A Woman with GN Presenting during Pregnancy

Susan Hou

Summary
The combination of kidney disease and pregnancy has long been recognized as a high-risk situation. When renal disease is recognized for the first time during pregnancy, it presents unique problems for both the obstetric and the renal teams. Particularly difficult can be distinguishing preeclampsia from preexisting kidney disease in women presenting for the first time with hypertension, proteinuria, and reduced GFR during pregnancy. Decision-making regarding performing a kidney biopsy and treatment of glomerular disease during pregnancy is often much more complicated by safety concerns for both the mother and the developing fetus.


Introduction
A 28-year-old woman (G2P0) presented for her first prenatal visit at an outside hospital at 12 weeks’ gestation. Her first pregnancy 2 years earlier was a molar pregnancy complicated by hypertension. She did not have her BP checked between pregnancies. She had hypertension and proteinuria at the time of her first prenatal visit at 12 weeks’ gestation. She was not aware of any kidney disease and had no family history of kidney disease. She had no diabetes and no symptoms of collagen vascular disease. She had not recently had sore throat or skin infection. She had not noted foamy urine or change in the color of her urine. She was not taking any medications, including nonsteroidal antiinflammatory drugs. She had no history of smoking, alcohol, or illicit drug use. Her BP was 145/95 mmHg, and she had no edema.

Her serum creatinine level was 0.9 mg/dl, and her creatinine clearance was 79 ml/min. A urinalysis showed 2–5 red cells/high-power field and 2+ protein. The 24-hour urine protein was 1130 mg. Her hemoglobin level was 11.2 g/dl, and her white blood cell and platelet counts were normal. Her fasting blood glucose level was 76 mg/dl. Her antinuclear antibody test result was negative, her C3 level was 186 mg/dl (normal, 88–201 mg/dl), and her C4 level was 22 mg/dl (normal, 16–47 mg/dl). Results of antiphospholipid antibody testing were negative. Test results for hepatitis B core antigen and core antibody, HIV, and antibodies to hepatitis C virus were negative. Her hypertension was treated with a-methyldopa.

Identifying Kidney Disease in a Pregnant Woman
Routine prenatal visits include measurement of BP and a urine dipstick examination. Abnormalities in either of these should prompt screening for kidney disease. Because this woman’s hypertension was present in the first trimester, it is likely that the problem was not preeclampsia, the most common cause of hypertension and proteinuria in a pregnant woman. Preeclampsia occurs late in pregnancy, so when hypertension and proteinuria are seen before 20 weeks’ gestation, another process is likely to be present (1). Hydatidiform moles are associated with preeclampsia and may occur earlier in gestation (1). With her history of a molar pregnancy, this patient is at higher risk for another molar pregnancy, which can be ruled out by ultrasound and quantitative β human chorionic gonadotropin. With more severe degrees of renal insufficiency, β human chorionic gonadotropin levels are elevated because of reduced renal clearance and can lead to a mistaken diagnosis of hydatidiform mole (2). Increases in urinary protein up to 250–300 mg in 24 hours can be seen in normal pregnancy, but our patient’s 24-hour urine protein is clearly abnormal (3). Her serum creatinine and creatinine clearance should be interpreted in the context of expected changes in renal function during pregnancy.

Normal pregnancy is accompanied by a 30%–50% increase in GFR; the expected serum creatinine would be 0.5–0.8 mg/dl, with a creatinine clearance in the 125–175 ml/min range (1). Commonly used formulas for calculating GFR (Cockcroft-Gault and Modification of Diet in Renal Disease methods) generally underestimate the GFR in pregnant women (4). In one study in pregnant patients with preeclampsia and CKD, the Modification of Diet in Renal Disease equation underestimated “true” GFR, as measured using inulin clearance, by about 25 ml/min. In healthy pregnant women, the measured GFR was 40 ml/min higher than the calculated GFR (4). Cystatin C levels do not correlate with GFR by inulin clearance in pregnancy (5). Measurement of creatinine clearance provides the most accurate assessment of GFR in a pregnant woman, in whom radioisotopes obviously cannot be used (6). Timed urine collections may be affected by stasis of urine in the dilated collecting system, which commonly occurs in pregnancy; thus, a 24-hour urine collection is preferable to a 4-hour collection.

