephropathy, glomerulonephritis, nephrolithiasis, reflux nephropathy, polycystic kidney disease and lupus nephritis. The kidney disease may have been diagnosed prior to conception, or may have been relatively silent and first appreciated during pregnancy, as pregnant women are scrutinized more closely, and also because the renal haemodynamic alterations in pregnancy may cause proteinuria to become clinically detectable for the first time. The true prevalence of CKD in pregnancy is not known since many individuals with stage 1 CKD are undiagnosed. During pregnancy frequent measurement of blood pressure may also lead to diagnosis of renal diseases accompanied by hypertension. In patients with stage 1 CKD who become pregnant, consideration must be given to the possible harmful effects of pregnancy on renal function, as well as the impact of kidney disease on pregnancy outcome. Relevant pregnancy outcomes may be divided into maternal (e.g. renal deterioration, nephrolithiasis, lupus flare, urinary infection or pyelonephritis), fetal (e.g. growth restriction, fetal death or stillbirth) and obstetric (e.g. pre-eclampsia, thrombosis). Assessment of maternal hypertension is also crucial, as it contributes significantly to the risk for pre-eclampsia, pre-term delivery, intrauterine growth restriction and perinatal mortality.

Although some areas in obstetric medicine have been extensively studied with randomized controlled trials, renal disease in pregnancy is less common, and the quality of evidence guiding clinical practice is not of the highest level. Most evidence consists of case series with modest numbers of subjects.

Diagnosis of stage 1 kidney disease in pregnancy

Determining GFR in pregnancy is less straightforward than in non-pregnant states, as GFR and creatinine (Cr) clearance increase by 40–65% in pregnancy while Cr production is unchanged, so Cr level normally falls. One study reported average Cr values in non-pregnant women of 0.83 mg/dL (73 μ mol/L), while in first, second and third trimester of pregnancy Cr was respectively 0.74, 0.58 and 0.53 mg/dL (65, 51 and 46 μ mol/L), with an upper limit of normal of 0.96, 0.90 and 1.02 mg/dL (85, 80 and 90 μ mol/L),² although of note, values depend on the assay used and lab reference points. Currently, Cr clearance measured by 24-hour urine collection is the best approximate of the gold standard of inulin clearance, and is the most well-validated method for measuring renal function in pregnancy. In the non-pregnant population, the most common formulae utilized to assess kidney function are the Cockcroft-Gault (C-G) and MDRD formulae, but in pregnancy the MDRD appears to substantially underestimate³ and the C-G overestimates⁴ GFR, so neither can be used in place of the 24-hour urine Cr clearance.

Proteinuria in pregnancy

Owing to a normally increased GFR in pregnancy, the tubular transport maximum is exceeded and there is increased urinary excretion ('spilling') of glucose, amino acids, calcium and urinary protein. The basis for increased protein excretion in pregnancy is likely to be multifactorial and may involve alterations in glomerular basement membrane filtration slit size as well.⁵ The upper limit of normal for urinary protein excretion is 300 mg/day in pregnant (versus 150 mg/day in non-pregnant patients). Evaluation of abnormal proteinuria has been studied performing 24-hour urine collection, urine dipstick and protein/Cr ratio, but the gold standard remains the 24-hour urine protein measurement. A 24-hour protein level greater than 300 mg is abnormal in pregnancy and correlates roughly with a urine dipstick 1+ protein measurement. Though commonly used in an obstetrician's office to detect significant proteinuria, urine dipstick testing is susceptible to error due to variations in urine

