Pregnancy is associated with many physiological changes in the renal system. Pregnancy can alter the course of some renal diseases as also pre-existing renal diseases may affect pregnancy outcomes. Pregnancy may be complicated by hypertension which warrants proper management. Acute kidney injury may complicate pregnancy. With chronic kidney diseases on the rise, it is important for the physician to be aware of management of pregnancy in these patients. Kidney transplant recipients have their unique set of problems and management of these patients poses a challenge for the physician. Hence this review highlights the management of pregnant patients with renal diseases including issues related to dialysis and transplantation.

**PHYSIOLOGICAL CHANGES IN RENAL FUNCTION IN PREGNANCY**

The kidney undergoes monumental physiologic and anatomic changes during a normal pregnancy. Renal plasma flow increases by 50-70%. Plasma volume increases by 50% and there is hemodilutional anemia. Cardiac output increases by 40%. Glomerular Filtration Rate (GFR) can reach levels up to 150% of normal. The intraglomerular pressure remains normal. Serum creatinine falls by an average of 0.4 mg/dl to a pregnancy range of 0.4 to 0.8 mg/dl. Hence, a serum creatinine of 1.0 mg/dl, although normal in a non pregnant individual, reflects renal impairment in a pregnant woman. S creatinine rises near term and value of 1 mg% is considered normal. There a blood pressure fall of approximately 10 mm Hg in the first 24 weeks. The blood pressure gradually returns to prepregnancy level by term. Glycosuria and aminoaciduria occur. Increased uric acid clearance results in low uric acid level (2.5-5.5 mg%) but increase later and reach pre-pregnancy values at term. A value of >6 mg% reflects PIH. Potassium and 900 meq of sodium are retained. Calcium excretion increases but stone formation is not increased as there is increased excretion of inhibitors of stone formation. A reset in the osmostat occurs, resulting in increased thirst and decreased serum sodium levels (by 5 mEq/L) and low plasma osmolality (10 mOsm/kg less ). Clearance of ADH is increased by placental vasopressinase (transient Diabetes insipidus of pregnancy) which may respond to DDAVP. On the other hand there are reports of transient SIADH in pregnancy. Urine concentration and dilution are adequate. There is mild respiratory alkalosis. 1

**ANATOMIC CHANGES**

A dilatation of ureters and pelvis occurs till pelvic brim (iliac sign) with dilatation more pronounced on right secondary to dextrorotation of uterus and dilatation of right ovarian venous plexus. This leads to urinary stasis and an risk of urinary tract infections (UTIs). There is an increase in kidney size by 1-1.5 cm. All the physiologic changes maximize by the end of the second trimester and then start to return to the prepartum level, whereas changes in the anatomy take up to 3 months postpartum to subside. 2,3

**HORMONES**

There is increase in aldosterone, desoxycorticosterone, progesterone, relaxin, oxytocin, and vasodilating prostaglandins and a decrease in vasopressin (due to vasopressinase) and also resistance to action of aldosterone and renin. 4

**RENAL FUNCTION TESTS**

- Microscopic hematuria may be seen in 20%, disappears after delivery.
- GFR –
  - MDRD formula-The Modification of Diet in Renal Disease (MDRD) formula underestimates GFR by 40 ml/min while Cockroft-Gault formula overestimates GFR by 40 ml/min. Creatinine clearance by 24-h urine collection is the gold standard in pregnancy.
- Estimating of Proteinuria during Pregnancy

Urine protein excretion increases and up to 300 mg/d is normal. Albumin excretion is also increased. These values return to normal by 6th month post partum. Twenty-four hour urine collection, although the gold standard for proteinuria quantification is cumbersome, and inaccurate. The use of the P:C ratio to estimate 24-h protein excretion is controversial in pregnancy. Most misclassifications occur in women with borderline proteinuria (250 to 400 mg/d). Hence, it is reasonable to use urine P:C ratio for diagnosis, with 24-h collection undertaken when result is equivocal.
Pregnancy and Renal Disease

- Renal biopsy in pregnancy - Indications include severe symptomatic nephrotic syndrome, rapidly progressive renal failure. Biopsy can be done in 2nd trimester with patient in lateral position.