Differential Diagnosis
At this point, it appears that this patient’s elevated BP is the result of a renal process, but it is not clear

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Renal Biopsy in Pregnancy

whether it is glomerular or tubular. It is also unclear whether her kidney disease is acute or chronic. In CKD, a definitive diagnosis can often be postponed until after delivery, even when proteinuria is discovered early in pregnancy. Most CKDs, with the exception of lupus, have similar risks in pregnant women. Pregnant women with CKD are at risk for increasing proteinuria, pre-eclampsia, and premature delivery. Whether pregnancy accelerates the decline of kidney function depends on the prepregnancy GFR. Women with a serum creatinine level of 1.4 mg/dl or less are unlikely to have permanent worsening of their kidney disease during pregnancy (6). As is often the case, a prepregnancy measurement of GFR is unavailable for this woman. Not all pregnant women with CKD have the expected pregnancy-associated increase in GFR and decrease in creatinine, but a substantial fraction do, so our patient’s serum creatinine of 0.9 mg/dl may actually be lower than her prepregnancy level.

The processes that need to be ruled out at this point are primarily the acute glomerulonephritides. Lupus is the most common of these in women of child-bearing age, regardless of pregnancy status; because lupus nephritis not uncommonly begins during pregnancy, this is certainly a major consideration in our patient. Patients with diffuse proliferative lupus nephritis require prompt treatment regardless of renal function. The patient with lupus is at risk for rapid and irreversible loss of kidney function, as well as life-threatening extrarenal complications. The fetus is at increased risk for spontaneous abortion, and the risk is greatest in women with anticardiolipin antibodies. Infants born to women with high titers of anti-SSA antibodies are at risk for congenital heart block. Other lupus-associated antibodies include IgG and cross the placenta, sometimes resulting in transient rashes and hematologic abnormalities in the baby. Antinuclear antibody, complement levels, and anti–double-stranded DNA titers should be measured. C3 and C4 levels are usually elevated in pregnancy, so borderline-low complement levels are suspect. Goodpasture syndrome and ANCA-associated vasculitides are uncommon during pregnancy, but serologic tests for these disorders should be done. The most important indicators of acute glomerular disease are changes in renal function and proteinuria during the next few weeks. An active urine sediment with dysmorphic red cells and red cell casts may also indicate an acute process.

Other common causes of proteinuria in a woman of childbearing age include infections with hepatitis B virus, hepatitis C virus, and HIV. In many places, tests for these diseases are included in routine prenatal testing. Diabetes is a common cause of proteinuria in pregnancy, but the diagnosis of type 1 diabetes would have been made years before the development of proteinuria. Type 2 diabetes is increasingly common in young people and sometimes goes undetected even as kidney failure develops. Blood glucose would have been tested during her previous pregnancy, and she would not have had time to develop diabetic nephropathy.

Renal Biopsy in Pregnancy

Packham and Fairley reported a very low complication rate (4.5%) among 104 women undergoing 111 kidney biopsies during pregnancy (7). However, few nephrologists have as much experience doing renal biopsies during pregnancy and might expect more complications. Even in this series, in which biopsies were done by very experienced practitioners, one woman sustained retroperitoneal bleeding followed by prepartum intrauterine bleeding. She gave birth to a premature baby who died, and she required transfusion of 7 units (7). Renal blood flow is increased during pregnancy, and later in pregnancy the biopsy has to be done with the patient lying on her side or sitting because of the gravid uterus.