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concentration, and may miss up to 1/11 pregnant women with true proteinuria.⁶ Conversely, 'negative' or 'trace' proteinuria rules out true proteinuria in most cases. Total protein/Cr ratio has been shown to accurately estimate 24-hour urine protein in non-pregnant patients, and in a systematic review of 13 studies of pregnant patients, it appears to be of value in ruling out proteinuria if less than 0.25 g/24-hour equivalent. Misclassifications tend to occur when the proteinuria is borderline (protein/Cr ratio of 0.25–0.40 mg/day) and so the 24-hour collection should be done to make the diagnosis of stage 1 CKD or pre-eclampsia if the protein/Cr results are equivocal. The protein/Cr measurement also underestimates severe proteinuria in pregnancy, so cannot be recommended as an alternative to 24-hour measurement in those cases.⁷

Haematuria in pregnancy

Dipstick-positive haematuria is common in pregnancy, and though it is seen in 16–20% despite careful collection of mid-stream urine, almost 40% of these are false-positive, with subsequently normal urine microscopic results.⁸ If positive on repeated measures, the clinician should perform urine microscopy to exclude casts, and document normal renal function, screen for proteinuria, measure the blood pressure and perform a urine culture. A renal ultrasound is the imaging modality of choice in pregnancy, but in the absence of renal dysfunction, a comprehensive evaluation of haematuria may be delayed until after delivery.

Renal structural abnormalities

Stage 1 CKD also includes women with structural radiographic renal abnormalities, such as reflux nephropathy, solitary kidney, nephrolithiasis, polycystic kidney disease; these diagnoses often predate the pregnancy and will be reviewed below.

STAGE 1 KIDNEY DISEASE IN PREGNANCY

There have been few studies specifically identifying patients with stage 1 CKD in pregnancy. In one study, 61 women were identified as having stage 1 CKD, and had a wide variety of diagnoses including glomerulonephritis, interstitial nephritis, pyelonephritis, nephrolithiasis, renal transplant and polycystic disease. When compared with 267 low-risk pregnancies, women with stage 1 CKD had significantly worse outcomes: early delivery <37 weeks in 33% versus 4.9% in controls, delivery <34 weeks in 14.8% versus 1.5% in controls, mean fetal weight 2795 g versus 3268 g in controls, and admission of the infant to the neonatal intensive care unit in 18% versus 1.1% controls. Hypertension was noted in 26% of women with stage 1 CKD in this study; the incidence of pre-eclampsia was not reported.⁹

Chronic glomerulonephritis

Child-bearing women may be afflicted with any of the forms of chronic glomerulonephritis (GN) including IgA nephropathy, focal and segmental glomerulosclerosis, membranoproliferative GN, minimal change nephritis and membranous nephropathy. GN may be pre-existing and diagnosed prior to conception, or may become apparent for the first time in pregnancy, especially if proteinuria is detected before 20 weeks of

gestation (before pre-eclampsia is a possibility). Similarly, patients who present with pre-eclampsia may fail to have resolution of proteinuria by 3–6 months postpartum, signalling renal pathology. Patients with preserved renal function (stage 1 CKD) and normal or well-controlled blood pressure tend to have favourable maternal and fetal outcomes. In a landmark study, 121 pregnancies in 89 women with stage 1 CKD were studied; increased proteinuria was seen in nearly half, hypertension in 23% and transient renal function decrease was noted in 16%. Pregnancy outcomes in this series: preterm delivery (≤ 36 weeks gestation) in 20%, small for gestational age infants 24.3% of all live births, fetal deaths 5.7% and neonatal deaths 4.9%.¹⁰ In another case-control study of 360 women with primary glomerulonephritis stage 1 CKD and absent or well controlled hypertension, pregnancy appeared to have little or no adverse effect on long-term renal function up to 25 years postpartum.¹¹

