RENAL DISEASE IN PREGNANCY

Laura Colicchia, MD

Minnesota Perinatal Physicians
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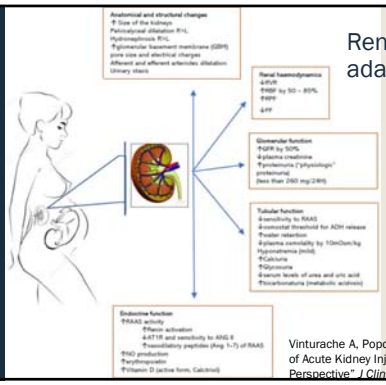
Overview

- Acute kidney injury in pregnancy
- Chronic kidney disease in pregnancy
- Dialysis and renal transplant

Renal physiologic adaptations to pregnancy



**Creatinine 0.9 or higher is potentially abnormal in pregnancy

Vinturache A, Popoola J, Watt-Coote I, "The Changing Landscape of Acute Kidney Injury in Pregnancy from an Obstetrics Perspective" *J Clin Med* 2019; 8(9): 1396.

Acute Kidney Injury

- Official definition:
  - *A rise in serum creatinine by >0.3mg/dL within 48 hours*
  - *OR an increase of >1.5 times baseline creatinine within 7 days*
  - *OR urine output <0.5mL/kg for >6 hours.*

BUT: in pregnancy pre-pregnancy baseline creatinine values may not apply – be suspicious of any rapid rise in creatinine or drop in UOP

What kind of acute kidney injury?

- Pre-renal (decreased renal blood flow)
- Intrinsic renal (ATN, glomerulonephritis, TTP/HUS, pre-eclampsia, drug-related)
- Post renal (obstruction)

*Individual patients may have multiple types of AKI simultaneously

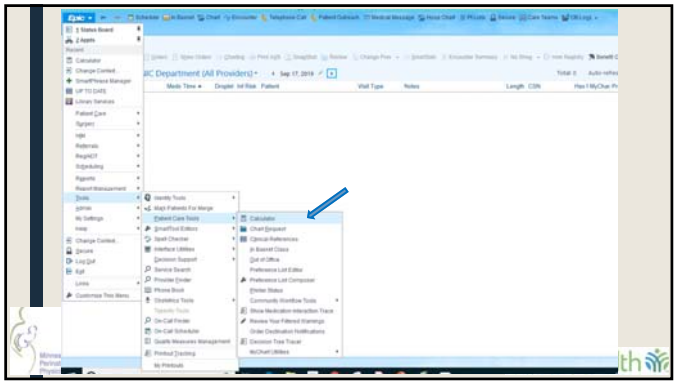
What kind of acute kidney injury?

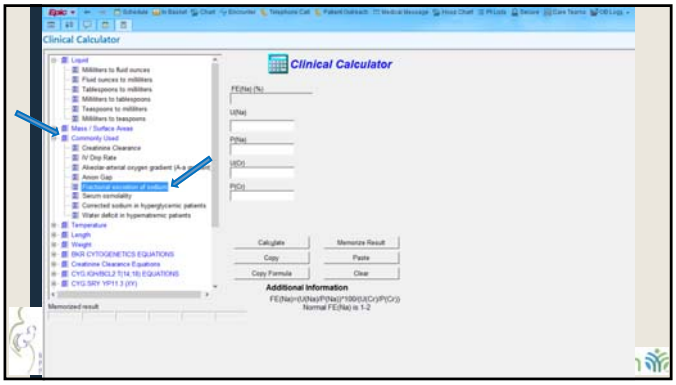
$$FENa = \frac{Urine\ Sodium \times Plasma\ Creatinine}{Urine\ Creatinine \times Plasma\ Sodium} \text{ x } 100$$

Pre-renal: FENa<1%; BUN:Cr >20:1

Intrinsic renal: FENa>2%; BUN:Cr < 10:1

Post-renal: equivocal FENa and BUN:Cr





Acute kidney injury – Prerenal disease

Decreased renal perfusion → Decreased filtration → Increased creatinine and decreased urine output

- Hypovolemia (hemorrhage, hyperemesis, diarrhea)
- Decreased intravascular volume (pre-eclampsia)
- Decreased renal perfusion (sepsis)
- Decreased cardiac output (cardiac failure, peripartum cardiomyopathy)

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Acute kidney injury – Prerenal disease