There are three widely accepted indications for kidney biopsy during pregnancy. First, new-onset lupus nephritis necessitates a biopsy because diffuse proliferative lupus nephritis must be treated immediately with toxic drugs, whereas other classes of lupus nephritis may not. Any unexplained deterioration of kidney function is a second indication for renal biopsy. A kidney biopsy should be done in our patient if her kidney function deteriorates during the next 1–2 weeks. In some women, glomerular disease is associated with severe nephrotic syndrome with massive edema and a profound decrease in serum albumin. If treatment with steroids or cytotoxic drugs is contemplated, it is advisable to perform a biopsy to better anticipate the likelihood of a response. The third indication for biopsy during pregnancy is massive proteinuria.

Late in pregnancy, it is often difficult to distinguish between primary renal disease and preeclampsia. Although kidney biopsy might be helpful in this setting, the patients are often too hypertensive to safely undergo this test.

Monitoring

The most common complication of pregnancy in women with kidney disease is severe hypertension/preeclampsia, which can be life-threatening for both mother and baby. Hypertension can have a sudden onset. Pregnant women with kidney disease should be taught to measure their BP at home and should check it twice a day. Measuring BP in the third trimester needs to be reinforced because weeks of good BP earlier in pregnancy may tempt the patient to decrease BP measurements at a time when the risk for severe hypertension is greatest.

Once it has been established that the kidney disease is not rapidly progressive, a serum creatinine and a urine protein-to-creatinine ratio should be measured every 1–2 weeks. If kidney function does deteriorate, terminating the pregnancy will not reverse the decline in function unless it is from preeclampsia. Kidney function may decline so rapidly that dialysis becomes necessary (8,9).

Treatment of Hypertension

In women with essential hypertension, the level at which antihypertensive medication should be started is a matter of debate. Although nephrologists may be inclined to treat pregnant patients with even mild hypertension, randomized controlled trials have shown conflicting results regarding the benefit of treating women with a history of hypertension and a BP < 160/100 mmHg. A review of antihypertensive drug therapy for mild to moderate hypertension (systolic BP, 140–169 mmHg; diastolic BP, 90–109 mmHg) in pregnant patients found no convincing decrease in poor maternal and fetal outcomes with treatment. Guidelines from several obstetric groups in the United States, Europe, Australia, and Canada recommend starting treatment...
at a higher BP (10). A diastolic BP > 110 mmHg during pregnancy has been associated with increased risk for stroke. I would argue for starting antihypertensive medications during pregnancy using a threshold of 140/90 mmHg because control of hypertension is central to preventing progression of kidney disease and safe drugs are available.

α-Methyldopa
α-Methyldopa has been used in pregnant women for more than 50 years and owes its survival in the antihypertensive armamentarium largely to its safety in pregnancy. Developmental testing in children exposed to α-methyldopa in utero has shown no ill effects (11). The drug is often poorly tolerated because of somnolence.

Calcium-Channel Blockers
These drugs were once reserved for refractory hypertension but are now widely used as first-line drugs for the treatment of hypertensive pregnant women. Nifedipine is the most commonly used. No increase in congenital anomalies has been reported, but the drug may cause profound hypotension when magnesium is given (12). When used acutely, nifedipine can suppress uterine contractions and has been used to stop premature labor. When used over the long term for hypertension, it generally does not have this effect (13).

β-Blockers and Labetalol
Labetalol combines α and β blockade and is the most widely used adrenergic blocker for hypertension in pregnancy. Although pure β-blockers have been associated with symptoms of autonomic blockade in the newborn, such is not the case with labetalol (14). Other β-blockers have been associated with intrauterine growth restriction and decreased tolerance of hypoxic insults (15). There have also been several case reports of neonatal bradycardia, hypoglycemia, and respiratory depression associated with β-blockers (16).

Diuretics
Some obstetricians are reluctant to use diuretics in pregnancy. These agents may aggravate the decreased intravascular volume seen with preeclampsia or interfere with the normal volume expansion of pregnancy. In an observational study of 20 pregnant women with hypertension, the mean increase in plasma volume was lower in 10 women who continued diuretics than in 10 women in whom they were stopped (17). However, a meta-analysis of nine randomized trials involving more than 7000 pregnant women receiving diuretics found no increase in the incidence of adverse fetal effects (18).