RENA L DISEASES OCCURRING IN PREGNANCY

Certain renal diseases are common in pregnancy.1,6

Urinary tract infections (UTI)

UTIs are the most common renal disease occurring during pregnancy and range from asymptomatic bacteriuria to pyelonephritis. UTIs have been associated with small for gestational age (SGA) babies, premature labor, intrauterine fetal death (IUD), anemia and hypertension in mother. Pregnant females are at risk for development of UTIs (2-10%), because of anatomic and physiologic changes that occur in normal pregnancy.

- Asymptomatic bacteriuria- A clean-voided specimen containing more than 100,000 organisms per milliliter suggests infection. 30% of patients develop pyelonephritis if asymptomatic bacteriuria is left untreated. Universal screening is therefore recommended in all pregnant females. Dipstick has a sensitivity of <50% and routine microscopy and culture are needed. Treatment with a 10-day course of oral antibiotics (nitrofurantoin, ampicillin, amoxicillin, sulfonamides, cephalexin or co-amoxiclav) reduces incidence of pyelonephritis to 3%. Urinalysis with culture should be performed on a monthly basis after resolution. Recurrence occurs in 35%. If bacteriuria is persistent, suppressive therapy (Nitrofurantoin 100 mg at night, cephalexin or amoxicillin) is indicated.

- Cystitis-(3%) is associated with dysuria, urgency and frequency, without systemic signs. Occurs in 2nd trimester. Common even in patients with negative urine cultures. Cystitis recurs in 17% and does not progress to acute pyelonephritis. It should be aggressively treated with oral antibiotic regimens. The symptoms of cystitis and pyuria accompanied by a “sterile” urine culture finding may be due to Chlamydia trachomatis urethritis. Mucopurulent cervicitis coexists, and erythromycin therapy is effective.

- Pyelonephritis-(3%)- 70% patients with PN have asymptomatic bacteriuria. 50% occur in 2 nd trimester. Onset is abrupt with fever, chills, flank pain, anorexia, nausea, vomiting and costovertebral tenderness. The etiologic organisms include Escherichia coli, Klebsiella, Enterobacter, and Proteus. 10% are due to Gram+ organisms. 15% patients have concurrent bacteremia. Other complications include hemolysis, sepsis, adult respiratory distress syndrome, hepatic dysfunction and death. Pyelonephritis requires hospitalization and intravenous antibiotics and fluids till fever resolves. Effective regimens include ampicillin plus gentamicin or a third-generation cephalosporin followed by oral administration of antibiotics (14 days). This leads to complete resolution of infection in 70%. In infections recurring in 2 weeks, 2-3 wks of treatment and suppressive therapy throughout the pregnancy should be given. Post coital cephalexin 250mg or NFT 50 mg may be preventive. Perinephric or cortical abscesses may be seen.

HYPERTENSION

Terminology of hypertensive disorders varies according to source, but the system recommended by the National High Blood Pressure Education Program describes the following 5 entities (NHBPEP, 2000):

- Gestational hypertension/ Transient hypertension- is defined as blood pressure of 140/90 mm Hg or greater with no hypertension before pregnancy. Preeclampsia does not develop, with blood pressure returning to normal levels within 12 weeks postpartum. Patients are usually asymptomatic or have symptoms or signs like preeclampsia. It usually affects nulliparous females mostly in third trimester. It is a retrospective diagnosis and is confused with preeclampsia at the time of onset and with essential hypertension postpartum until the blood pressure returns to normal. Proteinuria does not occur; serum uric acid is normal. It may predict the development of hypertension later in life. It is prudent to manage it as preeclampsia when first diagnosed.

- Chronic hypertension- is associated with underlying or preexisting hypertension. The diagnosis is established by a blood pressure of 140/90 mm Hg or greater before pregnancy or before 20 weeks’ gestation, or by persistent hypertension long after delivery. This diagnosis can be difficult to make, especially if no prior blood pressure readings are available or if the patient is not seen until late in pregnancy. Complications of chronic hypertension include superimposed preeclampsia, abruptio placenta, growth restriction and fetal death.