The level of blood pressure at the time of conception is an important variable in pregnancy outcome; in the absence of hypertension, there is significantly less chance of deterioration in renal function during pregnancy.¹¹ In those with hypertension, the risk of pre-eclampsia approaches 30%. BP treatment targets in women with glomerulonephritis (proteinuria) and stage 1 CKD are somewhat lower than pregnant hypertensives without renal risk. We treat to below 140/90 mmHg (Table 1) and patients are asked to obtain a home BP monitor to record their pressures, particularly in the latter half of pregnancy when pre-eclampsia may occur, notifying the physician if higher levels are recorded. The absolute level of BP varies in patients; we tend to advise notification if a >10–20 mmHg rise from baseline pressure is recorded over 1–2 hours, or the patient notes other signs and symptoms of pre-eclampsia (e.g. weight gain >1 kg per week, occipital headache, worsening oedema, right upper quadrant abdominal pain). Patient education is important, and all signs of pre-eclampsia should be reviewed with the patient. Bloodwork (particularly complete blood and platelet count, uric acid, liver function profile, Cr) and urine analysis for the detection of proteinuria are routinely performed at baseline and during pregnancy to screen for pre-eclampsia. Urine protein excretion may increase markedly in pregnant women with underlying renal disease, and may triple from baseline. This makes pre-eclampsia difficult to diagnose, as the clinician must rely on blood pressure and clinical symptoms. Patients with hypertension and increasing proteinuria may require hospitalization to allow ongoing monitoring of blood pressure and fetal wellbeing. The degree of proteinuria, however, does not generally factor into decisions about the timing of delivery and in some cases can be >10 g/day yet the patient may continue to be managed conservatively. In women with nephrotic range proteinuria, thromboprophylaxis with low molecular weight heparin should be considered. We suggest using similar thresholds for treatment as in the non-pregnant population, since there are no data that specifically address pregnancy. There are unfortunately not many known preventive measures that patients can take to avoid hypertension and pre-eclampsia; an individual patient meta-analysis of over 30,000 women at risk for pre-eclampsia found that low dose (75–150 mg/day) aspirin conferred a 10% reduction in the risk of adverse pregnancy outcomes particularly pre-eclampsia.¹²

IgA nephropathy

Hypertension frequently complicates pregnancy in women with IgA nephropathy and stage 1 CKD (50–100% depending

Table 1 Renal conditions and management considerations in pregnant patients with stage 1 CKD

Disease	Management considerations
Glomerulonephritis	May target BP somewhat lower, i.e. <140/90 mmHg. If nephrotic range proteinuria or low albumin, thromboprophylaxis with low molecular weight heparin (LMWH) should be considered. If managed with steroid, supplement with CaCO ₃ and vitamin D. Steroids increase risk of urinary and other infections, consider surveillance cultures
Diabetic nephropathy	If hypertensive may target BP somewhat lower, i.e. <140/90 mmHg. Prior to conception, switch ACEI or ARB to another antihypertensive. Consider surveillance urine cultures. Proteinuria may double or triple from baseline during pregnancy
Lupus nephritis	Disease should be inactive (normal urine sediment) for 6 months prior to conception. Antiphospholipid antibodies are associated with spontaneous fetal loss of 50–75%. Thromboprophylaxis with LMWH should be considered. Distinguishing pre-eclampsia from lupus flare is difficult; complement levels, presence of urine red cells help to distinguish; patient may require treatment for both lupus flare and pre-eclampsia
Autosomal-dominant polycystic kidney disease	Child has 50% chance of inheritance; consider genetic testing and <i>in vitro</i> fertilization with preimplantation genetic testing of embryos. Screen for hypertension, urinary infection
Reflux nephropathy	Perform surveillance urine cultures; prophylactic antibiotics may be necessary after first infection. Screen for hypertension
Nephrolithiasis	Increase fluid intake to 2.5–3 L per day, ultrasound for diagnosis, 80% stones will pass with fluids/analgesia. Extracorporeal shock wave lithotripsy contraindicated. Culture urine
Post kidney donation	Monitor for hypertensive complications of pregnancy
All diagnoses	Consider home BP monitor to record BP especially in latter half of pregnancy when pre-eclampsia may occur, notify treating physician of a 10–20 mmHg rise from baseline BP over 1–2 hours, or if signs and symptoms of pre-eclampsia, e.g. weight gain >1 kg per week, occipital headache, worsening oedema, right upper quadrant abdominal pain. Patient education: review signs of pre-eclampsia