Decreased renal perfusion → Decreased filtration → Increased creatinine and decreased urine output

- Treatment: correct hypovolemia, improve cardiac output, treat underlying disease
- Prerenal disease can lead to acute tubular necrosis if not corrected quickly

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Acute Kidney Injury – Intrinsic Renal Disease

- Can involve the renal vasculature, tubules, and/or glomeruli
- Glomerulonephritis
- Interstitial or Tubular
  - *Acute tubular necrosis caused by hemorrhage, sepsis*
- Renal vascular changes
  - *Pre-eclampsia*
  - *Vasculitis*
  - *Thrombotic microangiopathies (TTP/HUS)*
- Acute Fatty Liver of Pregnancy (AFLP)
- Lupus nephritis
- Antiphospholipid antibody syndrome

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Acute tubular necrosis

Decreased renal perfusion → Decreased filtration → Increased creatinine and decreased urine output

Decreased renal perfusion → Severe renal hypoperfusion and vasoconstriction → Acute tubular necrosis

- Presentation: clinical picture c/w hypotension (sepsis or hypovolemia), urinalysis with granular casts, elevated FENa
- Treatment: fluid resuscitation, treat underlying cause (sepsis, hemorrhage, etc), supportive therapy until renal recovery (dialysis if necessary)

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TTP/HUS (thrombotic thrombocytopenic purpura/ hemolytic uremic syndrome)

- TTP – Fever, Anemia, Thrombocytopenia, Renal and Neurologic disease (FAT-RN)
  - *Caused by a deficiency of ADAMTS-13 (either familial genetic mutation or acquired autoantibodies)*
  - *Can be precipitated during pregnancy in women with underlying predisposition*
  - *Treated with plasmapheresis*
- HUS – similar to TTP but rare neuro involvement and more significant renal disease
  - *Caused by excessive activation of complement pathways or by shiga toxin (e.coli 0157-H7)*
  - *Treated with plasmapheresis or monoclonal antibody therapy*
  - *Shiga toxin mediated always accompanied by severe diarrhea*
  - *Complement mediated can present or flare in the postpartum period*

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TTP/HUS (thrombotic thrombocytopenic purpura/ hemolytic uremic syndrome)

- TTP and HUS are both 10 times more common in pregnancy and the postpartum period
  - *Likely due to normal complement changes in pregnancy, normal falling ADAMTS13 levels in pregnancy*
- Majority of cases in third trimester and postpartum
- High risk of recurrence in subsequent pregnancies

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Table 2

Signs and Symptoms of Overlapping Syndromes of Acute Kidney Injury in Pregnancy

	Preeclampsia/HELLP	TTP	aHUS	AFLP	APS	Lupus flare
Timing in pregnancy	>20 weeks	Higher incidence in 2nd trimester	Higher in postpartum	Higher incidence in 3rd trimester	All gestational ages	All gestational ages
Blood pressure >140/90 mmHg	3+	0 to 3+	2+	0 to 2+	0 to 3+	0 to 3+
Neurologic involvement	0 to 3+	2+ to 3+	0 to 1+	0	0 to 3+	0 to 3+
Fever	0	1+ to 3+	0 to 3+	0	2+	2+
Schistocytes (more than 1%)	0 to 2+	3+	2+	0 to 1+	2+	0
Low platelet count (cells/ μL)	0 to 3+	2+ to 3+	3+	1+ to 2+	2+	1+ to 2+
Elevated liver enzymes	0 to 3+	0 to 1+	0 to 1+	2+ to 3+	0 to 1+	0
Proteinuria*	1+ to 3+	1+ to 3+	1+ to 3+	1+	0 to 3+	1+ to 3+
Low ADAMTS13 activity (<10%)	0 to 1+	3+	1+	0	0	0
Treatment	Delivery of fetus	Plasma exchange	Plasmapheresis/eculizumab	Delivery of fetus	Aspirin + anticoagulatio n	Immune suppression

ADAMTS13: A disintegrin and metalloprotease with a thrombospondin type 1 motif, member 13.