- Preeclampsia- is associated with intrauterine growth retardation and SGA babies. Occurs in 7% of all pregnancies mostly in primigravidas. It is a triad of hypertension, proteinuria and oedema occurring after the 20th week of gestation with few cases developing postpartum within hours. Hypertension is defined as rise in systolic BP >30 mmHg and diastolic BP >15 mmHg. Proteinuria is defined as >300mg protein in urine per day. The risk factors associated with the development of preeclampsia include age older than 35 years or younger than 16 years, multiple pregnancies, chronic hypertension, obesity and African American race. HELLP syndrome (Hemolysis, ELevated liver enzymes, and Low Platelets) is observed when severe preeclampsia or eclampsia is accompanied by significant liver involvement. Acute renal failure (ARF) may develop.8

- Eclampsia-is the occurrence of seizure activity with no other explainable cause in setting of preeclampsia.

- Preeclampsia superimposed on chronic hypertension- defined as new-onset proteinuria (i.e., >300 mg/d) after 20
weeks’ gestation in a hypertensive patient or as a sudden increase in proteinuria or blood pressure in a patient with hypertension and proteinuria before 20 weeks’ gestation.

PATHOPHYSIOLOGY

Utero-placental ischemia: A combination of genetic and environmental factors results in inadequate invasion of uterine spiral arteries by placental trophoblasts resulting in inability of uterine vessels to transform from low-caliber resistive channels to a high-caliber capacitance system. This results in utero-placental ischemia. In normal pregnancy vascular endothelial growth factor (VEGF) and Placental induced growth factor (PIGF) are made by placenta and circulate in high concentrations in pregnancy. VEGF and PIGF induce synthesis of nitric oxide and vasodilating prostacyclin in endothelial cells decreasing vascular tone and blood pressure. In PIH the utero-placental ischemia results in oxidative stress and release of a soluble cytokine, the sFlt-1 (soluble fms-like tyrosine kinase-1). sFlt-1 is a potent antagonist of VEGF and PIGF. In PET concentrations of sFlt-1 rise in the 2nd trimester with a decrease in VEGF and PIGF. Overproduction of sFlt-1 explains increased susceptibility to PET in multiple gestation, hydantidiform mole, trisomy 13 and first pregnancy. In addition, increased concentration of circulating pre-eclamptic factors—antihypertensin I, Bradykinin B2 receptor heterodimers, agonistic antibodies to angiotensin I receptor and soluble endoglin are seen in PET. 

Screening tests- Laboratory data reveals proteinuria, high uric acid, thrombocytopenia. Schistocytes and anemia may be present in more severe disease, thus indicating microangiopathic hemolytic anemia. Recently, urinary PIGF values and sFlt-1 values have shown great promise as a means of identifying preclinical preeclampsia. 

Management of hypertension- Patient should be advised bed rest. Weight loss and salt restriction are not recommended. ACE inhibitors are contraindicated. Teratogenic effects of angiotensin-converting enzyme inhibitors (ACEis/ARBs) include fetal hytponension, anuria-oligohydramnios, growth restriction, pulmonary hypoplasia, renal tubular dysplasia, neonatal renal failure, limb contractures, hypocalvaria. congenital abnormalities of cardiovascular, central nervous system. Diuretics lead to intravascular volume depletion, organ and placental hypoperfusion. They are used with caution if significant edema. If preeclampsia develops diuretics must be discontinued. Beta-blockers have no major contraindications, although neonatal bradycardia, hypoglycemia, and respiratory depression are reported. Labetalol is not associated with neonatal bradycardia. Alpha-methylldopa is the drug of choice for essential hypertension. Clonidine is also used. Calcium channel blockers may cause tocolysis in 3rd trimester hence are limited to hypertension unresponsive to other medications. Hydralazine is a first-line agent for hypertensive emergencies. Experience with minoxidil and prazosin is limited.

Management of preeclampsia- Basic management includes early prenatal detection by serial blood pressure measurements, weight determination and duration of gestation, hospitalization if worsening hypertension or proteinuria. In mild preeclampsia, physical activity should be reduced. If symptoms worsen (eg, headache, visual disturbances, epigastric pain, oliguria), it can be assumed that eclampsia is imminent, and pregnancy must be terminated. Controversial prevention strategies include calcium supplementation, fish oils, sodium restriction, low-dose aspirin and antioxidants.