Hydralazine
Hydralazine has been widely used in pregnancy and is considered safe in pregnancy. Although the drug does cross the placenta, neonatal arrhythmia and transient thrombocytopenia have been seen. However, these complications are rare.

Angiotensin-Converting Enzyme Inhibitors and Angiotensin-Receptor Blockers
Angiotensin-converting enzyme (ACE) inhibitors and angiotensin-receptor blockers (ARBs) are widely used to control BP, reduce proteinuria, and slow the progression of renal disease. These two classes of antihypertensive medications are strongly contraindicated in pregnancy. Adverse effects of ACE inhibitor use in the second and third trimesters are well recognized and include oligohydramnios, renal dysplasia, and pulmonary hypoplasia; in addition, the newborn may have anuria and die of respiratory failure (19). Similar problems have been noted when ARBs were used in the second and third trimesters, with chronic renal insufficiency affecting surviving infants. More recently, one observational study reported an increased incidence of major congenital malformations with first-trimester exposure to ACE inhibitors (20).

At 22 weeks the patient began to notice peripheral edema, and proteinuria increased from 1+ to 3+ on dipstick. Her BP was 140/92 mmHg with 500 mg of α-methyldopa twice daily. At 28 weeks she noted markedly increased edema, including facial edema. At 31 weeks, the edema worsened and she began having headaches, so she was admitted to the hospital. Her BP was 180/120 mmHg. Her physical examination was remarkable for facial edema. Her chest was clear and her heart sounds normal. She had no right-upper-quadrant tenderness. Her uterus was appropriate for gestational age. She had 3+ pretibial edema. Laboratory values are shown in Table 1.

Her BP was treated with hydralazine and labetalol. She received magnesium for preeclampsia at an initial dose of 4 g, followed by an infusion of 2 g/hr. The infusion was later stopped because of hypermagnesemia (serum magnesium level, 6.4 mg/dl). She received dexamethasone to mature the fetal lungs. Her BP remained difficult to control, and on the third hospital day labor was induced. After failed induction, a baby girl was born via cesarean delivery. The baby weighed 1596 g and had Apgar scores of 3, 8, 19.9

Table 1. Laboratory results

<table>
<thead>
<tr>
<th>Test</th>
<th>Day 1</th>
<th>Day 2</th>
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<tbody>
<tr>
<td>Creatinine (mg/dl)</td>
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<td>1.9</td>
</tr>
<tr>
<td>Sodium (mEq/L)</td>
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<td>Potassium (mEq/L)</td>
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<td>Bicarbonate (mEq/L)</td>
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<td>16</td>
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<tr>
<td>Hemoglobin (g/dl)</td>
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<td>White blood cell count (K/UL)</td>
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<td>Platelets (K/UL)</td>
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<td>340,000</td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
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<td>1.3</td>
</tr>
<tr>
<td>Aspartate aminotransferase (IU/L)</td>
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<td>27</td>
</tr>
<tr>
<td>Alanine aminotransferase (IU/L)</td>
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<tr>
<td>Uric acid (mg/dl)</td>
<td>6.6</td>
<td>7</td>
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<tr>
<td>Urinary protein (g/24 hr)</td>
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<tr>
<td>Urinalysis pH, 6.0; 3+ protein; 0–2 red blood cells</td>
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</table>
and 8. Three days after the delivery of the baby, the mother’s serum creatinine was 1.3 mg/dl.

Our patient was thought to have preeclampsia, for which the definitive treatment is delivery of the baby. She had massive proteinuria, increased serum creatinine, and difficult-to-control hypertension. Her uric acid level was elevated. The low serum sodium level is normal in a pregnant woman in whom there is a reset osmostat. The low bicarbonate and the alkaline urine are an expected response to the respiratory alkalosis seen in pregnancy. Worsening proteinuria, elevated serum creatinine and uric acid levels, and hypertension can all be manifestations of worsening kidney disease rather than preeclampsia. However, the inability to control BP was consistent with preeclampsia, and the risk to the mother’s life dictated delivery. Her BP was never stable enough to perform kidney biopsy to confirm that she had preeclampsia.