CKD, chronic kidney disease; BP, blood pressure; ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocker

on the study), despite normal blood pressure and renal function prior to pregnancy.^{13,14} The incidence of pre-eclampsia is reported to be 25–30%. Long-term outcomes in 245 pregnant patients with IgA nephropathy and preserved kidney function are favourable when compared with pregnant normals, and in follow-up at 10 years those with IgA did not fare differently from healthy controls.¹⁵

Stage 1 CKD as acute glomerulonephritis

A comprehensive review of this complex topic is beyond the scope of this paper; these patients are challenging as immunosuppressants are toxic to the fetus, and high-dose steroids have not been studied during pregnancy. Acute GN presenting in pregnancy should be treated with close collaboration between the obstetrician and nephrologist. Prednisone crosses the placenta, but fetal adrenal insufficiency and thymic hypoplasia are unlikely if the dose is 15 mg/day or less^{16,17} whereas doses of greater than 20 mg/day are associated with maternal infection and placental abruption.¹⁸ The use of high-dose steroids in pregnancy is largely unguided by the literature. If there is morbid nephrotic syndrome it may be beneficial to treat empirically with oral steroids (e.g. prednisone 0.5 mg/kg pre-pregnancy weight or maximum 40–50 mg/day) and supplemental vitamin D and calcium. If glomerulonephritis is biopsy-proven and the diagnosis is amenable to calcineurin therapy, cyclosporine 2–5 mg/kg/day, aiming for CyA levels of 75–100 ng/mL may allow partial remission, resulting in elevations of maternal albumin which may ameliorate fetal growth. If the patient is nephrotic (>3 g/day proteinuria) or albumin levels are <2.0 mg/dL (20 g/L) thromboprophylaxis with subcutaneous low molecular weight heparin is advisable. If there is acute renal deterioration after 28–32 weeks gestation, delivery should be considered.

Renal biopsy

Renal biopsy is usually deferred until after delivery unless there is acute deterioration in renal function, or morbid nephrotic

syndrome, in which case biopsy is performed in the second trimester; in one study this resulted in a change in management in 40%.¹⁹ Although experienced operators have reported few complications of renal biopsy during pregnancy, increased renal blood flow, hypertension and difficulty positioning the patient are concerns.^{20–22} The timing of renal biopsy after delivery depends on the clinical circumstances. If renal function is normal, and only proteinuria is present, it is reasonable to delay biopsy by up to six months postpartum, since proteinuria may improve once the pregnancy-associated haemodynamic alterations have resolved. However, if renal function is impaired, or nephrotic syndrome is morbid with oedema, ascites or very low albumin, then biopsy may be considered either mid-pregnancy or within a few days or weeks of delivery.

Diabetes

Pre-existing diabetes poses significant risks to pregnancy, and if present for 10–15 years, patients may have developed diabetic nephropathy. Diabetic women with microalbuminuria, well-preserved renal function and normal blood pressure have a good prognosis for pregnancy, although they are at increased risk for pre-eclampsia and urinary infection.^{23,24} In one prospective cohort study from Denmark, 240 pregnant women with type 1 diabetes were followed during pregnancy, 11% of whom had microalbuminuria and 5% had diabetic nephropathy. Of this cohort, preterm deliveries (<37 weeks gestation) occurred in 62% of women with microalbuminuria and normal renal function, and in 91% of women with overt diabetic nephropathy (compared with 35% of diabetic women with no albuminuria). Pre-eclampsia developed in 6% of women with no albuminuria compared with 42% and 64% of women with microalbuminuria and diabetic nephropathy, respectively.²⁴ With respect to progression of maternal renal disease as a consequence of pregnancy, a study from Denmark reported that 26 women with type 1 diabetes who became pregnant had similar rates of deterioration in renal function over a 16-year follow-up, when compared with 67 control subjects with comparable disease who had never been