RENAL FAILURE

Incidence of ARF in pregnancy is 1:20,000. Causes of renal failure in pregnancy can be divided into (i) Early pregnancy- Hyperemesis gravidarum, Septic abortion .(ii) Late pregnancy-PIH and its complications, HELLP Post partum HUS, Acute fatty liver of pregnancy, Volume loss –APH, PPH, Sepsis

Septic abortion-Commonest causative organism is Clostridium. It manifests few hours to 1-2 days after abortion with fever, vomiting and pain abdomen. Progression to shock and death is rapid. Jaundice may occur. Anemia, leucocytosis and thrombocytopenia with DIC may be seen. Management consists of antibiotics, volume resuscitation, hysterectomy, hyperbaric oxygen, antitoxin and exchange transfusion.

Pregnancy induced hypertension-

PIH alone is an uncommon cause of AKI.

PIH may be associated with HELLP (hemolytic anemia, low platelets and elevated liver enzymes) and is commonly associated with AKI, jaundice and bleeding. Usually occurs antepartum but can occur peripartum or post partum. DIC can complicate HELLP. HELLP is the commonest cause of renal failure in pregnancy, Outcome is good, maternal mortality is 1%. Rarely placental abruption, subcapsular liver hematoma, retinal detachment, ARDS, ascites, pleural effusion may occur.

Eclampsia may be associated with bleeding, jaundice and oliguric renal failure. Renal failure is unusual even with severe cases, unless there is significant bleeding or hemodynamic instability or marked DIC. Severe preeclampsia may be associated with a true DIC state with prolongation of the prothrombin, partial thromboplastin times, low levels of clotting factors, elevated FDP and positive D-dimer test. There is activation of the coagulation cascade. Fibrin forms crosslinked networks in the small blood vessels (MAHA). The abnormalities typically resolve spontaneously within the first two weeks postpartum. In some cases, however, preeclampsia begins in postpartum period without prior proteinuria and may be difficult to initially differentiate from postpartum HUS. Only the subsequent spontaneous recovery will point toward preeclampsia. Treatment consists of delivery of the baby, Mag sulphate decreases risk of seizures, anti hypertensive drugs are used as described for PIH. For DIC- Fresh frozen plasma, Blood transfusion, Anti thrombin 3 concentrate are indicated. Incidence 0.2-0.6% of all pregnancies, occurs in 10-20% of women with preeclampsia.

Hemolytic uremic syndrome (HUS)/Idiopathic post partum
failure occurs in primipara and is characterized by renal failure, anemia and HT. Onset is within hours to days. Symptoms can begin before delivery, but the onset in most cases is delayed for 48 hours or more after delivery (mean four weeks). HUS may follow a normal pregnancy or be preceded by findings indistinguishable from preeclampsia. The cause is obscure and viral illness, retained placental fragments, drugs eg oxytocics, ergot and oral contraceptives have been implicated. Labs reveal Microangiopathic hemolytic anemia (MAHA), thrombocytopenia, LDH (>600 U/liter). Biopsy shows mesangiolysis, glomerular simplification. There may be hypocomplementemia, deficiency in PG or antithrombin levels. Outcome is poor, high maternal mortality 18-44% and fetal loss 80%. 45% have residual neurologic or chronic renal failure. Recurrences occur in 50%. Recurrence in subsequent pregnancies is low. History (eg, preceding proteinuria and hypertension favor preeclampsia), the absence of DIC, onset more than two days after delivery, and/or persistent disease for more than one week are the main findings that differentiate the HUS from preeclampsia.

Treatment includes Plasmapheresis, Plasma infusion, Steroids, anti-platelet therapy, Immunoabsorption, splenectomy, IV gamma globulin, hemodialysis and antihypertensives. Platelet transfusions should be avoided. Heparin and fibrinolytic agents, anti thrombin III concentrates may be used. Dilatation and curettage should be considered when occurs very close to delivery.

