

# **PREGNANCY WITH RENAL DISEASES**

**or**

# **RENAL DISEASES WITH PREGNANCY**

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# **There are two questions that need to be addressed when a woman with underlying kidney disease (KD) becomes pregnant**

- What is the effect of pregnancy on the KD
- What is the effect of the KD on pregnancy

# The effect of pregnancy on renal disease

- Proteinuria increases
- Hypertension develops or worsens;
- Severe hypertension can occur, leading
  - Maternal injury,
  - Premature delivery,
  - Poor fetal outcome.
- Marked worsening of edema also can be seen in NS.
- **These changes generally resolve after delivery.**

# Effect of renal function

- Renal function may decline as a result of pregnancy among patients with renal disease, (by the severity of underlying renal disease)
- Renal functions decline in between 0-10% of women when the GFR is initially normal or only mildly reduced

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# Evaluated 360 women with chronic glomerulonephritis and normal renal function:

- 171 became pregnant, while the remainder did not conceive.
- After follow-up for as long as 30 years, there was no difference in renal survival between the two groups.
- Patients with **hypertension** were much more likely to develop progressive disease independent of pregnancy status.

# The physiological Changes on Renal and urinary tract in normal pregnancy

- Normal pregnancy is characterized by profound changes in almost every organ system.
- Ureteral tone, peristalsis, and contraction pressure reduce.
- Ureters becomes elongated, and displaced laterally
- Ureters compression causes pain and urinary obstruction,
- Bladder mucosa becomes edematous and hyperemic
- Intermittent vesicoureteral reflux risk occurs.

# Urinary tract changes

- Both kidneys increase in size by 1 to 1.5 cm.
- The renal pelvises and caliceal systems dilate,
- Hydroureter,hydronephrosis occurs (>80%).
- The resulting urinary stasis can serve as a reservoir for bacteria, which may contribute to pyelonephritis

# Urinary Symptoms

- Urinary frequency (voiding >7 times per day) , %80-95%
- Nocturia (voiding  $\geq 2$  times at night) , %80-95%
- Dysuri ,
- Urgency
- Stress incontinence are common during pregnancy.

[van Brummen HJ et al, Neurourol Urodyn 2006; 25:135.](#)

[Nel JT et al. J Pelvic Floor Dysfunct 2001; 12:21.](#)



## Postpartum changes:

- Mucoal congestion,
  - Submucosal hemorrhage,
  - Detrusr atony,
  - Increased postvoid residual urine,
  - Bladder overdistention,
  - Urinary retention are frequently encountered in women in the first few days after delivery.
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- **These symptoms are typically mild, transient, and completely reversible.**

## Hemodynamic and renal changes during normal pregnancy

Systemic hemodynamics	
Increase in cardiac output	
Fall in vascular resistance and blood pressure	
Blood volume expansion	80%
Renal function and electrolyte balance	
Increase in glomerular filtration rate	50%
Chronic respiratory alkalosis	
Hyponatremia due to resetting of osmostat	
Increased ADH metabolism and polyuria in selected women	

- The physiologic increase in GFR during pregnancy results in a decrease in serum creatinine concentration, **Thus, a serum creatinine of 1.0 reflects renal impairment in a pregnant woman**

## Normal reference range of renal function tests in pregnant women

Test	Normal (reference) range		
	First trimester	Second trimester	Third trimester
Sodium (mEq/L)	133 to 148	129 to 148	130 to 148
Potassium (mEq/L)	3.6 to 5.0	3.3 to 5.0	3.3 to 5.1
Chloride (mEq/L)	101 to 105	97 to 109	97 to 109
BUN (mg/dL)	7 to 12	3 to 13	3 to 11
Creatinine (mg/dL)	0.4 to 0.7	0.4 to 0.8	0.4 to 0.9
Calcium (mg/dL)	8.8 to 10.6	8.2 to 9.0	8.2 to 9.7
Magnesium (mg/dL)	1.6 to 2.2	1.5 to 2.2	1.5 to 2.2
Phosphate (mg/dL)	3.1 to 4.6	2.5 to 4.6	2.8 to 4.6
Uric acid (mg/dL)	2.0 to 4.2	2.4 to 4.9	3.1 to 6.3
Albumin (g/dL)	3.1 to 5.1	2.6 to 4.5	2.3 to 4.2
24 hour protein excretion (mg)	19 to 141	47 to 186	46 to 185

