Pregnancy in patients with Chronic Kidney Disease – risks and rewards

KCC Education Rounds
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Objectives

- Review the principles of pre-pregnancy counselling for patients with CKD
  - What do patients want to know?
- Discuss what is known about pregnancy outcomes in women with CKD and post transplantation

Case – Mrs. WB

- 32 year old G_0 who is 2 years post kidney transplant. Her renal disease was IgA nephropathy
- Her creatinine is 110 (eGFR 45 mL/min), her urine ACR is 4 mmol/L
- She wants to get pregnant

Common preconception questions

How will my kidney disease affect the pregnancy?

- Will I have a healthy baby?
- Are the medications that I need to take safe?

How will the pregnancy affect my kidney disease?

- Will it make my kidneys fail faster?
- Will it hurt my transplant?

When is the best time to get pregnant for me?

- What do I need to do to prepare?
- Is there anything that can reduce my risk?

Women with CKD are at increase risk for adverse maternal and fetal events

Pregnancy in CKD has been associated with loss of maternal renal function

Creatinine	Chance of worsening CKD?	Will it stay lower after delivery?	
< 125	Up to 10%	Possibly	
125-180	40%	50%	
> 180	70%	Almost always	23% progress to ESKD within 6 months of delivery

Jones DC et al. N Engl J Med 1996;335:226-232

Quantifying risks of adverse pregnancy outcomes

Creatinine	Successful obstetric outcome (%)	Preterm (%)	Small for gestational age (%)	Preeclampsia (%)
< 125	96	30	25	22
125-180	90	60	40	40
> 180	78	> 95	65	60

Other counselling points to consider

- Pregnancy is a sensitizing event
  - Can result in the formation of anti-HLA antibodies
  - May make finding a future suitable donor more difficult

Pregnancy and CKD— optimizing outcomes

Low-dose Aspirin

ASA 81mg/d if increased risk of preeclampsia (so anyone with CKD, Proteinuria, HTN)

Start at 12 weeks, continue to 36wks or delivery

Calcium supplementation

Evidence strongest if dietary intake low

If intake <1000mg/d, increase to 1000-2500mg/day with diet or supplementation

Not routinely recommended

Vitamin C, Vitamin E, Fish oil, etc.

Common renal diagnosis – Lupus nephritis

- Quiescent disease for at least 6 months before attempting conception
- Kidney flares most common post-partum vs in pregnancy
- Continue hydroxychloroquine to reduce risk of flares +/- preeclampsia

Common renal diagnosis – Diabetic Nephropathy

- Best if tight glycemic control for at least 6 months pre-pregnancy
- Patients with diabetic kidney disease are at risk of progression with or without pregnancy
- Stop ACE/ARB in most patients prior to pregnancy and in all patients during pregnancy
- Pre-existing proteinuria increases significantly during pregnancy (avg. 7 fold increase) and usually returns to baseline by 12 weeks post-partum

Pregnancy in patients on dialysis

- Fertility significantly diminished
  - Pregnancy rare but still possible
- Intensive dialysis has been shown to improve
  - Chances of conceiving
  - Maternal and fetal outcomes
- Amount of dialysis required depends on residual renal function
  - Better outcomes with increased frequency and length of dialysis
  - Aim for as close to normal physiology as possible
  - Goal of 36 hours per week in studies

Pregnancy in patients on dialysis

- Control blood pressure
- Estimate volume removal/dry weight □ a moving target!
- Manage anemia with increasing doses of ESA
- Attention to ensuring adequate nutrition/protein intake, folate, vitamin, zinc supplements
- Fetal monitoring during/post hemodialysis once viability reached
- If conceive on PD, general recommendation is to stay on PD

Pregnancy post renal transplantation

- Kidney transplant improves reproductive function
  - Fertility generally returns a few months after renal transplantation
- Preconception counselling, family planning and contraception important components of care

Pregnancy post renal transplantation

- Advised to wait 1-2 years post transplantation
  - Individualized to the patient
- Kidney function stable and optimized
- No episodes of rejection in the previous year
- No concurrent fetotoxic infections, such as cytomegalovirus (CMV)
  - Preferable to wait 6-12 months since resolution of disease before conception
- On no teratogenic or fetotoxic medications
- Immunosuppressive regimen is stable at maintenance levels