Preeclampsia is a multisystem disease occurring after 20 weeks’ gestation, characterized by hypertension (BP $\geq 140/90$ mmHg on two measurements 6 hours apart) and proteinuria ($\geq 300$ mg/24 hr). The diagnosis can be difficult to make in a woman with preexisting kidney disease who has hypertension and proteinuria from the beginning of pregnancy.

We now know that preeclampsia is characterized by increases in angiogenic factors, soluble fms-like tyrosine kinase 1 (sFlt-1), and endoglin, which are thought to play a major role in its pathogenesis (21). The increase in angiogenic factors is accompanied by a decrease in placental growth factor and vascular endothelial growth factor. Little is known about changes in these substances in CKD and whether they will someday be helpful in distinguishing preeclampsia from preexisting kidney disease. In our patient, the prompt improvement in her BP and serum creatinine level after delivery was consistent with preeclampsia.

Seizure Prevention with Magnesium
Magnesium is more effective than other anticonvulsants in preventing seizures in preeclamptic women, but in the setting of renal insufficiency and changing kidney function, the loading dose may be given and a continuous infusion started at a lower rate. Serum magnesium should be carefully monitored to avoid hypermagnesemia, which can cause flaccid paralysis, apnea, bradycardia, and hypotension.

After delivery, this patient’s serum creatinine level decreased to a low of 1 mg/dl and her 24-hour urine protein decreased to 2.9 g. She underwent a kidney biopsy 2 months postpartum. The biopsy showed 12 glomeruli; 1 glomerulus showed global sclerosis, 3 showed segmental scars, and 1 had a fibrous crescent occupying 20%. Immunofluorescent studies showed intense staining for IgA and less intense staining for light chains (without $\kappa$ or $\lambda$ predominance) and C3. Electron microscopy showed electron-dense deposits in the mesangium and partial foot-process effacement. These findings are consistent with IgA nephropathy. She was treated with fish oil and lisinopril. A year after her pregnancy, CKD began to progress; 11 years later her serum creatinine level is 5.87 mg/dl. She is currently being evaluated for kidney transplant. Her daughter, now 11 years of age, is developing normally.

Discussion
The stability of the patient’s renal function until she developed preeclampsia at 31 weeks is consistent with a chronic process. However, the prolonged interval between the development of edema and the severe hypertension, as well as the increased protein on dipstick testing, suggests that she had worsening proteinuria before preeclampsia developed. If this patient had been seen with worsening proteinuria and hypoalbuminemia without hypertension, treatment would have been considered and she would have had one of the indications for biopsy discussed above. Treatments that might apply to nephrotic syndrome of any cause, as well as disease-specific treatment, would have been considered.

Venous Thromboembolism
Patients with nephrotic syndrome are at risk for deep-vein thrombosis and other thrombotic complications because of the loss of such proteins as antithrombin 3 and protein S and C as part of their proteinuria. The risk for thrombosis increases with profound hypoalbuminemia and is higher in membranous nephropathy than in IgA nephropathy (7.85% versus 0.36%) (23). Pregnancy, even in the absence of nephrotic syndrome, is also a state associated with increased risk for thromboembolic disease. There are no evidence-based guidelines for deep-vein thrombosis prophylaxis in pregnant women with nephrotic syndrome. Warfarin is avoided in pregnancy because of the occurrence of a constellation of birth defects known as warfarin embryopathy, which includes nasal hypoplasia and epiphyseal stippling, as well as problems related to bleeding. Heparin does not cross the placenta to the fetus but has effects on the placenta that are not completely understood (24). Nonetheless, both unfractionated and low-molecular-weight heparins are thought to be safe in pregnancy, and it seems

Treatment of Severe Hypertension in Pregnancy

Hydralazine
Intravenous hydralazine at doses of 5–10 mg every 20–30 minutes is the drug of choice for hypertensive crisis in pregnancy.

Labetalol
Intravenous labetalol is the second most commonly used drug for treating hypertensive emergencies in pregnant women. It is given as a 20-mg loading dose followed by 20–30 mg every 30 minutes or as a 1–2 mg/min drip. The newborn should be monitored for bradycardia and hypotension.

