Renal disease in pregnancy

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Abstract

The diagnosis of acute kidney injury (AKI) in pregnancy is complicated by haemodynamic and urinary tract changes in pregnancy, and non-pregnant references intervals for serum creatinine should not be used. Pre-eclampsia is the most common cause of AKI in pregnancy. Although pregnancy-associated haemolytic microangiopathies are rare, it is useful for physicians and nephrologists to be aware of potential clinical discriminators as different, timely management is required. Pregnancy is successful for most women and pregnant individuals with chronic kidney disease (CKD). There is, however, an increased risk of adverse parental and neonatal outcomes at all stages of CKD, including pre-eclampsia, growth restriction, preterm delivery, low birthweight, neonatal unit admission and postpartum loss of parental kidney function. Pregnant persons with CKD should therefore have access to pre-pregnancy counselling to be able to make an informed decision about proceeding with pregnancy. A multidisciplinary team with expertise in obstetric nephrology should coordinate the care of pregnant individuals with CKD, which includes obstetric and kidney disease surveillance, monitoring of immunosuppression, and the initiation and/or intensification of haemodialysis if required. The diagnosis of superimposed pre-eclampsia remains clinically challenging.

Keywords Acute kidney injury; chronic renal insufficiency; dialysis; pre-eclampsia; pregnancy; renal transplantation

Key points

- Acute kidney injury in pregnancy can be missed if non-pregnancy reference ranges for serum creatinine are used
- Pregnancy is successful for most individuals with chronic kidney disease (CKD)
- An increased risk of adverse pregnancy outcomes mandates prepregnancy planning and multidisciplinary expertise in pregnancy
- Pre-eclampsia is a common cause of acute kidney injury in pregnancy, and making the diagnosis in those with CKD can be difficult

Acute kidney injury (AKI)

Clinicians often miss pregnancy-associated-AKI, which can be masked by the use of non-pregnant reference intervals. The normal haemodynamic changes of pregnancy lead to a decrease in serum creatinine during the first trimester, from a mean pre-pregnancy concentration of 60 micromol/litre to a nadir of 47 micromol/litre in the second trimester, before increasing back to prepartum concentrations at term. Systematic review shows that upper reference limits for creatinine in pregnancy are 85%, 80% and 86% of the non-pregnant limits in the first, second and third trimesters, respectively. Therefore, if the upper reference limit for non-pregnant individuals is 90 micromol/litre, values >77 micromol/litre in pregnancy should trigger investigations to exclude AKI (or undiagnosed chronic kidney disease (CKD)).

Definitions of AKI outside pregnancy are based on threshold levels of an increase in creatinine and decrease in urine output. These cannot, however, be used in pregnancy as gestational variations in serum creatinine mean there is no baseline against which relative change can be reliably assessed. In addition, a physiological oliguria impacts urine output in the peripartum period.

Causes of AKI in pregnancy mirror those in non-pregnant populations, with the addition of pregnancy-specific aetiologies (Table 1). Initial management of AKI is an assessment of parental and fetal well-being. Volume status should be optimized, nephrotoxic medications stopped, acute obstruction excluded with appropriate imaging, urinary tract infection treated, and investigation of primary kidney disease determined by urinary sediment, systemic features and gestation. Indications for renal replacement mirror those in non-pregnant persons and include refractory hyperkalaemia/acidosis and oligoanuric fluid overload. The fetotoxicity of urea is a factor in initiating dialysis in CKD (see below), but there are no data on the serum urea concentration at which dialysis confers clinical benefit in AKI.