**Thrombotic thrombocytopenic purpura** : TTP is characterized by the pentad of microangiopathic hemolytic anemia, thrombocytopenia, renal insufficiency, fever, and neurologic abnormalities. The degree of renal impairment is often mild. Thrombotic thrombocytopenic purpura almost always occurs antepartum, many cases begin before 24 weeks but the disease also occurs in the third trimester.

Cortical necrosis-50% of all cortical necrosis is pregnancy related. Causes include Abruptio, septic abortion, placenta previa, prolonged IUD or amniotic fluid embolism. Commoner in Post partum than antepartum AKI. Renal cortical necrosis may be patchy or total. Patients develop abrupt onset of oligoanuria, gross hematuria, flank pain and hypotension. The diagnosis can be established by ultrasonography. Renal calcifications on plain film of the abdomen suggest cortical necrosis (6 weeks). CT scanning demonstrates hypoechoic or hypodense areas in renal cortex or may demonstrate cortical tram track calcification. Angio- abrupt cut off of vascularity. No specific therapy is effective. Many patients develop chronic kidney disease.

**ACUTE PYELONEPHRITIS**: Although renal function is well maintained during acute pyelonephritis, some pregnant women develop acute renal failure. Renal biopsy may reveal focal microabscesses and recovery after antimicrobial therapy may be incomplete due to irreversible injury.

**ACUTE FATTY LIVER OF PREGNANCY**: It is a rare complication of pregnancy that is associated with AKI in 60%. It is due to mutation in enzyme for long chain 3 hydroxy acyl CoA dehydrogenase. It is characterized by jaundice, mild renal failure in last trimester, DIC, PIH, hypoglycemia, pancreatitis and encephalopathy. The diagnosis should be suspected in a woman with preeclampsia who has hypoglycemia, hypofibrinogenemia, and a prolonged PTT in the absence of abruptio placentae, high bilirubin, normal/ high transaminases, microvesicular steatosis and rarely liver necrosis. Renal biopsy shows acute tubular necrosis (ATN). Treatment-IV fluids, cryoprecipitate, Fresh frozen Plasma, glucose. It reverses with delivery, C section is preferred. Liver transplant is the treatment of choice in patients with liver necrosis. Outcome 20-25% maternal and fetal mortality, 25% recur.

**URINARY TRACT OBSTRUCTION**: Functional hydronephrosis rarely cause renal failure. The diagnosis can be established in some cases by the normalization of renal function in the lateral recumbent position and its recurrence when supine. In some cases, either insertion of a ureteral catheter or delivery of the fetus is required. Rarely, acute urinary tract obstruction in pregnancy is induced by a kidney stone.

**PREGNANCY IN THE SETTING OF CKD /DIALYSIS/ TRANSPLANT**

1. **Effects of the renal insufficiency on pregnancy.**

Renal insufficiency-Current consensus suggests degree of renal insufficiency, rather than underlying renal diagnosis, is the primary determinant of outcome. Women with only mild renal impairment (S Cr <1.4mg%), normal BP, and little or no proteinuria have good maternal and fetal outcomes, (95% live births, 75% AGA) with 16% showing a mild decline in renal function, only 6% having increased risk for accelerated progression toward ESRD or preterm delivery. There is increased PIH and nephrotic syndrome. Moderate CKD (S Cr 1.5-2.5mg%)-live births 90% but fetal growth retardation or preterm exceed 50%.40% have decline in renal function and 50% of these recover postpartum. More than 70% of women who become pregnant with a serum creatinine 2.5 mg/dl (Severe CKD) experience preterm delivery and 40% develop preeclampsia. 70% have an accelerated decline in renal function and 1/3 rd progress to ESRD. The normal increase in GFR during pregnancy is attenuated in these women and they should be counseled to avoid pregnancy.