HELLP: hemolysis, elevated liver enzymes, low platelets

TTP: thrombotic thrombocytopenic purpura

AFLP: acute fatty liver of pregnancy

APS: anti-phospholipid syndrome

Proteinuria: defined as either >1+ on urinalysis or urine protein of more than 300 mg/24 hours or urine protein/creatinine ratio of > 0.3 g/g

Ratings: 0, unlikely or not present; 1+, mild or low likelihood; 2+, moderate or moderate likelihood; 3+, severe or high likelihood

Jim B, Garovic VD. "Acute Kidney Injury in Pregnancy". *Semin Nephrol* 2017; 37(4): 378-385.

Acute Kidney Injury – Postrenal disease

- Ureteral injury
- Urinary retention
- Hydronephrosis due to uterine compression (very rare for this to cause actual AKI, but more common with solitary kidney or congenital urologic abnormalities)
- Nephrolithiasis

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Table 3. Causes of acute kidney injury in pregnancy classified by the time of occurrence.

Pre-Renal	Intrinsic Renal	Post-Renal
Early Pregnancy		
Bleeding—miscarriage Hyperemesis gravidarum Ovarian hyperstimulation syndrome Ectopic pregnancy	Anticardiolipin antibody syndrome Sepsis (i.e., septic abortion) Autoimmune disease Glomerulonephritis, interstitial nephritis, lupus nephritis CKD progression	Renal stones Ureteral obstruction
Late Pregnancy		
Bleeding—second-trimester miscarriage, placenta praevia, placental abruption	Severe pre-eclampsia, HELLP Acute fatty liver of pregnancy HUS/TTP Pyelonephritis Chorioamnionitis CKD Progression Glomerulonephritis, interstitial nephritis, lupus nephritis	Polyhydramnios Multifetal gestation Large uterine fibroids Ureteral obstruction Renal stones
Postpartum		
Bleeding—uterine atonia, uterine rupture, obstetrical trauma (vulvo-vaginal and perineal tears and lacerations)	Severe pre-eclampsia, HELLP HUS Puerperal sepsis Glomerulonephritis, interstitial nephritis, lupus nephritis Nephrotoxic drugs (NSAIDS, antibiotics, proton-pump inhibitors, H2 antagonists) CKD Progression	Renal stones

Abbreviations: HELLP, haemolysis, elevated liver enzymes and low platelet count; HUS, haemolytic uremic syndrome; NSAIDs, non-steroidal anti-inflammatory drugs; TTP, thrombotic thrombocytopenic purpura; CKD, chronic kidney disease.

Vinturache A et al "The Changing Landscape of Acute Kidney Injury in Pregnancy from an Obstetrics Perspective" *J Clin Med* 2019; 8:1396.

Acute Kidney Injury – Initial Workup

- Assess the overall clinical scenario/vitals/etc
  - *Signs of hypovolemia?*
  - *Hypertension/pre-eclampsia?*
  - *Risk factors for kidney disease (cardiac disease, diabetes, lupus/autoimmune illness, hypertension)?*
  - *Recent medication exposures?*
  - *Signs of infection? (pyelonephritis, sepsis)*
- Check BMP, LFTs, CBC, urine protein (P:C ratio or 24h urine), U/A with micro, consider FENa, consider renal U/S
- Renal consult if not pre-renal or pregnancy-related
- If renal biopsy is needed, risk of hemorrhage higher than outside of pregnancy, consider delaying until after delivery if >32 weeks

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Acute Kidney Injury in Pregnancy– Outcomes

- AKI in pregnancy 6.3/10000
- AKI requiring dialysis 1/10000
  - *4-13% mortality*
  - *4-9% still required dialysis at 4 months postpartum*
- Evolution over the past 40 years – decline in cases due to septic abortion and peurpural sepsis, increase in cases due to hypertensive disorders, thrombotic microangiopathies

Jim B, Garovic VD, "Acute Kidney Injury in Pregnancy" *Semin Nephrol* 2017; 37(4): 378-385.
Rao S, Jim B. "Acute Kidney Injury in Pregnancy: The Changing Landscape for the 21st Century" *Kidney Int Rep* 2018; 3(2): 247-257.
Vinturache A et al. "The Changing Landscape of Acute Kidney Injury in Pregnancy from an Obstetrics Perspective." *J Clin Med* 2019; 8:1396.

Chronic kidney disease

TABLE 57-2 Stages of Chronic Kidney Disease

Stage	Description	Estimated GFR (mL/min/1.73 m²)
1	Kidney damage with normal or increased GFR	≥90
2	Kidney damage with mildly reduced GFR	60-89
3	Moderately reduced GFR	30-59
4	Severely reduced GFR	15-29
5	End-stage renal failure	<15 or dialysis

GFR, glomerular filtration rate.
From National Kidney Foundation: K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification, Am J Kidney Dis 39(2 Suppl 1):S1–S266, 2002.