Kidney biopsy is difficult to perform in the prone position with increasing gestation, and the risk of bleeding is higher (around 7%) in the late second and third trimesters compared with the postpartum period (around 1%). Kidney biopsy is therefore advocated only where a histological diagnosis will inform or change management during pregnancy

The most common cause of AKI in pregnancy is pre-eclampsia. Standard diagnostic criteria for pre-eclampsia are the development of *de novo* hypertension (≥140/90 mmHg) after 20 weeks' gestation in conjunction with either *de novo* proteinuria (urinary protein:creatinine ratio (uPCR) >30 mg/mmol), organ dysfunction (AKI, transaminitis, neurological symptoms, thrombocytopenia) or evidence of uteroplacental dysfunction (fetal growth restriction, abnormal umbilical artery Doppler recordings).[1]

Fluid balance in pre-eclampsia is complicated by hypoalbuminaemia, endothelial dysfunction and capillary leak. Individuals with pre-eclampsia are therefore vulnerable to

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Causes of AKI in pregnancy

Gestation	Diagnosis	Clinical features
Early	Hyperemesis gravidarum	Vomiting, ptyalism
	Septic abortion/miscarriage	Abdominal pain, vaginal bleeding, sepsis
Mid to late	Pre-eclampsia (see text)	*De novo* hypertension after 20 weeks' gestation with any of: • *De novo* proteinuria (uPCR >30 mg/mmol) • Parental organ dysfunction • Evidence of uteroplacental insufficiency
	HELLP (see text)	Haemolysis, elevated liver enzymes, low platelets. A severe variant of pre-eclampsia
	Bladder outflow obstruction	Consider risk factors: single kidney, neuropathy, polyhydramnios, multiple pregnancy, obstructed labour Physiological dilatation of the urinary tract in pregnancy can mimic hydronephrosis. Look for failure of decompression in the prone position and an absence of urinary jets
	Placental abruption	Abdominal pain, uterine tenderness, vaginal bleeding
	Acute fatty liver of pregnancy	Elevated transaminases, hypoglycaemia, lactic acidosis. New nausea/vomiting in the third trimester
	Microangiopathic haemolytic anaemia (TTP/aHUS) (see text)	Platelet consumption leading to haemolysis and end-organ damage including kidney failure (aHUS) and neurological symptoms (TTP). Non-resolution/progression after delivery
Peripartum	Chorioamnionitis	Sepsis, uterine tenderness, abnormal lochia, prolonged rupture of membranes
	Postpartum haemorrhage	Intravascular volume depletion, hypotension
	Ureteric injury	Operative delivery, fever, leucocytosis, pain, persistent ileus
	Non-steroidal anti-inflammatory drugs	The most commonly used postpartum analgesia
Any	Urosepsis	Dysuria, back/flank pain, renal angle tenderness, sepsis
	Lupus nephritis	Proteinuria ± haematuria, malaise, joint pain, hair loss, rash, pancytopenia. Positive ANA/dsDNA, low C3/C4
	Glomerulonephritis	Persistent proteinuria (uPCR >30 mg/mmol) before 20 weeks should be investigated to exclude primary kidney disease
	Interstitial nephritis	New drug exposure
	Renal stone disease	Colic

ANA, antinuclear antibodies; dsDNA, anti-double-stranded DNA; HELLP, haemolysis, elevated liver enzymes and low platelets. C, complement; uPCR, urinary protein: creatinine ratio; TTP, thrombotic thrombocytopenic purpura; aHUS, atypical haemolytic uraemic syndrome.
Adapted from Wiles KS, Banerjee A. Acute kidney injury in pregnancy and the use of non-steroidal anti-inflammatory drugs. *Obstetr Gynaecol* 2016. doi.org/10.1111/tog.12257.

Table 1

pulmonary oedema with even small volumes of fluid, leading to increased parental morbidity and mortality, with no evidence of improved uteroplacental perfusion. Pre-eclampsia is therefore managed with replacement of insensible losses (30 ml/hour) along with anticipated urinary losses (0.5–1 ml/kg per hour), while restricting overall intake to 80 ml/hour to reduce the risk of pulmonary oedema.[1]

The association between pre-eclampsia and adverse parental and fetal outcomes is well established. This includes a measurably increased risk of cardiovascular and kidney disease in later life, with studies reporting a 5–9-fold increased risk of kidney disease requiring renal replacement therapy, although optimum postpartum surveillance and risk factor management are unknown.