3. **Nephrotic proteinuria- is associated with thromboembolism, variable IUGR, preterm labor and poor long term maternal and renal prognosis. These females need low molecular weight heparin prophylaxis till 6 weeks postpartum with double the usual dose as heparin clearance is increased in pregnancy. Mild proteinuria >500 mg/d is associated with 30% increased risk of PET,45% preterm,23% IUGR and also decline in GFR. These females need serial monitoring.**

Preconceptional hypertension leads to IUGR, preeclampsia, preterm labor, and accelerated decline in renal functions. Perinatal mortality is 23% versus 4% in normotensives with CKD.
Table 1: Changes in some common indices during pregnancy

<table>
<thead>
<tr>
<th></th>
<th>Nonpregnant</th>
<th>Pregnant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematocrit (%)</td>
<td>41</td>
<td>33</td>
</tr>
<tr>
<td>Plasma protein (g/dl)</td>
<td>7.0</td>
<td>6.0</td>
</tr>
<tr>
<td>Plasma osmality (mOsm/kg)</td>
<td>285</td>
<td>275</td>
</tr>
<tr>
<td>Plasma sodium (mmol/l)</td>
<td>140</td>
<td>135</td>
</tr>
<tr>
<td>Plasma creatinine (mg/dl, µmol/l)</td>
<td>0.8 (73)</td>
<td>0.5 (45)</td>
</tr>
<tr>
<td>Blood urea nitrogen (mg/dl, µmol/l)</td>
<td>12.7</td>
<td>9.3</td>
</tr>
<tr>
<td>Plasma urea (mmol/l)</td>
<td>4.5</td>
<td>3.3</td>
</tr>
<tr>
<td>pH units</td>
<td>7.40</td>
<td>7.44</td>
</tr>
<tr>
<td>Arterial PCO₂ (mmHg)</td>
<td>40</td>
<td>30</td>
</tr>
<tr>
<td>Plasma bicarbonate (mmol/l)</td>
<td>25</td>
<td>20</td>
</tr>
<tr>
<td>Plasma uric acid (mg/dl, µmol/l)</td>
<td>4.0 (240)</td>
<td>3.2 (190) early</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>115</td>
<td>105</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>70</td>
<td>60</td>
</tr>
</tbody>
</table>

II. Effect of pregnancy on renal disease

Pregnancy may result in deterioration in renal function in some renal diseases-Lupus, scleroderma, MPGN and Periarteritis nodosa. Effect of pregnancy on FSGS, IgA and Reflux nephropathy is controversial. ¹

DN- has accelerated progression in 45% of patients. ²⁻¹²

Lupus nephritis- 50% experience a flare during pregnancy, although it is less common in patients who have been in remission for > 6 months. Exacerbations (flares) increase risk of renal failure. Fetal loss occurs in 50% of patients. Lupus anticoagulant and anticardiolipin antibody increase risk. Therapeutic abortion is generally recommended if a lupus flare is associated with worsening renal function or worsening hypertension prior to 34 weeks’ gestation. Delivery is recommended after 34 weeks’ gestation. Infant should be screened for neonatal lupus. Treatment for flares includes prednisone or azathioprine. Cyclophosphamide is avoided because it is teratogenic. Fetal survival rates are good (95%). Complications, including SGA, preterm labor and stillbirth, are increased even in mild renal insufficiency.²⁻¹²

Pregnancy in patients on dialysis- Pregnancy occurs only in 1% of patients. The cause of infertility is multifactorial. Upto 42% of women receiving dialysis have regular menses, but many are anovulatory. Anemia probably also plays a role. The fetal outcome is quite poor. Only 23-55% of pregnancies result in surviving infants and a large number of second-trimester spontaneous abortions occur. Approximately 85% of surviving infants are born premature and 28% are SGA. Polyhydramnios is seen in 50%. Premature rupture of membranes may occur. Maternal complications including death may occur. Hypertension worsens in more than 80% of pregnant females on dialysis. The diagnosis of pregnancy is also difficult because levels of beta-human chorionic gonadotropin (beta-hCG) are normally elevated in patients receiving dialysis and ultrasound should be done to aid in diagnosis. The patient should be placed on transplant list because outcomes with allograft transplant patients are markedly better. During hemodialysis uterine and fetal monitoring is needed, hypotension should be avoided. Judicious use of erythropoietin and aggressive dialysis to keep BUN levels less than 50 mg/ may improve mortality and morbidity. PD can also be done but is inferior to HD.²³