Thadhani RI, Manish RM, "Renal Disorders" *Creasy and Resnik's Maternal-Fetal Medicine: Principles and Practice*. 2013. 949.964.e4

Types of CKD – IgA Nephropathy

- Most common type of glomerulonephritis in the developed world
- Renal biopsy shows mesangial IgA deposition
- 50% present with gross hematuria in the setting of upper respiratory infection, most others have occult hematuria or proteinuria picked up on routine U/A
- 15% of cases are familial
- 20-30% progress to end-stage renal disease over 20 years (higher risk with elevated Creatinine, hypertension or >1g proteinuria)
- Treatment: control blood pressure, ACE/ARB to slow progression, select patients may benefit from chronic glucocorticoids to slow progression

Types of CKD – Diabetic Nephropathy

- Initial presentation – microalbunuria (30-300mg protein/day) or nephropathy (>300mg protein/day)
  - *Once nephropathy develops, often a steady progressive decline in renal function*
  - *Baseline proteinuria may significantly worsen during the normal course of pregnancy*
- 20-30% of women with diabetes eventually develop renal disease
- Treatment: blood glucose control, blood pressure control, ACE/ARB

Types of CKD – Diabetic Nep thy

Table 2. Comparative Studies of Outcomes in Class F Diabetes Mellitus

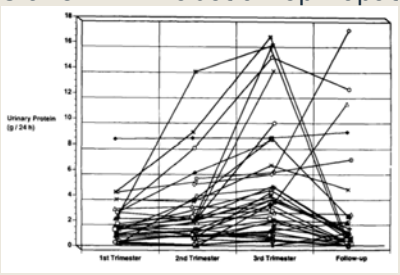
	Kitzmiller[2] (1981)	Grenfell[4] (1986)	Reece[3] (1988)	Present study
N	26	20	31	45
Chronic hypertension	31%	27%	22%	27%
Initial creatinine >1.0 mg/dL	38%	10%	22%	11%
Initial proteinuria >3.0 g/24 h	8.3%	NA	22%	13%
Preeclampsia	15%	55%	35%	53%
Cesarean delivery	NA	72%	70%	80%
Perinatal survival	88.9%	100%	93.5%	100%
Major anomalies	3 (11.1%)	1 (4.3%)	3 (9.7%)	2 (4%)
Fetal growth restriction	20.8%	NA	19.4%	11.0%
Delivery (wk)				
<34	30.8%	27%	22.5%	15.5%
34–36	40.7%	23%	32.3%	35.5%
>36	28.5%	50%	45.2%	49%

NA = not available.

45
27%
11%
13%
53%
80%
100%
2 (4%)
11.0%
15.5%
35.5%
49%

Gordon M et al, "Perinatal Outcome and Long-Term Follow-up Associated with Moder of Diabetic Nephropathy" *Obstet Gynecol* 1996; 87(3):401-409.

Types of CKD – Diabetic Nephropathy



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Types of CKD – Lupus Nephritis

- Is there an increased risk of flare during pregnancy? (maybe)
- Vascular, glomerular and tubulointerstitial renal damage
- Measurable disease activity present in 40-50% of women with lupus during pregnancy
  - *Up to 70% of women have renal involvement during flares*
  - *Risk factors for flare: last flare <6 months before pregnancy, renal involvement, discontinuation of immunosuppressants in early pregnancy*
- Increased risk of pre-eclampsia (30%), preterm birth (26.7%), IUGR (5-20%)
- Lupus flares in pregnancy can present with HTN and worsening proteinuria → common pre-eclampsia mimic
- Treatment: immunosuppression

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Jim [redacted] Garovic VD. "Acute Kidney Injury in Pregnancy" *Semin Nephrol* 2017; 37(4): 378-385.