Although rare, thrombotic thrombocytopenic purpura (TTP) and atypical haemolytic–uraemic syndrome (aHUS) can present in pregnancy or the postpartum period because of a gestational fall in ADAMTS13 (a Distntegrin and Metalloproteinase with a Thrombospondin Type 1 motif, member 13) or peripartum activation of the alternative complement pathway, respectively. Such conditions have phenotypic overlap with HELLP (haemolysis, elevated liver enzymes and low platelets) syndrome, which is a severe manifestation of pre-eclampsia; however, rapid clinical distinction is required to start timely treatment with plasma exchange to increase ADAMTS13 activity in TTP or eculizumab to therapeutically block complement activation in aHUS (Table 2).

CKD and pregnancy

An overview of the management of CKD in pregnancy is shown in Figure 1.

Before pregnancy

Fertility and contraception: CKD is associated with mechanistic effects on fertility via disruption of the hypothalamic–pituitary–ovarian axis.[2] However, unintended pregnancies can and do occur in individuals with CKD, including those on dialysis. It is therefore vital that all reproductive-age females with CKD have

Possible distinguishing features of aHUS/TTP and HELLP

Feature	HELLP	HUS/TTP
Incidence	Around 1% of pregnancies	1 in 25,000 pregnancies
Gestation	After 20 weeks' gestation Prepartum (70%) Postpartum (30%)	TTP: second and third trimesters and postpartum period HUS: >75% postpartum Can occur before 20 weeks' gestation
Blood pressure	140/90 or more	Haemolysis can occur in the absence of hypertension
Platelet count	$<100 \times 10^9$/litre, rare $<10 \times 10^9$/litre	Usually $<70 \times 10^9$/litre; $<10 \times 10^9$/litre is suggestive of aHUS/TTP
Haemoglobin	>11 g/litre favours HELLP	<80 g/litre in the absence of another cause
Abnormal liver function	Transaminitis. LDH:AST <10:1 suggests HELLP	Normal liver function, unconjugated hyperbilirubinaemia
LDH	Typically <1000 U/litre	Typically >1000 U/litre
AKI	3–15% of HELLP Serum creatinine typically <180 micromol/litre	Serum creatinine typically >180 micromol/litre in aHUS
Coagulopathy	20% of HELLP	None. Elevated antithrombin and fibrinogen may be seen
Postpartum progress	Clinical improvement by 48–72 hours postpartum	Persistent laboratory abnormalities >72 hours after delivery
ADAMTS13	Deficiency may be found in HELLP	Activity <10% in TTP
Complement abnormalities	Described in HELLP	Detected in >80% pregnancy associated aHUS
Treatment	Delivery, supportive	Plasma exchange (TTP), eculizumab (aHUS)

AST, aspartate aminotransferase; LDH, lactate dehydrogenase.

Table 2

access to contraceptive counselling, and that safe and effective contraceptive methods are offered to those taking teratogenic medication, those in the first year after kidney transplantation or with active vasculitis, and for all those who do not wish to conceive.

Progesterone-only contraceptives avoid the risks of venous thromboembolism, arterial thrombosis and cervical cancer that are associated with oestrogen-containing agents, adverse effects of particular relevance to women with nephrotic syndrome, with advanced CKD or on long-term immunosuppression. The progesterone-only pill (desogestrel), subdermal progesterone implant and progesterone-containing intrauterine system are considered safe and effective in CKD.[2] In addition, all emergency contraceptives in the UK (levonorgestrel, ulipristal) act via progesterone and can be safely prescribed within 72 hours of unprotected intercourse to those with CKD.

Pre-pregnancy counselling: this provides an individualized, evidence-based assessment of the risk of adverse pregnancy outcomes, prevents exposure to teratogenic medication and offers an opportunity to optimize health for pregnancy.