Nifedipine
Short-acting nifedipine is rarely used in the United States now but is still used to treat severe hypertension in pregnancy in other countries.

Nicardipine
Nicardipine has been used as an alternative to labetalol and hydralazine, with similar efficacy. A loading dose of 10 mg is given, followed by infusions of 12.5–15 mg/hr (22).
reasonable to administer prophylactic heparin to women with nephrotic syndrome and either membranous nephropathy or profound hypoalbuminemia (\(<2 \text{ g/dl}\)) who are on bed rest.

**Hyperlipidemia**

Hydroxymethylglutaryl coenzyme A reductase inhibitors are contraindicated in pregnancy, and hyperlipidemia is usually left untreated.

**Immunosuppressive Drugs in Pregnancy**

The reason for a biopsy during pregnancy would be an illness that required immediate treatment. IgA nephropathy has a wide spectrum of courses. At one end of the spectrum, crescentic IgA nephropathy can present as aggressive GN requiring treatment with steroids and cytotoxic drugs. At the other end, IgA nephropathy can be an indolent disease with few if any symptoms. One biopsy study found IgA nephropathy in 16.1% of kidney donors at the time of transplant (25). When treatment is indicated, both corticosteroids and cytotoxic drugs have been used in addition to angiotensin-blocking agents, but with mixed results (26). Observation over a few weeks convinced us that this patient did not have a rapidly progressive disease that required immediate treatment. She had both clinical and histologic features that predicted she would have progression in the long run, with >1 g of proteinuria, segmental sclerosis in 25% of glomeruli, and a glomerular crescent. What are the options for a woman who needs immunosuppressive therapy during pregnancy (Table 2)?

**Corticosteroids.** Prednisone crosses the placenta poorly, with a 10:1 maternal-to-cord blood ratio (27). In doses used for induction therapy, fetal exposure may be significant and neonates should be monitored for adrenal insufficiency. Maternal risks include increased risk of infection, hypertension, gestational diabetes, and premature rupture of membranes.

**Azathioprine.** Azathioprine is listed by the U.S. Food and Drug Administration as a category D drug, but it has been used in thousands of pregnant women. One recent study that compared 189 women exposed to azathioprine and 230 women not exposed found no difference in the frequency of congenital anomalies (28).

**Tacrolimus and Cyclosporine.** Transient neonatal anuria and hyperkalemia have been occasionally seen with tacrolimus, more often than with cyclosporine. Congenital anomalies in the infants of renal transplant recipients receiving these drugs are increased compared with the general population, but the anomalies show no distinct pattern (29,30). One study found a decrease in some T cell subsets in the baby at age 1 year and suggested delaying live virus vaccinations (31).

**Cyclophosphamide and Mycophenolic Acid.** These drugs are teratogenic and rarely used (32). Congenital anomalies occurred in 11 of 48 (23%) live-born infants exposed to mycophenolic acid (29). Cyclophosphamide has been used late in pregnancy, but there may be an increased risk of cancer in the children exposed *in utero.*

**Sirolimus and Everolimus.** These drugs have been used during some pregnancies, but not enough to allow conclusions to be drawn about their safety (29).

**Rituximab.** Rituximab is a human/murine chimeric monoclonal IgG directed against the CD20 protein on B lymphocytes that causes B cell depletion. All types of IgG cross the placenta with increasing efficiency as pregnancy progresses; the greatest chance of crossing occurs during the last 4 weeks of pregnancy. This pattern would decrease the risk of congenital anomalies in women who received rituximab in the first trimester. However, the drug may persist in the maternal circulation, has been reported to cause hematologic abnormalities, and predisposes to infections, including with cytomegalovirus (33). Women are advised not to conceive for a year after receiving rituximab.