Pregnancy post renal transplantation

- Live birth rate and miscarriage rate similar to general population
- No effect on graft function or rejection if baseline GFR “normal”
- Increased risk of:
  - Preeclampsia (27% vs 3.8%)
  - Gestational diabetes (8% vs 3.9%)
- Preterm delivery (46% vs 12.5%)
  - Average gestation 35.6 wks
  - Average weight 2420 gms

Pregnancy post renal transplantation

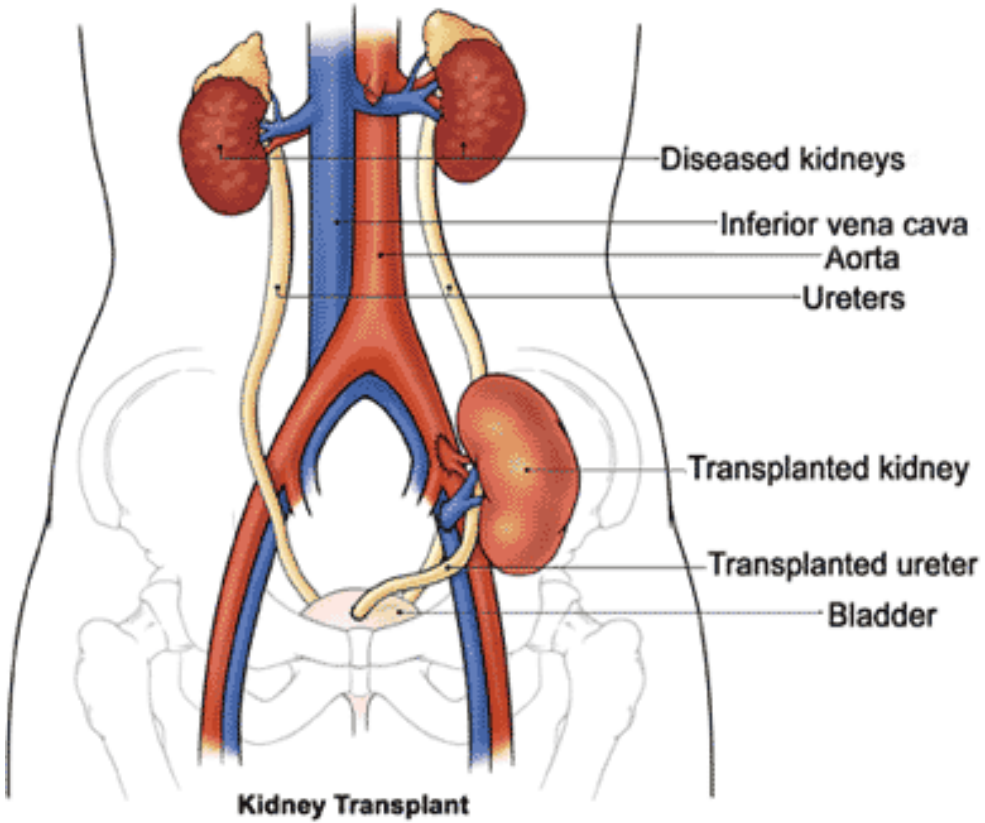
- Immunosuppressive regimen needs to be modified preconception
  - Azathioprine, tacrolimus/cyclosporine +/- prednisone
  - Change at least 3 months before conception
- Tacrolimus doses often need to be increased substantially
  - Whole blood tac levels in pregnancy may not accurately reflect free levels
- Breastfeeding is encouraged for most women post delivery

Medications in pregnancy

Drug	Adverse Effects During Pregnancy
Safe	
Hydroxychloroquine	No known risk for teratogenicity; withdrawal may cause flare
Glucocorticoids	Risk for gestational diabetes; risk for cleft lip and palate; risk for premature rupture of membranes
Azathioprine	No known risk for teratogenicity
Cyclosporine	Increased risk for cholestasis
Tacrolimus	Risk for gestational diabetes and hypertension
Hazardous	
Cyclophosphamide	Fetal malformations, higher rates of pregnancy loss
Mycophenolate mofetil	Teratogenic (lip, palate, ear abnormalities), higher rates of pregnancy loss
Unknown	
Rituximab	Transient fetal B-cell depletion

Pregnancy in renal transplant patient

- Vaginal delivery generally safe
- Location of allograft and ureter should be noted on US in case cesarean required