The risk of adverse pregnancy outcomes including pre-eclampsia, fetal growth restriction, preterm delivery, low birthweight, neonatal unit admission and loss of parental kidney function increases with a higher stage of CKD pre-pregnancy (Table 3). In individuals with pre-pregnancy CKD stages 3–5, pregnancy results in a stepwise decline in kidney function equivalent to 2–5 years of pre-pregnancy kidney function.[3] However, even those with stage 1 CKD and preserved glomerular filtration have an increased pregnancy risk compared with individuals without kidney disease, even after correction for systemic disease, proteinuria, hypertension and late referral, suggesting that CKD per se confers risk in pregnancy.[4]

Chronic hypertension and proteinuria are independent risk factors for adverse pregnancy events. In those with CKD stages 3–5, chronic hypertension is the strongest predictor of preterm delivery, and pre- or early-pregnancy proteinuria is associated with an increased risk of fetal growth restriction.[3] Evidence from observational cohorts shows that optimizing these parameters ahead of pregnancy is associated with improved pregnancy outcomes. Reassuringly, kidney transplantation is not independently associated with adverse pregnancy outcomes.[3]

Known teratogens should be discontinued before pregnancy and converted to pregnancy-safe alternatives. The most commonly prescribed teratogen in persons with CKD is mycophenolate, which should be discontinued at least 6 weeks before pregnancy; however, a longer time might be needed to ensure disease/transplant stability on a pregnancy-safe alternative, commonly azathioprine.

Angiotensin-converting enzyme (ACE) inhibitors are toxic to the fetal kidney if exposure is in the second or third trimester; however, population data demonstrate no additional exposure risk in the first trimester when data are corrected for parental co-morbidities including diabetes mellitus and chronic hypertension. In individuals with proteinuric CKD, ACE inhibitors can therefore be continued for nephroprotection provided regular pregnancy testing is undertaken to ensure early confirmation of pregnancy.

There are limited data on angiotensin receptor antagonist exposure in pregnancy, so these agents are usually discontinued in advance of attempts to conceive. Sodium glucose co-transporter-2 (SGLT2) inhibitors are contraindicated in pregnancy because of fetotoxicity concerns based on animal data. Non-live vaccinations against SARS-CoV-2 and influenza are recommended to all pregnant individuals, including those with CKD and kidney transplants, because of the increased risks of infection in pregnancy. Medication considerations for pregnancy and lactation are shown in Table 4.