pregnant.²⁵ Women with stage 1 diabetic CKD with normal renal function and blood pressure are not likely to experience accelerated progression of diabetic nephropathy,²⁵ although it is not unusual for urinary protein excretion to increase significantly due to the haemodynamic changes in pregnancy. Women with non-nephrotic range proteinuria pre-conception may develop nephrotic range proteinuria during pregnancy, which will usually reverse after delivery. Women with overt nephropathy pre-conception, particularly those with impaired renal function and hypertension, have a high incidence of preterm delivery, pre-eclampsia and deterioration in maternal renal function.²³ On the other hand, women with type 1 diabetes and stage 1 CKD with microalbuminuria and normal renal function and normal blood pressure should be encouraged *not* to postpone pregnancy, because of the worse prognosis once overt nephropathy develops. They still need to be appraised of the heightened risks of pre-eclampsia and preterm delivery, and the need to be followed closely, but delaying pregnancy is likely to only worsen risk.

Many patients with albuminuria are treated with angiotensin blockade; however, angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers are contraindicated in all three trimesters of pregnancy due to a two-fold increased rate of fetal central nervous system (CNS) and cardiovascular malformations when given in the first trimester,²⁶ and up to a 64% rate of neonatal renal failure or mortality in the second and third trimesters.^{27,28} Women should be switched to other agents safe in pregnancy such as methyldopa, labetalol or nifedipine, prior to conception. Prior to the 12th week of pregnancy if patients were unknowingly pregnant and taking these medications, termination is not advised, rather patients are referred for ultrasound to assess cardiac and CNS risk. After delivery if ACEI is to be re-started, and the patient wishes to breast feed, enalapril has been deemed safe by the American Pediatrics Association; this is likely a class effect, but safety data are lacking in other ACEI. There are no published studies of pregnancy and nephropathy associated with type 2 diabetes, but given the increasing prevalence of this condition, it is an important area for future study.

Lupus nephritis

During pregnancy lupus nephritis is an unpredictable illness, because of the tendency of the disease to flare. Recent data suggest that disease duration, disease activity and renal damage prior to pregnancy are associated with increased organ damage after pregnancy.²⁹ Whether or not pregnancy *per se* is a risk factor for lupus flares has been disputed. Although some studies report no increase in flares attributable to pregnancy in patients in remission, prospective data suggest that pregnancy is in fact associated with a greater chance of disease exacerbation.³⁰ Women with lupus nephritis are advised not to conceive unless their disease has been 'inactive' for the preceding six months as there is a higher incidence of fetal demise with active disease. Optimal criteria for conception include a serum Cr measurement of <0.7 mg/dL or $62 \mu\text{mol/L}$, proteinuria less than 0.5 g/day and on spun urine examination, fewer than five red blood cells per high-powered field. If there is active disease with a Cr of >1.2 mg/dL or $106 \mu\text{mol/L}$, fetal loss occurs in 25–50%.³¹ Women with lupus are also more likely to have elevated titres of antiphospholipid antibodies (e.g. anticardiolipin, lupus anticoagulant) which may be

associated with spontaneous fetal loss of 50–75%, hypertensive syndromes indistinguishable from pre-eclampsia and thrombotic events including deep vein thrombosis, pulmonary embolus, myocardial infarction and strokes.³² Thus all women with systemic lupus erythematosus should be screened for antiphospholipid antibodies prior to pregnancy or early in gestation. When titres are elevated (more than 40 GPL), daily aspirin (80–325 mg) is recommended and low molecular weight heparin is generally prescribed. If there is a history of thrombotic events or pregnancy loss, then heparin in combination with aspirin is recommended.