Table 2. Anti-inflammatory and immunosuppressive drugs in pregnancy

Drug Name	Comments	FDA Class*
Corticosteroids	Risks of use often outweighed by risk of underlying disease. Potential risks for orofacial clefts (3 of 1000 births) and premature birth	C
Hydroxychloroquine	Considered safe in pregnancy at 200–400 mg/d. Discontinuation during pregnancy associated with increased risk of lupus flare. May use for maintenance or mild flares	Not assigned
NSAID	Avoidance after 28 weeks of gestation because of the effects of NSAID-related prostaglandin inhibition on the fetal cardiovascular system (closure of ductus arteriosus)	C
Cyclosporine	Can be maintained in pregnancy at lowest effective dose. No significant increase in rate of congenital malformations	C
Tacrolimus	Can be maintained in pregnancy at lowest effective dose. Potential risks of neonatal hyperkalemia and renal dysfunction	C
Rituximab	Limited safety data. May alter fetal and neonatal B cell development	C
IVIG (γ globulin)	Data are lacking, but may be helpful for lupus nephritis flare refractory to medical therapy	C
Azathioprine	May use for flare during pregnancy. Consider as alternative to mycophenolate. Avoid doses >1.5–2 mg/kg per day due to risk of suppressed neonatal hematopoiesis	D
Mycophenolate mofetil	Contraindicated during pregnancy due to teratogenicity	D
Cyclophosphamide	Useful when maternal disease is life threatening. High risk of fetal loss, but less pronounced in more recent studies	D
Methotrexate	High risk of miscarriage and congenital abnormality. Treatment should be withdrawn 3 months before pregnancy	X

Stanhope TJ et al, "Obstetric Nephrology: Lupus and Lupus Nephritis in Pregnancy" *Clin J Am Soc Nephrol* 2012; 7:2089-99

Types of CKD – Autosomal Dominant Polycystic Kidney Disease

- Most women of childbearing age are stage 1 (asymptomatic with normal BP, no proteinuria, normal Cr)
- Pregnancy outcomes similar to other forms of CKD by stage
- Risk of intracranial aneurysms
  - *Consider MRI in all patients with AD-PKD and family history of aneurysms*
- Autosomal dominant inheritance → fetus has a 50% risk of being affected

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Other types of CKD

- Hypertensive nephrosclerosis
- Reflux nephropathy
- Alport Syndrome
- Minimal change disease
- Focal segmental glomerulosclerosis
- Membranous nephropathy
- IgA vasculitis (Henoch-Schonlein purpura)
- Wegner's granulomatosis
- Polyarteritis nodosa
- Systemic sclerosis

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Nephrotic Syndrome

Edema + hypoalbunemia (<3.0) + massive proteinuria (>3.5g/day) + hyperlipidemia

Possible causes: IgA nephropathy, diabetes, SLE, HIV, hepatitis B or C, focal segmental glomerulosclerosis, minimal change disease, membranous nephropathy

-- minimal increased risk to pregnancy unless HTN or elevated Cr

-- Increased risk of venous thromboembolism (consider anticoagulation if >5g protein per day)

-- Most common cause after 20 weeks == pre-eclampsia

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How does pregnancy impact chronic kidney disease?

- Outcomes depend on clinical stage
- Stage 1-2 CKD: low risk of progression of renal disease due to pregnancy
  - *Especially with well-controlled BP and minimal proteinuria*

Jones DC and Hayslett JP, "Outcome of Pregnancy in Women with Moderate or Severe Renal Insufficiency" *NEJM* 1996; 335:226-232.

How does pregnancy impact chronic kidney disease?

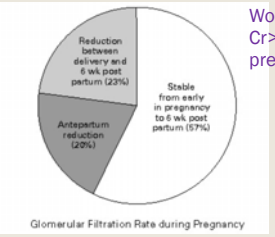
Stage 3-5 CKD

TABLE 2. EFFECT OF PREGNANCY ON RENAL DISEASE.*

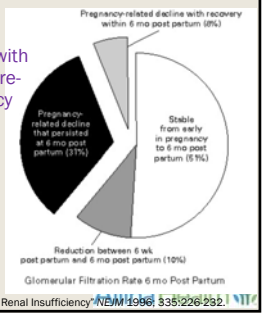
		GESTATIONAL CHANGES
Glomerular filtration rate		
No. of pregnancies	70	
Change in serum creatinine (mg/dl)	+0.5¶	
Remained stable — no. (%)	55 (79)	
Decreased by 25% — no. (%)	14 (20)	
Increased by 25% — no. (%)	1 (1)	
Arterial blood pressure		
No. of pregnancies	74‖	
Change in mean arterial blood pressure (mm Hg)	+6.1**	
Persistent normotension — no. (%)	35 (47)	
Stable hypertension — no. (%)	17 (23)	
New-onset hypertension — no. (%)	19 (26)	
Exacerbation of hypertension — no. (%)	3 (4)	
Proteinuria		
No. of pregnancies	59	
Stable — no. (%)	36 (61)	
Decreased — no. (%)	6 (10)	
Increased — no. (%)	17 (29)††	

Jones DC and Hayslett JP, "Outcome of Pregnancy in Women with Moderate or Severe Renal Insufficiency" *NEJM* 1996; 335:226-232.