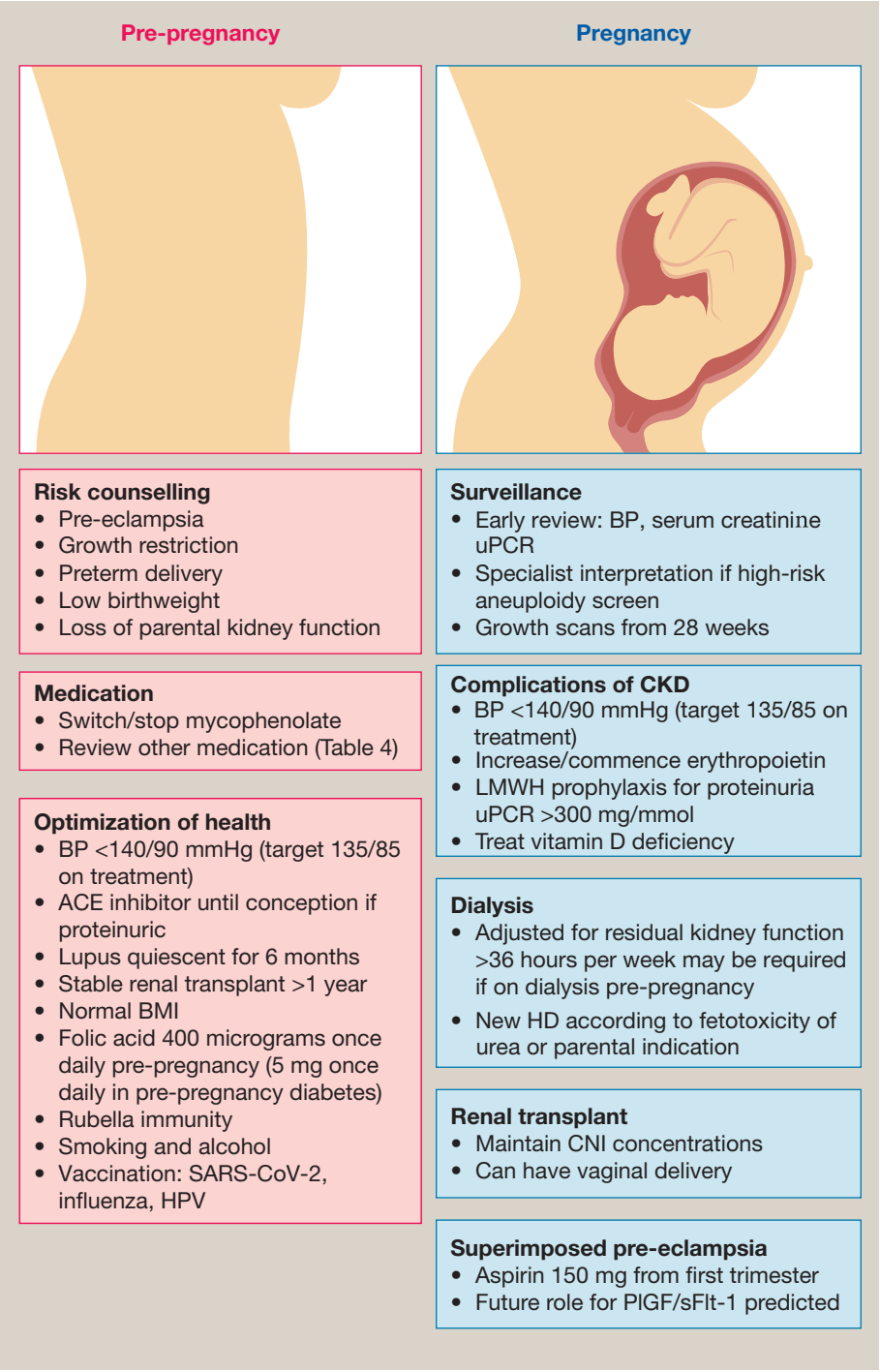

Figure 1 An overview of the management of CKD in pregnancy. ACE, angiotensin converting enzyme; BMI, body mass index; BP, blood pressure; CNI, calcineurin inhibitor (tacrolimus/ciclosporin); HD, haemodialysis; HPV, human papilloma virus; LMWH, low molecular weight heparin; PlGF, placental growth factor; sFlt-1, soluble fms-like tyrosine kinase-1.

Active lupus nephritis confers a risk of hypertension and preterm delivery; thus advice is to delay pregnancy until the disease has been quiescent on stable treatment for at least 6 months. Hydroxychloroquine is advocated for all those with lupus nephritis in pregnancy to minimize corticosteroid exposure, prevent flares and reduce fetal growth restriction. SSA (Ro) and SSB (La) antibodies can undergo placental transfer, conferring an estimated 15% risk of self-limiting neonatal cutaneous lupus and 2–5% risk of congenital heart block; fetal heart rate and echocardiography surveillance is recommended for the latter, although the optimum surveillance and treatment are unknown. Hydroxychloroquine reduces the risk of congenital heart block in those with previously affected infants, and these data are generalized for primary prevention.

Individuals with diabetic nephropathy should be supported in optimizing their blood glucose concentrations as any reduction in pre-pregnancy glycated haemoglobin towards an optimum of <48 mmol/litre (<6.5%) confers a decrease in the risks of

Rates (%) of adverse pregnancy outcomes from contemporaneous prospective cohorts according to pre-pregnancy CKD stage

		CKD stage (pre-pregnancy eGFR ml/minute/1.73 m^2)				
	Controls	1**	2**	3a*	3b*	4–5*
Outcome		>90	60–89	45–59	30–44	<30
Preterm delivery <37/40 weeks	6	23	51	41	62	88
Preterm delivery <34/40 weeks	1	8	16	20	25	40
Birthweight <10th centile	9	13	18	24	32	64
Neonatal unit admission	2	10	28	24	41	48
CKD stage shift or 25% reduction in eGFR at 1 year	–	8	13	34	35	86

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.
* = reference 3.
** = reference 4.