Lupus versus pre-eclampsia

One of the difficulties in managing lupus nephritis during pregnancy is that increased activity of lupus may be difficult to distinguish from pre-eclampsia; both are characterized by an increase in proteinuria and hypertension. Thrombocytopenia may also be observed in both conditions. A distinguishing feature of pre-eclampsia is the increase in liver function tests, which are not characteristic of lupus activity. Conversely, hypocomplementaemia is a feature of lupus but not pre-eclampsia, and spun urine microscopy for red blood cell casts can also uniquely signal lupus nephritis activity. If disease activity is present before 20 weeks of gestation, then the diagnosis is more likely to be a lupus flare and amenable to steroid therapy. In the latter half of pregnancy, it may be impossible to distinguish between a renal lupus flare and pre-eclampsia; frequently, both are present simultaneously, and what starts as increased lupus activity may appear to trigger pre-eclampsia. It may be necessary to treat for both conditions, e.g. steroid therapy for lupus and bed rest and blood pressure control for pre-eclampsia. Unfortunately, delivery may be necessary if blood pressure cannot be controlled, HELLP syndrome (haemolysis, elevated liver enzymes and low platelets) is present, or if there is renal function deterioration and rising Cr. The approach to treatment of lupus nephritis during pregnancy is based largely on anecdotal experience, principles of treatment used in non-pregnant patients and avoidance of immunosuppressants with fetal toxicity. Steroid and azathioprine are the mainstays of treatment. Hydroxychloroquine during pregnancy appears to be associated with improved outcomes and does not appear to be toxic to the fetus.³³ Cyclophosphamide is generally not recommended during pregnancy, because of potential fetal toxicity, and should only be used when the mother's life is in jeopardy. Mycophenolate mofetil has been characterized as a teratogen due to associated craniofacial deformities, and should not be used during pregnancy.³⁴

Polycystic kidney disease

Young women with autosomal-dominant polycystic kidney disease (ADPKD) frequently have stage 1 CKD; they may be asymptomatic, with normal renal function and normal blood pressure, and may be unaware of their diagnosis. Little has been written about polycystic kidney disease and pregnancy, since many patients with this condition have well-preserved renal function until after childbearing. A report of 235 women with autosomal-dominant polycystic kidney disease and 108 unaffected family members demonstrated an increased incidence of maternal complications such as pre-eclampsia (11% versus 4%) in affected compared with unaffected women.³⁵

Pre-existing hypertension was the most common risk factor for maternal complications during pregnancy, as hypertension is a well-known risk factor for pre-eclampsia.³⁵ Fetal mortality is higher in patients with pregnancies complicated by hypertension than in non-hypertensive pregnancies.^{36,37} Pregnant women with polycystic kidney disease should be considered at increased risk of urinary tract infection and surveillance urine cultures should be considered. Oestrogen is reported to cause liver cysts to enlarge, and repeated pregnancies may result in symptomatic enlargement of liver cysts. Given the association between cerebral aneurysms and ADPKD in some families, screening for such aneurysms may be considered prior to natural labour. In women with fewer than four pregnancies, age at time of end-stage renal disease was 52 years.³⁵ All patients should undergo genetic counselling before pregnancy to ensure they are aware that their offspring have a 50% chance of being affected. To avoid ADPKD in the offspring, preconception, women may be counselled to consider the option of *in vitro* fertilization, with the goal of preimplantation genetic testing of the embryos and transfer of only those free of the mutation.³⁷

Reflux nephropathy

Chronic pyelonephritis usually refers to nephropathies associated with recurrent urinary tract infection often in association with urinary tract abnormalities, e.g. vesicoureteral reflux. Chronic pyelonephritis, due to further physiological dilation and stasis in the urinary tract, may worsen in pregnancy. Women with reflux nephropathy have been reported to have an adverse prognosis during pregnancy. A prospective study of 54 pregnancies in 46 women with reflux nephropathy found that pre-eclampsia was present in 24%, most commonly in women with pre-existing hypertension.³⁸ One-third of the infants were delivered preterm, and 43% had vesicoureteral reflux. These women should maintain a high fluid intake and should be screened with urine cultures at least monthly for bacteriuria, with prompt treatment when infections are present. After a first infection, suppressive antibiotic therapy with agents safe in pregnancy (see below) may be warranted for the rest of the pregnancy.