Pregnancy in patients after transplantation-Fertility rates increase after 6 months of transplantation and pregnancy occurs in up to 12%. Uncontrolled hypertension, worsening proteinuria, and poor prepregnancy renal function are prognostic indicators for the risk of renal function deterioration. Patients should wait a year after a living related donor transplant and 2 years after a cadaveric transplant before planning pregnancy. The renal function should be stable, (serum creatinine< 2.0 mg/dL). Attempts should be made to decrease prednisone to 15 mg/d or less, azathioprine to 2 mg/kg/d or less, and cyclosporine to 5 mg/kg/d or less. Prednisone crosses the placenta and may cause neonatal adrenal insufficiency and thymic hypoplasia. These are rare if the dose is less than 15 mg/d. If acute rejection of the kidney occurs during pregnancy high-dose steroids, OKT3 and ATG may be used. Azathioprine is teratogenic in animals, but not in humans. Although azathioprine crosses the placenta, the immature fetal liver cannot convert it to its active form, 6-mercaptopurine. Use of azathioprine is associated with SGA babies and dose-related myelosuppression in the fetus. Cyclosporine has been associated with SGA babies and Preeclampsia(29%). Tacrolimus crosses the placenta and has been associated with hyperkalemia and renal insufficiency. Mycophenolate mofetil(MMF) has potentially teratogenic effects in pregnancy, eg fetal bone marrow suppression and structural malformations including hypoplastic nails, shortened fingers, microtia and cleft lip/palate. Women should discontinue MMF at least 6 wk before conception.
Although there are few human data on the safety of sirolimus in pregnancy, animal studies suggest teratogenicity, so it should be avoided. All pregnant post transplant patients should receive antibiotic prophylaxis before all surgical procedures. Any UTI in pregnancy warrants continuation of long term prophylaxis. Most evidence suggests that pregnancy after transplantation does not increase risk for rejection, so long as renal function is good. There is no increased risk for birth defects. 20% pregnancies end in spontaneous abortions with 90% successful outcomes in pregnancies completing 1st trimester. An elevated prepregnancy creatinine level (ie, >1.4 mg/dL) is not only associated with a higher risk of renal decline but also with a decreased fetal survival rate (74% with creatinine level > 1.4 mg/dL, 96% if < 1.4 mg/dL). Obstruction of the transplant ureter by the pregnant uterus is rare but has been reported. The dose of steroids needs to be increased in the peripartum period. Neonatal outcome in pregnancies among renal transplantation patients is good except a higher rate of preterm birth (50 to 54%), SGA (33 to 45%), and neonatal mortality (1 to 3%) as compared with the general population (12.3, 5, and 0.68%, respectively). Long-term outcome of surviving infants is good.

Management of pregnancy in CKD and transplant-Prenatal visits should be frequent—every 2 weeks until 28 weeks’ gestation and then weekly. Prenatal monitoring should include daily blood pressure measurements. Biweekly visits with laboratory work consist of urine protein by dipstick (24 hr protein if dipstick abnormal) CBC counts, electrolytes, BUN and creatinine levels. Monthly ultrasounds and urine cultures and determination of CMV-IgM, Toxoplasma IgM for seronegative women (every trimester). IgM for HSV(last trimester) should be done. Biweekly fetal surveillance with a biophysical profile is indicated in the third trimester. If rubella titers are low, administer the vaccine before transplant because this live virus vaccine is contraindicated after transplantation.22

Obstetric management-The most common cause of mortality and morbidity in patients with any renal disease is preterm labor. Magnesium can be cautiously used to avoid toxicity and respiratory depression. The literature is divided about elective early delivery (34-36 wk) in patients with chronic renal insufficiency or those receiving dialysis, especially when fetal lung maturity is present. In patients who have had a transplant, however, delaying delivery until the onset of labor is generally thought to be the most prudent step, provided that the mother and fetus show no signs of distress. Vaginal delivery is preferred.

REFERENCES
14. Sibai, BM, Villar, MA, Mabie, BC. Acute renal failure in hypertensive disorders of pregnancy. Pregnancy outcome and remote prognosis in...