Table 3

miscarriage, congenital malformation, stillbirth and neonatal death.

Meta-analysis data examining transplant-to-pregnancy intervals have shown that an interval of <2 years from transplant to conception is associated with a higher live birth rate and lower miscarriage rate, although pre-eclampsia, gestational diabetes mellitus, caesarean delivery and preterm birth are common.[5] Standard immunosuppression regimens routinely include mycophenolate in the first year after transplantation; therefore a delay of at least a year after transplantation is advised before attempting to conceive, provided a switch to azathioprine is feasible and subsequent graft function remains stable. Additional considerations include a history of transplant rejection, transplant function, cytomegalovirus infection, hypertension and proteinuria.

Pregnancies in individuals requiring dialysis are high risk, both in absolute terms and in comparison to pregnancies after successful kidney transplantation. Delaying pregnancy until after transplantation should therefore be considered for those who are established on or approaching dialysis, provided kidney transplantation is anticipated during reproductive age.

During pregnancy

There is no evidence specifically addressing the schedule of care for pregnancy in persons with CKD. Expert consensus is that all those with CKD should have a plan for pregnancy made by a multidisciplinary team with expertise in obstetric nephrology, including appropriate surveillance and plans for delivery. Clinical review in early pregnancy is important to establish baseline concentrations of serum creatinine and proteinuria, to optimize blood pressure control and to ensure that low-dose aspirin (150 mg) is commenced as prophylaxis against preterm pre-eclampsia.

No specific evidence exists to guide gestational blood pressure targets for individuals with CKD. Data from two multicentre randomized controlled trials in general obstetric cohorts with chronic hypertension support the use of blood pressure control to <140/90 mmHg to reduce adverse parental outcomes, without evidence of increased fetal risk. In the UK, national guidance advocates a target blood pressure of 135/85 mmHg throughout pregnancy for all individuals taking antihypertensive medication.[1]

Kidney function in pregnancy is monitored by serum creatinine as the estimated glomerular filtration rate variably underestimates kidney function and is not valid. The greatest risks of a decline kidney function in pregnancy occur with chronic hypertension and in those whose serum creatinine falls by less than 10% compared with pre-pregnancy concentrations.[3]

Pregnant individuals with CKD should be offered routine trisomy screening, which includes a quantification of β-human chorionic gonadotropin (β-HCG). This can be elevated in CKD as a result of reduced renal clearance, so positive screening based on a high β-HCG concentration requires specialist interpretation, with consideration of non-invasive prenatal testing using circulating fetal DNA if available. Ultrasound assessment of fetal growth and well-being should occur every 4 weeks from 28 weeks' gestation, and more frequently if there is any clinical concern.

Physiological adaptation to pregnancy results in an increase in proteinuria and circulating erythropoietin concentration. Although the threshold concentration of proteinuria that confers a clinically significant thromboembolic risk remains unknown, expert consensus is to commence low-molecular-weight heparin prophylaxis if uPCR is >300 mg/mmol, or >100 mg/mmol with other risk factors. The need to initiate and/or titrate synthetic erythropoietin should be anticipated.

Kidney transplants: regular monitoring of tacrolimus/ciclosporin concentrations is required as these fall in pregnancy. Doses should be increased to maintain pre-pregnancy concentrations. Antibiotic prophylaxis should be considered after confirmed and treated urinary tract infection, including asymptomatic bacteriuria. Women with kidney transplants can have a vaginal delivery, with transplant team input into a surgical plan made in advance in case obstetric indications for caesarean delivery arise.