How does pregnancy impact chronic kidney disease?



Women with Cr>1.4 pre-pregnancy



Jones DC and Hayslett JP, "Outcome of Pregnancy in Women with Moderate or Severe Renal Insufficiency" *NEJM* 1996; 335:226-232.

Table 2. Renal and Pregnancy Outcomes According to Chronic Kidney Disease Stage

Outcome	Control Group (n=836)	Stage 1 (n=370)	Stage 2 (n=87)	Stage 3 (n=37)	Stage 4–5 (n=10)
Progressed to next stage of CKD	NA	7.6	12.6	16.2	20
New-onset HTN	5.5	7.9	17.6	47.1	50
New-onset or doubling of proteinuria	NA	20.5	37.9	86.5	70
Gestational age at delivery (wk)	39.0±1.7	37.6±2.6	35.7±3.2	34.4±2.4	32.6±4.2
Delivery at less than 37 wk of gestation	6.1	23.5	50.6	78.4	88.9
Delivery at less than 34 wk of gestation	1.0	7.3	20.7	37.8	44.4
Birth weight (g)	3,242±480	2,966±659	2,484±707	2,226±582	1,639±870
SGA less than 10%	10.3	13.3	17.9	18.9	50
NICU	1.8	10.3	27.6	44.4	70

CKD, chronic kidney disease; NA, not applicable; HTN, hypertension; SGA, small for gestational age; NICU, neonatal intensive care unit. Data are % or mean±SD.

Piccoli GB et al, "Risk of Adverse Pregnancy Outcomes in Pregnancies with CKD" *J Am Soc Nephrol* (2015) 26:2011-22.

How does chronic kidney disease impact pregnancy?

- Stage 1-2 CKD
  - *13%-24% IUGR*
  - *20%-50% preterm delivery (largely iatrogenic due to IUGR and pre-E)*
- Stage 3-5 CKD
  - *50%-59% preterm delivery with baseline serum creatinine 1.4-2.5*
  - *78%-86% preterm delivery with baseline serum creatinine >2.5*
  - *18%-66% IUGR*
- Pre-eclampsia rate uncertain due to pre-existing HTN and proteinuria complicating diagnosis (certainly higher than baseline)
- Poor prognostic factors: creatinine>1.4, proteinuria >1g/24h, needing >1 antihypertensive medication

Piccoli GB et al, "Risk of Adverse Pregnancy Outcomes in Pregnancies with CKD" *J Am Soc Nephrol* (2015) 26:2011-22.
Jones DC and Hayslett JP, "Outcome of Pregnancy in Women with Moderate or Severe Renal Insufficiency" *NEJM* 1996; 335:226-232.

Management of pregnancy with CKD

- Baseline assessment (patients with known or suspected CKD): serum BUN/creatinine, electrolytes, 24 urine for protein and creatinine clearance
  - *Referral to nephrology (if not already established) for Cr>1.4 or proteinuria>300mg/24h*
  - *Consider referral for Cr>0.9 and risk factors for CKD*
- Labs: urine P:C ratio, serum BMP, Hgb, urine culture at least every trimester
- Continue immunosuppressants in many cases
- Serial growth US
- Antenatal testing starting at 32 weeks (sooner if poorly controlled HTN)
- Close monitoring of BP (home BP cuff) and pre-E symptoms
- Delivery 37-39 weeks (depending on fetal growth and BP control)
- Consider aspirin 81-150mg to decrease pre-eclampsia risk

Management of pregnancy with CKD – Antihypertensive goals

- ACOG guidelines – start antihypertensives when BP>160/110s
  - *Based on lack of improved pregnancy outcomes with tight control*
- CHIPS study – RCT of 987 women assigned to tight (<140/90) or traditional BP control
  - *No significant differences in pregnancy outcomes between the groups*
  - *No increase in adverse fetal outcomes with tight control*
- Cochrane review – 63 trials of antihypertensives for mild-moderate HTN
  - *Decreased risk of severe hypertension with tight control, no change in pre-eclampsia, IUGR, preterm delivery*