Data from: Abbassi-Ghanavati M, Greer LG. Reference Table of Normal Laboratory Values in Uncomplicated Pregnancies. In: Cunningham FG, Leveno KJ, Bloom S, Hauth JC, Rouse DJ, Spong CY. *Williams Obstetrics*, 23rd Edition. New York: McGraw-Hill, 2010.

## Other changes

Mild hyponatremia,

Increased protein excretion,

Chronic respiratory alkalosis,

Hypourcemia,

Decreased in serum union gap,

**Impaired tubular function:**

Thus, pregnant patients may exhibit glucosuria and aminoaciduria in the absence of hyperglycemia or renal Disease

# Kidney biopsy during pregnancy

## Indications:

- Sudden unexplained deterioration in renal function,
- Markedly symptomatic nephrotic syndrome occurring before 32 weeks gestation.

## The procedure:

- Can be performed safely by experienced operators in women with **well-controlled blood** pressure and normal coagulation indices.
- Biopsy after week 32 is not recommended.

# Effect of kidney on pregnancy

## The pregnancy in mild to moderate CRD:

- The rate of live births is above 90 percent in women with normal renal function and
- Lower with modest chronic kidney disease (CRD),
- **If the blood pressure is well controlled**
- **Hypertension** is the major risk factors for permanent exacerbation of underlying RD.

# Major risks of kidney disease in pregnancy:

The results of a meta-analysis of 13 cohort studies:

- Pregnant women with preexisting renal impairment were significantly more likely to develop:
- **Gestational hypertension,**
- **Preeclampsia,**
- **Eclampsia,**
- **Die (12 versus 2 percent).**

# Pregnancy with CKD

- Preeclampsia may be more difficult to diagnose,
- Features of the preeclamptic syndrome of
- Hypertension,
- Proteinuria,
- Decreased platelet count or
- Increased liver enzymes may include significant worsening.
- Women with underlying renal disease are at greater risk for **second-trimester preeclampsia**.
- Maternal mortality is more frequent in those with CKD (4 versus 1 percent),

# Fetal survival is lower when hypertension is uncontrolled

- The relative risk of fetal death has been estimated to be approximately 10-fold higher in women with a mean arterial pressure  $>105$  mmHg at conception, compared with those with spontaneous or therapeutically achieved normotension



# Drug therapy

- Angiotensin-converting enzyme inhibitors,
- Angiotensin II receptor blockers, and some
- Immunosuppressive drugs (particularly cyclophosphamide) should be discontinued at the earliest indication of pregnancy.
- In addition, women who are not pregnant, but are of childbearing age, should be warned about the potential consequences of these agents

# Pregnancy with dialysis

- The diagnosis of pregnancy may be difficult in women with end-stage renal disease (ESRD),
- Because serum levels of beta-human chorionic gonadotropin (beta-hCG) may be increased in the absence of pregnancy.
- Perform USG to women suspected of being pregnant who have elevated serum beta-hCG,

# Conception in dialysis patients

- The reported frequency of conception among women of childbearing age on dialysis ranges from 0.3 to 1.5 percent per year.
- Although fetal wastage is markedly increased when pregnancy occurs, improvements in management have resulted in an enhanced frequency of live births (40 to 75 percent of all pregnancies)

# In one survey of 1281 women of childbearing age undergoing maintenance dialysis

- 1.5% became pregnant in a two-year period;
- 52% of these pregnancies resulted in surviving infants,
- In dialysis clinics (6230 women) noted successful outcomes 40 percent of pregnancies,.