Dialysis: individuals established on dialysis before pregnancy are likely to require increased haemodialysis in pregnancy. More than 36 hours/week has been shown to improve neonatal outcomes,[5] though this may be adjusted if there is residual kidney function. New haemodialysis in pregnancy is most commonly initiated because of a concern about the fetotoxicity of urea,

Safety of medication used in CKD in pregnancy and lactation

Pre-pregnancy		Pregnancy		Lactation	
Considered safe	**Unsafe or unknown**	**Considered safe**	**Unsafe or unknown**	**Considered safe**	**Unsafe or unknown**
Labetalol	ARB	Labetalol	ACE inhibitors[b]	Labetalol	Methyldopa[d]
Nifedipine	Mycophenolate	Nifedipine	ARB	Nifedipine	ARB
Methyldopa	Cyclophosphamide	Methyldopa	Mycophenolate	Enalapril/captopril	Mycophenolate
ACE inhibitors	Allopurinol	Corticosteroids	Cyclophosphamide	Corticosteroids	Cyclophosphamide
Corticosteroids	Cinecalcet	Azathioprine	Warfarin	Azathioprine	Allopurinol
Azathioprine	HIF stabilizers	Ciclosporin	Allopurinol	Ciclosporin	Cinecalcet
Ciclosporin	SGLT2 inhibitors	Tacrolimus	Cinecalcet	Tacrolimus	HIF stabilizers
Tacrolimus	Statins	Hydroxychloroquine	HIF stabilizers	Hydroxychloroquine	SGLT2 inhibitors
Hydroxychloroquine		Aspirin	SGLT2 inhibitors	Aspirin	Statins
Aspirin		LMWH	Statins	LMWH	
LMWH		Colchicine		Colchicine[c]	
Colchicine		Iron[a]		Iron	
Iron		Erythropoietin		Erythropoietin	
Erythropoietin					

Limited data:

- Rituximab: no evidence of teratogenicity. Placental transfer in the second and third trimesters. Treatment pre/early pregnancy minimizes risk of neonatal B cell depletion, but live vaccines should be appropriately delayed. Trace amounts in breast milk, but neonatal absorption is unlikely. No long-term outcome data.
- Eculizumab: no evidence of teratogenicity. Benefit is likely to be greater than theoretical risk given the morbidity of the underlying condition. Trace amounts in breast milk, but neonatal absorption is unlikely. No long-term outcome data.

ARB, angiotensin receptor blockade; HIF, hypoxia inducible factor; LMWH, low molecular weight heparin.
Source: Adapted from Wiles et al. (2018).[2]
[a] No data on intravenous iron in the first trimester.
[b] Toxic to the fetal kidney in the second and third trimesters.
[c] Estimated 10% of dose is received by the infant.
[d] Risk of postnatal depression.

Table 4

rather than for standard indications including refractory fluid overload, hyperkalaemia or acidosis. The optimum urea threshold at which dialysis should be commenced in pregnancy remains unknown as the limited historical data fail to reflect contemporary obstetric practice. Discussions are recommended if serum urea concentrations are >15 mmol/litre so haemodialysis can be commenced at a concentration of >17–20 mmol/litre depending upon the trajectory of kidney function decline, stage of gestation and risks of iatrogenic preterm delivery.

Residual kidney function is thought to be important in those who are new to dialysis in pregnancy, which begins 'gently' (e.g. for 2 hours three times per week) and is titrated according to parental parameters; this aims for a midweek pre-dialysis serum urea concentration of <12.5 mmol/litre. No additional benefit has been shown for long, frequent dialysis in a single small cohort newly starting dialysis in pregnancy.[5]

Pre-eclampsia: the risk of pre-eclampsia is increased in individuals with CKD, and rises in increments with CKD stage (see Table 3). Low-dose aspirin (150 mg) is given from the first trimester to reduce the risk of preterm pre-eclampsia, based on high-quality evidence from pregnant individuals without CKD. For those with hypertension and/or proteinuria before pregnancy, there are no standard diagnostic criteria for superimposed pre-eclampsia. Relative changes in blood pressure and proteinuria after 20 weeks' gestation are difficult to interpret in the context of gestational change, but should trigger increased surveillance for uteroplacental and parental organ dysfunction.[1]

It can be challenging to distinguish between pre-eclampsia and lupus flare because of overlapping phenotypes that include proteinuria, hypertension and thrombocytopenia. Systemic features, double-stranded DNA titres and complement concentrations can help. Placental growth factor and sFlt-1 (soluble fms-like tyrosine kinase-1) concentrations can be used for the prediction and prognosis of pre-eclampsia in the absence of CKD. A recent study showed that serum placental growth factor concentrations <150 pg/ml predict delivery with superimposed pre-eclampsia in CKD, although the predictive value is lower in the higher stages of pre-pregnancy CKD.