Chronic Hypertension in Pregnancy. ACOG practice bulletin No.203. American College of Obstetricians and Gynecologist. *Obstet Gynecol* 2019;133:e26-50.
Magee et al. "Tight Versus Less-Tight Control of Hypertension in Pregnancy," *NEJM* 2015; 372:407-417.
Abalos et al. "Antihypertensive Drug Therapy for Mild to Moderate Hypertension in Pregnancy." Cochrane Database of Systematic Reviews 2018

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Management of pregnancy with CKD – Antihypertensive goals

- ACOG guidelines – start antihypertensives when BP>160/110s
  - *Based on lack of improved pregnancy outcomes with tight control*

Given significant improvement in renal function with tight BP control, and lack of fetal harm shown in RCTs, recommend BP goal of <140/90 for any chronic kidney disease patients.

Chronic Hypertension in Pregnancy. ACOG practice bulletin No.203. American College of Obstetricians and Gynecologist. *Obstet Gynecol* 2019;133:e26-50.
Magee et al. "Tight Versus Less-Tight Control of Hypertension in Pregnancy," *NEJM* 2015; 372:407-417.
Abalos et al. "Antihypertensive Drug Therapy for Mild to Moderate Hypertension in Pregnancy." Cochrane Database of Systematic Reviews 2018

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Management of pregnancy with CKD – Postpartum considerations

- Avoid NSAIDs
- Restart ACE/ARB therapy
  - *If not breastfeeding, start pre-pregnancy agent*
  - *If breastfeeding, start Enalapril or Captopril*
    - Both agents have low transfer into breastmilk, considered safe for term infants
    - Discuss with NICU if the infant is premature (usually still considered safe)

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IBM Micromedex®

captopril

Home | Drug Interactions | IV Compatibility | Drug ID | Drug Comparison | CareNotes | NeoFax / Pediatrics | Other Tools ▾

captopril and enalapril [507].

B) Breastfeeding

1) American Academy of Pediatrics Rating: Maternal medication usually compatible with breastfeeding.

2) World Health Organization Rating: Compatible with breastfeeding.

3) Micromedex Lactation Rating: Infant risk is minimal.

a) The weight of an adequate body of evidence and/or expert consensus suggests this drug poses minimal risk to the infant when used during breastfeeding.

4) Clinical Management

a) Captopril has been detected in human breast milk at concentrations of approximately 1% of maternal blood levels. Due to a potential for serious adverse reactions in the nursing infant, consider discontinuation of either breastfeeding or captopril, taking into account the importance of the drug to the mother [503][510][511].

5) Literature Reports

a) Captopril is excreted in human milk. Concentrations of captopril in human breast milk are approximately 1% of maternal blood levels [503][510][511]. In 12 lactating women who were treated with 7 doses of captopril 100 mg three times per day, average maximum milk concentrations of 4.7 nanogram/mL occurred 4 hours after the last dose [510].

6) Drug Levels in Breastmilk

a) Parent Drug

1) Concentration in Breastmilk at Therapeutic Dose

a) 1% of maternal plasma concentration [533]

2) Milk to Maternal Plasma Ratio

a) 0.012 [510][534]

IBM Micromedex®

enalapril

Home | Drug Interactions | IV Compatibility | Drug ID | Drug Comparison | CareNotes | NeoFax / Pediatrics | Other Tools ▾

B) Breastfeeding

1) American Academy of Pediatrics Rating: Maternal medication usually compatible with breastfeeding.

2) Micromedex Lactation Rating: Infant risk is minimal.

a) The weight of an adequate body of evidence and/or expert consensus suggests this drug poses minimal risk to the infant when used during breastfeeding.

3) Clinical Management

a) Enalapril is considered compatible with breastfeeding by the American Academy of Pediatrics [542]. Advise the nursing mother to either discontinue nursing or discontinue enalapril therapy, considering the mother's clinical need and the benefits of breastfeeding to the infant [144].