Urinary infection

Asymptomatic bacteriuria occurs in up to 10% of normal pregnancies, is associated with preterm labour and intrauterine growth restriction, and should be treated in pregnancy. The risk of developing pyelonephritis in pregnancy is up to 40% in those with asymptomatic bacteriuria. In women with a history of frequent urinary infections, or those with reflux, diabetes or CKD, regular surveillance cultures and prompt treatment are prudent. Three days of treatment for bacteriuria is recommended, and a number of antibiotics are safe to use in pregnancy, including oral preparations of amoxicillin-clavulanic acid, nitrofurantoin and cephalexin. Pyelonephritis in pregnant women is more likely to be associated with significant azotemia compared with non-pregnant women, and should be treated in hospital with intravenous fluids and antibiotics. Parenteral ceftriaxone, ampicillin, ticarcillin and piperacillin have all been used safely in pregnancy, and women may be switched to oral treatment and continued for a further two weeks, with follow-up cultures done thereafter. In women

who have had pyelonephritis or more than one urine infection in pregnancy, a low-dose antibiotic may be given as prophylaxis; daily nitrofurantoin 50–100 mg or cephalexin 250 mg is usually sufficient.

Urinary tract obstruction

Pregnancy is associated with dilation of the collecting system, which is not usually accompanied by renal dysfunction. Occasionally, acute urinary tract obstruction in pregnancy is caused by a kidney stone. Diagnosis may be made by ultrasonography, though this has poor sensitivity and specificity for stone diagnosis, and ureteral dilation is a normal anatomical change in pregnancy. Computed tomography is not recommended in pregnancy due to concerns about radiation.³⁹ Often (80% of the time) the stone will pass spontaneously, but occasionally if there is acute obstruction with kidney injury, systemic infection or a solitary kidney, cystoscopy may be necessary for insertion of a stent to remove a fragment of stone and relieve obstruction. Extracorporeal shock wave lithotripsy is contraindicated during pregnancy because of possible adverse effects on fetal hearing.

Pregnancy post kidney donation

Outcomes after kidney donation appear favourable for the mother and baby, although there may be a slightly increased risk of hypertension and pre-eclampsia despite a normal GFR. As such, when pregnant, donors should have more frequent clinical surveillance than normal low-risk pregnancies, to evaluate hypertension, appearance of proteinuria and fetal growth.⁴⁰ Review of management of pregnancy in renal transplant recipients is beyond the scope of this paper, and has been reviewed elsewhere,⁴¹ though specific data on stage 1 CKD post-transplant are lacking.

CONCLUSIONS

Stage 1 CKD comprises a wide variety of diagnoses, and with the exception of lupus nephritis and those with morbid nephrotic syndrome (both of which have more complicated physiology and worse prognosis for maternal and fetal health), patients with preserved renal function and normal blood pressure tend to do well in pregnancy. All patients need to be closely monitored for hypertension and pre-eclampsia, which are more common in patients with stage 1 CKD overall. We rely on patient education and home blood pressure monitoring between clinic visits. Hypertension magnifies the risk of pre-eclampsia (25%), and aspirin may help in prevention.¹² In patients with renal disease, we treat hypertension to slightly lower levels than the standard goal of 140/90 mmHg, using agents safe in pregnancy.⁴² Select groups will need regular surveillance cultures for urinary infections (Table 1). Underlying renal disease may first become apparent after pre-eclampsia has developed, and patients need follow-up to ensure disappearance of proteinuria postpartum. Similarly, nephropathy first detected in pregnancy requires nephrological work-up and possibly renal biopsy postpartum. Since these disorders are relatively uncommon, multicentre efforts are needed to better identify risks and determine optimal therapeutic strategies.

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