Postpartum period

Breastfeeding can be supported in individuals with CKD. Drug regimens can and should be made safe for lactation (Table 4).

Numerous studies have shown that the lifespan of a kidney transplant is not significantly different in transplant recipients undertaking pregnancy compared with those who do not. However, for those with pre-pregnancy CKD stages 3–5, there is a

stepwise loss in kidney function during pregnancy that equates to approximately 4 years of background kidney disease. ◆

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TEST YOURSELF

To test your knowledge based on the article you have just read, please complete the questions below. The answers can be found at the end of the issue or online here.

Question 1

A 27-year-old with lupus nephritis and hypertension attended pre-pregnancy counselling. She wished to conceive. At her diagnosis 5 years previously, she had been given prednisolone and mycophenolate mofetil (MMF) induction therapy. She could not tolerate MMF, experiencing gastrointestinal adverse effects, so was changed to azathioprine and prednisolone maintenance therapy. Her lupus has been in remission for the previous 12 months. On examination, her blood pressure was 132/82 mmHg.

Investigations

- Creatinine 95 micromol/litre (non-pregnant 45–90)
- Urine protein: creatinine ratio 18 mg/mmol (non-pregnant <15)

Her current medications are listed below. Which medication should she be advised to discontinue in advance of attempts to conceive?

A. Azathioprine
B. Hydroxychloroquine
C. Irbesartan
D. Nifedipine
E. Prednisolone

Question 2

A 32-year-old presented at 34 weeks' gestation in her first pregnancy. She had had a persistent headache for the previous 24 hours. She had type 1 diabetes complicated by diabetic nephropathy. She was taking aspirin 150 mg daily and intermediate-acting and prandial insulin. On examination she had pitting oedema to the knees, her blood pressure was 154/98 mmHg (2 weeks previously 134/79 mmHg). Urine dipstick testing revealed 2+ protein.

Investigations

- Haemoglobin 90 g/litre (115–155[a])
- Platelets 89 × 10^9/litre (150–400[a])
- Serum creatinine 169 micromol/litre (45–90[a]) (2 weeks previously 122 micromol/litre)
- Alanine aminotransferase 55 U/litre (<45[a])
- Albumin 24 g/litre (35–45[a])
- Lactate dehydrogenase 720 U/litre (10–250[a])
- Urinary protein:creatinine ratio 156 mg/mmol (<30)
- Blood film showed schistocytes (red blood cell fragments)

[a] Reference ranges refer to non-pregnant values.

What is the most likely diagnosis?

A. Atypical haemolytic–uraemic syndrome (aHUS)
B. Focal segmental glomerulosclerosis
C. Haemolysis, elevated liver enzymes and low platelet syndrome
D. Progressive diabetic nephropathy
E. Thrombotic thrombocytopenic purpura (TTP)

Question 3

A 26-year-old was referred to the antenatal clinic at 12 weeks' gestation with blood 2+ and protein 3+ in her urine (leucocytes negative, nitrites negative). She had noticed that her rings felt tight on her fingers. She also had pains in the small joints of her hands. On clinical examination, she had a malar rash across the bridge of her nose and cheeks. Her blood pressure was 123/82 mmHg.

Investigations

- Haemoglobin 112 g/litre (115–155) [a]
- Platelets 156 x10^9/litre (150–400) [a]
- Creatinine 105 micromol/litre (non-pregnant 45–90)[a]
- Urine protein: creatinine ratio 314 mg/mmol (non-pregnant <15)

[a] Reference ranges refer to non-pregnant values.

Which is the best investigation to guide management in pregnancy?

A. Double-stranded DNA antibody concentrations
B. Antinuclear antibody profile
C. Antiphospholipase A2 receptor (PLA2R) antibody concentrations
D. Complement component C3 and C4 concentrations
E. Kidney biopsy