The outcomes were similar in patients treated with hemodialysis and peritoneal dialysis

# During dialysis

- More intensive dialysis with the blood urea nitrogen (BUN <50) should be planned.
- In clinical practice, this is usually achieved by increasing the frequency of dialysis (eg, increase to four to six sessions per week) or switching to long nightly dialysis.
- **Ameliorating the uremic milieu can avoid**
- Polyhydramnios,
- Help control hypertension,
- Increase birth weight and gestational age,
- Improve maternal nutrition.

# During dialysis

- Give higher doses of erythropoietin to maintain an adequate red cell mass.
- Correct the metabolic acidosis and hypocalcemia
- Perform careful uterine and fetal monitoring to:
  - Assess the fetal heart rate
  - Prevent dialysis-induced hypotension.
- Be alert for maternal hemodynamic instability??
- May compromise the uteroplacental circulation

# Attention to nutritional considerations and proper weight gain are essential for a successful pregnancy.

- The recommended weight gain in the second and third trimesters is between **0.3 to 0.5 kg/week**,
- But it is difficult to distinguish excess fluid gained between dialysis sessions from that due to pregnancy-associated weight gain.
- The clinician should perform a careful weekly physical examination to help and detect the presence of excess fluid unrelated to the pregnancy.

## Despite optimal therapy, mothers are at increased risk for severe hypertension, and prematurity

- **Preeclampsia** is the greatest risk factor for prematurity and other adverse outcomes.
- The mean gestational age at delivery was only 30.5 weeks (of 120 pregnant dialysis patients)\*

### **Preeclampsia is associated with\*\***

- A lower successful delivery rate (60 versus 92.9%),
- Extremely premature delivery rate (77.8 versus 3.3%),
- Lower gestational age and birth weight, compared with those without preeclampsia.

\*[Giatras I et al. Pregnancy during dialysis: case report and management guidelines. Nephrol Dial Transplant 1998; 13:3266.](#)

\*\*[Luders C et al. Obstetric outcome in pregnant women on long-term dialysis: a case series. Am J Kidney Dis 2010; 56:77.](#)



# Delay pregnancy

- It may be advantageous to delay pregnancy among hemodialysis patients until renal transplantation
- Transplant recipients have a higher incidence of successful pregnancies and fewer complications and birth abnormalities

# Pregnancy in the renal transplant recipient

- Fertility generally returns after renal transplantation.
- The rates of both pregnancy and successful pregnancy (resulting in a live birth) remain far lower than in the general population.

## **During the first three posttransplant years:**

- The unadjusted pregnancy rate was 33 per 1000 women,
- But, this rate is  $>100$  per 1000 women in the general population.

## **In transplant recipients:**

- 55% of pregnancies resulted in a live birth, while it is
- Nearly 70% in the general population.

**In addition to an increased risk of fetal loss, the frequency of preeclampsia, intrauterine growth restriction, and premature delivery are elevated in transplant recipients.**

A meta-analysis included 4706 pregnancies, 3570 kidney transplant recipients

	<b>Kidney transplant recipients</b>	<b>Normal pupulation</b>
<b>Preeclampsia</b>	27	4
<b>Gestational diabetes</b>	8	4
<b>Preterm delivery</b>	46	3

# The long-term effect of pregnancy on renal function is less clear.

- The data largely based on retrospective small studies suggest that:
- Pregnancy does not have long-term adverse effects on survival of either the allograft or patient.

# Women are usually advised to wait at least

- One year after living related-donor transplantation and
- Two years after deceased transplantation to avoid complications arising from immunotherapy and rejection.
- The renal allograft should be functioning well, with a stable serum creatinine level  $<1.5$  and urinary protein excretion  $<500$ .
- Although not recommended, women who become pregnant in the first 6 to 12 months posttransplantation are also likely to have a successful pregnancy.

# Delivery

- If the pelvic allograft does not obstruct the birth canal Vaginal delivery is recommended.

## **To avoid complications :**

- Prophylactic antibiotics and
- Careful wound closure are warranted.