4) Literature Reports

a) Enalapril and enalaprilat have been detected in human breast milk [144]. The milk serum ratio of enalapril and enalaprilat (the active metabolite) in 5 lactating mothers was minimal. The maximum milk concentrations of enalapril and enalaprilat were 5.9 nanograms (ng)/mL and 2.3 ng/mL, respectively. Assuming infant ingestion of 150 mL milk/kg/day (the population average), absolute infant exposure would be 885 ng/kg/day for enalapril and 345 ng/kg/day for enalaprilat, or only 0.27% of the weight-adjusted maternal dose of enalapril. Data are from a single dose study; milk concentrations may be higher at steady state [543]. Infant levels are further reduced due to poor oral bioavailability.

5) Drug Levels in Breastmilk

a) Enalapril Maleate

1) Parent Drug

a) Milk to Maternal Plasma Ratio

1) 0-0.14 [543]

2) Active Metabolites

a) Enalaprilat [571]

1) Milk to Maternal Plasma Ratio

a) 0.021-0.031 [543]

Management of pregnancy with CKD – Other considerations

- Renally dose meds if elevated Creatinine
  - *Lovenox*
  - *Magnesium*
- Watch for magnesium toxicity with pre-eclampsia
  - *Consider serial bolus doses instead of a continuous rate*
  - *4g bolus, check magnesium level at 4-6 hours, re-bolus or start continuous rate if significantly subtherapeutic*
- Watch closely for anemia, send iron studies if low Hgb to determine if iron responsive
  - *May require erythropoietin*

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Dialysis in pregnancy

- Decreased fertility on dialysis, **but women on dialysis can and do get pregnant**
  - *Fertility rate of 10-15%*
- Livebirth rate increases with more intensive dialysis regimens
  - *Ideally 36 hours per week (minimum of 20 hours/week)*
- Careful monitoring of electrolytes, fluid balance, post-dialysis BP (goal 140/90)
- Increase protein intake to 1.5-1.8g/kg, double prenatal vitamins due to dialysate losses
- Watch for fluid shifts during dialysis → preterm contractions, nonreassuring fetal testing
- Increase erythropoietin doses
- Delivery at 34-37 weeks (most deliver sooner)

Allina Health

Dialysis in pregnancy

TABLE 57-3 Estimates for Pregnancy Complications and Outcomes in Dialysis Patients

Pregnancy Complication	Estimate*
Polyhydramnios	33%-62%
Maternal hypertension	42%-80%
Cesarean section deliveries	46%-53%
Preterm delivery	85%
Average gestational age at delivery	32 weeks
INFANT SURVIVAL OUTCOME	
Conceived on dialysis	40%-50%
Conceived before dialysis	75%-80%

Thadhani RI, Manish RM, "Renal Disorders" *Creasy and Resnik's Maternal-Fetal Medicine: Principles and Practice*. 2013. 949.964.e4

Allina Health

Dialysis in pregnancy

Women who are candidates for renal transplant should be encouraged to delay conception until AFTER transplant

Allina Health

Pregnancy after renal transplant

- Overall 90% live birth rate
- Best outcomes if:
  - *No rejection episodes for >1 year post-transplant*
  - *Minimal proteinuria*
  - *Well controlled hypertension*
  - *Creatinine <1.5 (ideally <1.1)*
  - *Stable immunosuppressive regimen with drugs safe in pregnancy*

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Pregnancy after renal transplant

- No decrease in graft function due to pregnancy
  - *Possible worsening of graft function when baseline Cr>1.5*
- Pregnancy outcomes:
  - *Increased risks of HTN (54%), pre-eclampsia (27%), gestational diabetes (8%), IUGR (25%), preterm delivery (30%)*
- Need close monitoring of immunosuppressant levels
- Watch for reactivation of CMV/toxo

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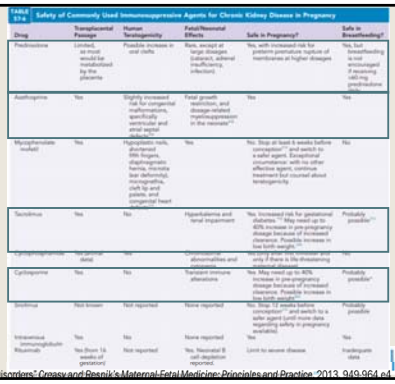

Thadhani RI, Manish RM, "Renal Disorders" *Creasy and Resnik's Maternal-Fetal Medicine: Principles and Practice*. 2013. 949.964.e4

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THANK YOU