**Pregnancy Counseling**

What would my colleagues and I have told this woman if we had seen her before her pregnancy? In all likelihood, she would have had a biopsy and we would have known that she had IgA nephropathy. We would have noted the clinical and histologic features that predicted a poor long-term prognosis. We would have warned her of the risk of hypertension and preeclampsia, worsening proteinuria, and premature birth but would also have told her that the safest time to become pregnant was while kidney function was still well preserved.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>FDA Category</th>
<th>Crosses the Placenta?</th>
<th>Effects on Fetus</th>
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<tbody>
<tr>
<td>Corticosteroids</td>
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<td>Poorly</td>
<td>Adrenal insufficiency</td>
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<tr>
<td>Prednisone</td>
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<td>Yes</td>
<td>Congenital anomalies</td>
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<tr>
<td>Betamethasone</td>
<td>C</td>
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<tr>
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<td>C</td>
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<tr>
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<td>C</td>
<td>Yes</td>
<td>No increase in congenital anomalies or leukopenia</td>
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<tr>
<td>Tacrolimus</td>
<td>C</td>
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<td>Decrease in B lymphocytes/infection</td>
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<tr>
<td>Azathioprine</td>
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</tr>
<tr>
<td>Rituximab</td>
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<td>Yes</td>
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</table>

FDA, U.S. Food and Drug Administration.
Would pregnancy change the course of her disease? Some investigators have thought that pregnancy in women with certain histologic lesions leads to progression of disease, including IgA nephropathy. Studies have been flawed by heterogeneous populations and lack of a control group. The best study to date comes from the Italian Society of Nephrology, in which 223 women with biopsy-proven IgA nephropathy and serum creatinine levels ≤1.2 mg/dl were followed for at least 5 years after biopsy (median, 10 years; range, 5–31 years) (34). In a comparison of the courses of 136 women who had had 229 pregnancies and 87 women who had no pregnancies, pregnancy was not associated with a faster progression of disease.

Care of a pregnant woman with kidney disease requires close collaboration among nephrologists, high-risk obstetricians, and neonatologists. Increased vigilance is necessary after the birth of the infant; even an infant born near term requires close observation during the first day for potential problems, such as immunosuppressive adverse effects or an osmotic diuresis if the mother had an elevated BUN level. The mother’s BP and kidney function should be monitored closely postpartum because severe hypertension can occur as long as 6 weeks postpartum. Deterioration of kidney function in lupus flares and in other kidney disease can occur postpartum even when the pregnancy has been uneventful. Breastfeeding is discouraged in women taking most immunosuppressive drugs except for prednisone (up to 40 mg/d), although the National Transplant Pregnancy Registry has reported no problems with breastfeeding by 64 women with 80 infants (35). Many women have breastfed while taking azathioprine and calcineurin inhibitors, but breastfeeding should still be discouraged in women taking cyclophosphamide and mycophenolate. Most antihypertensive drugs are safe during breastfeeding, but individual drugs should be reviewed. ACE inhibitors, ARBs, and diuretics can be used to treat hypertension postpartum.

In summary, kidney disease may be recognized for the first time during pregnancy. When kidney disease is chronic, kidney function is well preserved, and the woman does not have severe nephrotic syndrome, a biopsy can be postponed until after delivery. Permanent deterioration of kidney function usually occurs only when there is moderate pre-existing renal insufficiency, but the risk of severe hypertension, heavy proteinuria, and premature delivery are increased with any level of kidney function. Many antihypertensive and immunosuppressive drugs can be safely used in pregnancy.

Questions
Emily Robinson, MD, MPH. As you mentioned, pregnant women with pre-existing hypertension and proteinuria are at a higher risk for development of preeclampsia. Yet the pathophysiology of preeclampsia is so uniquely different from the hypertension and proteinuria that are common in primary glomerular diseases, such as IgA nephropathy. Why is it, then, that women with diseases such as IgA nephropathy are at a higher risk for development of preeclampsia?

Susan Hou, MD. Women with preexisting renal disease are at increased risk for preeclampsia, but we don’t understand why. We may have a better understanding of the reasons as we are able to look at newly recognized markers of preeclampsia in pregnant women with renal disease.

References
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