# Cyclosporine

- The safety of cyclosporine is not established
- Hypertension can be induced or exacerbated,
- The dose should be limited to 2 to 4 per day.
- Patients taking cyclosporine or tacrolimus require more frequent monitoring of renal function and drug levels during pregnancy

- **Mycophenolate** mofetil (MMF)
- Is listed as a category-D. It should be discontinued at least six weeks prior to attempted conception
- The complications are:
  - Spontaneous abortions,
  - Hypoplastic nails and shortened fifth finger,
  - Microtia with cleft lip and palate,
  - Microtia alone, and
  - Neonatal death with multiple malformations.
- It is recommended that kidney transplant recipients who wish to conceive should change from MMF to **azathioprine**,
- **Sirolimus** is **contraindicated**
- Effect of **tacrolimus** on pregnancy????



# Evaluation of renal dysfunction

- The differential diagnosis of renal dysfunction and the evaluation of the pregnant allograft recipient are similar to that in the nonpregnant transplant patient.

## Acute renal injury in pregnancy

ARF in pregnancy can be induced by any of the disorders leading to renal failure in the general population,

# A number of pregnancy complications may result in ARF

- **Early in pregnancy, the most common problems are:**
  - Prerenal disease due to hyperemesis gravidarum or
  - ATN, resulting from a septic abortion.
- **Later in pregnancy, ARF may result from**
  - Preeclampsia,
  - Thrombotic microangiopathies,
  - Acute fatty liver of pregnancy (AFLP),
  - Renal cortical necrosis,
  - Pyelonephritis,
  - Urinary tract obstruction, or
  - Nephrolithiasis

# TTP, HUS or severe preeclampsia with the HELLP syndrome

- May cause ARF with thrombocytopenia, anemia
- The treatment of TTP-HUS is the same as that in the nonpregnant patient.
- The treatment of preeclampsia with HELLP syndrome includes **delivery**.
- Delivery is important to prevent fetal complications from placental microthrombi

# Acute fatty liver is a rare complication of pregnancy

- ARF,
- Hypoglycemia ,
- Hypofibrinogenemia,
- Liver function test abnormalities, and a
- Partial thromboplastin time (PTT).

## **Therapy consists:**

- Treatment of DIC and
- Immediate delivery of the fetus

## **Acute pyelonephritis**

May cause ARF, even in the absence of septicemia or hypotension.

# Bilateral renal cortical necrosis can be a sequela of

- Sever hypotension
  - DIC,
  - Abruptio placentae,
  - Symptomatic placenta previa,
  - Prolonged intrauterine fetal death,
  - Amniotic fluid embolism.
- 
- Affected patients develop oliguria or anuria, gross hematuria, flank pain, and hypotension.
  - No specific therapy is effective in this disorder, and many patients require **dialysis**.

# **Occasionally, obstruction is sufficient to cause renal failure in pregnant.**

- Obstruction may be induced by a kidney stone
- Affected women usually present with acute flank pain and hematuria, rather than renal failure.
- In some cases,
  - Ureteral catheter or
  - Delivery of the fetus is required

# Obstetrical management of women with underlying renal disease

- Increase frequency of prenatal visits (every two weeks until the third trimester and then weekly).
- Early detection and treatment of asymptomatic bacteriuria.
- Serial monitoring (at least monthly) of maternal renal function.
- Close monitoring for the development of preeclampsia.
- Aggressive treatment of maternal hypertension.

- Fetal surveillance with USG and fetal heart rate monitoring to assess fetal growth and well-being.
- Preterm intervention in the presence of:
  - Deteriorating renal function,
  - Severe preeclampsia,
  - Fetal growth restriction,
  - Nonreassuring fetal testing (fetal distress).
- **Elective delivery** is indicated if labor has not occurred by the estimated date of confinement
- Consultaion of nephrologist and an obstetrician



# **Renal impairment is associated with both increased risk for adverse**

## **Adverse Maternal outcomes, including**

- Gestational hypertension,
- Preeclampsia,
- Eclampsia, and
- Death,

## **Adverse fetal outcomes, including**

- Premature birth,
- Intrauterine growth restriction,
- Small gestational age,

# Successful



# is a result of helaty



**Many thanks**