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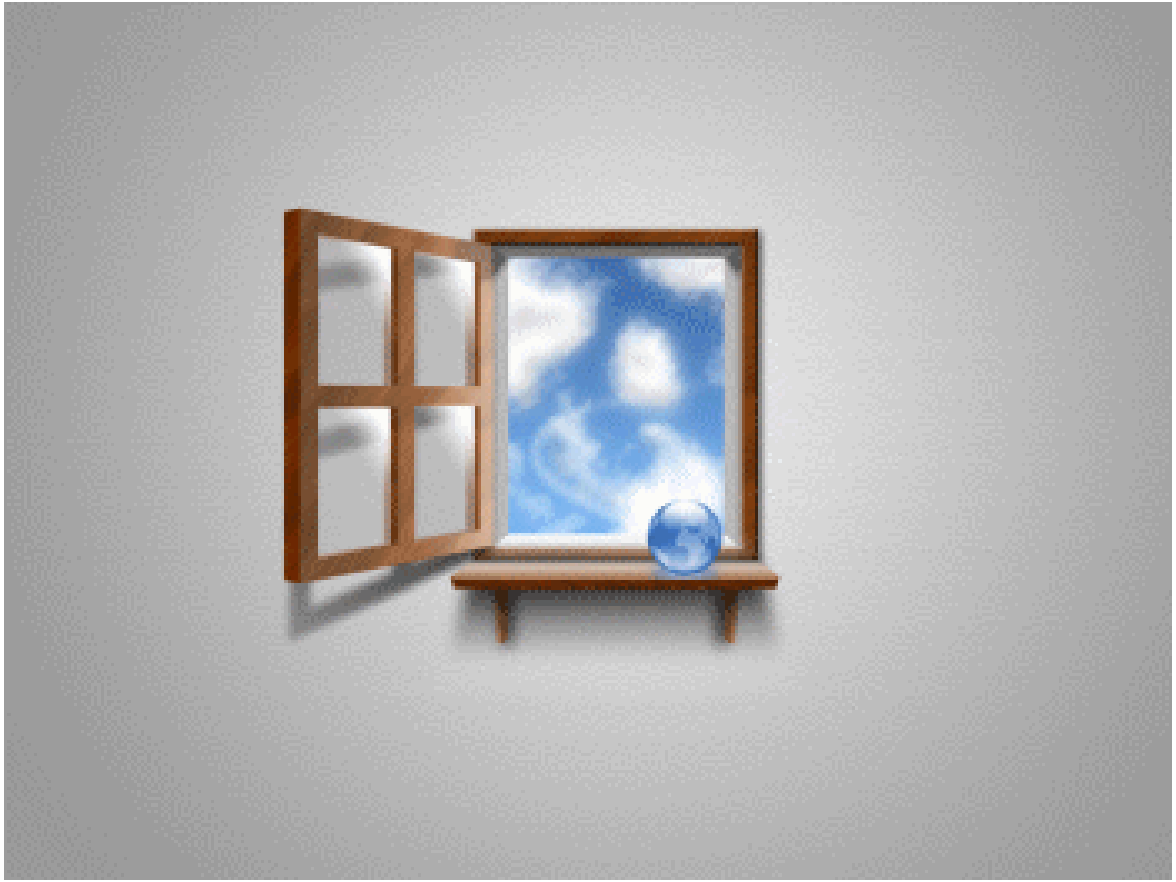
Case – Mrs. WB

- ACE-I discontinued prior to pregnancy, prepreg uACR was 60 mg/mmol
- Immunosuppressive medications changed to pregnancy safe regimen
- Started ASA 81mg po daily at 12 weeks
- Creat 90 umol/L in T2 and 118 umol/L prior to delivery
- uACR 120 mg/mmol at 37 weeks but no other signs preeclampsia
- SVD at 38 weeks
- Creatinine increased transiently to 130 and then improved to baseline over 6 months
- She is currently 6 years post-partum, Cr 125, uACR 10



Pregnancy in CKD patients – Timing is everything!

- Discuss family planning goals with all women of childbearing age and **in the context of their anticipated renal trajectory**
  - Both renal function/fertility declines over time!
  - CKD Stage 4/5 and progressive, age <35, may be able to delay until transplantation
  - CKD Stage 4/5 and progressive, age >35, maybe don’t delay, may need dialysis

Summary

- Patients with pre-existing kidney disease can and do have successful pregnancies
- No kidney disease is trivial in pregnancy
- Discuss family planning goals with all women of childbearing age and **in the context of their anticipated renal trajectory**
  - Both renal function/fertility declines over time!
- Patients should be evaluated by an obstetrician and a nephrologist with experience caring for pregnant patients with CKD to evaluate their risks particular to their disease processes and kidney function