# Acute Kidney Injury in Pregnancy

By Richard Lafayette

During pregnancy, the development of acute renal failure is especially daunting because two lives are involved and at risk. The outcomes of acute kidney injury (AKI), as in other settings, can be quite poor, with significant morbidity and mortality rates of 20–30 percent.

Variable definitions of AKI have been used for pregnancy. The normal baseline serum creatinine during pregnancy is approximately 0.5 mg/dL; thus, a rise over 48 hours to values greater than 1.0 mg/dL, or an increase from a baseline of more than 0.5 mg/dL in 48 hours, should trigger further evaluation for AKI. It has been suggested that the RIFLE criteria be used, focusing on the percent change in creatinine or the development of oliguria to define AKI in pregnancy (1), but validation is needed. Regardless, there is clear evidence that the incidence of AKI in pregnancy has fallen over the past several decades, likely because of improved access to prenatal care and emergency services for the care of obstetric complications in developing countries and among disadvantaged populations. Still, in some less developed nations, the rates of AKI related to septic abortion and other infectious and hemorrhagic complications remain high (2). Presently, the incidence of AKI in pregnancy has fallen to approximately 1 in 15,000 pregnancies (3), but the outcomes have not significantly improved (3, 4).

## Causes of AKI in pregnancy

Pregnant women are subject to many of the non–pregnancy-specific causes of AKI, and a general approach that considers prerenal, intrarenal, and obstructive causes is best. However, some specific issues are more common in pregnancy. One approach would be to evaluate AKI on the basis of its timing (Table 1).

## Early pregnancy

From the first trimester to about 20 weeks, AKI is quite rare; the major contributor is hyperemesis gravidum, which is generally easily supported with increased fluids and vigilance. Complications of tubal pregnancies and septic abortions also contribute to the prevalence of AKI, and in these areas, improved access to health care is extremely important in optimizing outcomes. From early in pregnancy, an increased incidence of urinary tract infection is demonstrable, but this only rarely causes AKI, with the development of bilateral pyelonephritis or systemic complications of sepsis. In women with significant chronic kidney disease (CKD) (creatinine >1.5–2.0 mg/dL), rapid progression of hypertension, proteinuria, and renal insufficiency can sometimes be seen early in pregnancy (5). Thrombotic microangiopathy can develop early in pregnancy, notably in women with anticardiolipin/antiphospholipid antibodies, who have a high risk of recurrent early fetal loss. Pregnancy-associated thrombocytopenic purpura (TIP) also occurs, related to immune depletion of ADAMTS 13 or caused by genetic deficiencies related to complement activation (6). Additionally, patients with autoimmune nephritis, especially systemic lupus erythematosus, sometimes experience a flare in early pregnancy, with active glomerular injury.

## Late pregnancy

After 20 weeks, AKI is more common and is more likely to be related to the classic complications of pregnancy. Complications of urinary tract infection remain rare but are easily assessed. Obstructive uropathy is another rare cause, as a consequence of dilation of the urinary tract and the effects of uterine size (7). Kidney stones related to increased urinary calcium excretion, polyhydramnios, or underlying uterine fibroids can also contribute to obstruction in pregnancy. As in early pregnancy, women with systemic lupus erythematosus and autoimmune nephritis can experience a flare during this time; there are also many reports of postinfectious glomerulonephritis in late pregnancy as well (8). Women with significant CKD are more likely to experience progression late in pregnancy, and their course is usually marked by increasing blood pressure and proteinuria. Beyond this, there are several specific risks of pregnancy after 20 weeks to consider separately.

*Pre-eclampsia* is a common complication of pregnancy (3–5 percent of all pregnancies) and is generally seen in primigravidas or in women with multiple pregnancies (e.g., twins, triplets). It is defined by new-onset hypertension (>140/90 mm Hg) and proteinuria (≥2+), often with edema. Generally, pre-eclampsia is associated with a mild reduction in GFR, and the increase in creatinine does not meet the definition of AKI (9). However, severe pre-eclampsia can be associated with AKI, especially when complicated by systemic thrombotic microangiopathy, often in association with the HELLP syndrome (hemolysis, elevated liver enzymes, low platelets). In this syndrome, renal failure is not uncommon (up to 10 percent of the time) and is associated with markers of coagulopathy (10). The treatment of severe pre-eclampsia focuses on preventing eclamptic seizures with magnesium, early delivery, and prevention/treatment of profound hypertension. It is often difficult to discern pre-eclampsia from disease progression in patients with CKD. Generally, pre-eclampsia is thought to progress more rapidly and may be associated with other laboratory and clinical changes. Screening for soluble angiogenic factors, such as soluble fms-like tyrosine kinase 1 and soluble endoglin, may be available in the future to help differentiate the causes of AKI (11).

*Acute fatty liver of pregnancy* typically presents as abdominal discomfort, mental status changes, and a rapid rise in bilirubin out of proportion to elevated liver enzymes. The incidence of acute fatty liver of pregnancy seems to be on the rise (more than 1 in 10,000 pregnancies) (12). Renal involvement is common, with AKI reported in at least 30–35 percent of patients. Features of the hepatorenal syndrome are usually present, although acute tubular necrosis also occurs. Definitive diagnosis requires liver biopsy showing microsteatosis, but clinical diagnosis generally prevails, and treatment, again, is early delivery and supportive care. Most patients recover well over time, but liver transplant has been necessary in some cases.

*Hemolytic uremic syndrome* usually occurs in the early postpartum period and is marked, of course, by thrombocytopenia, microangiopathic anemia, and renal failure (13). This can occur before delivery and is easily confused with pre-eclampsia. Plasma exchange, avoiding platelet transfusions, and more controverisal treatments (e.g., steroids, antiplatelet agents) are available to treat this syndrome.

*Postpartum AKI* is generally related to sepsis, shock, hemorrhage, or amniotic fluid emboli. Complications related to placental catastrophes or uterine hemorrhage can commonly lead to acute tubular necrosis, and pregnant women are almost uniquely vulnerable to acute cortical necrosis (14), which is likely to leave the patient dependent on renal replacement therapy, or occasionally with substantial CKD.

## Management

Acute kidney injury profoundly risks the outcome of pregnancy. Mortality rates and other complication rates remain high. It is key to make an appropriate diagnosis and to treat the underlying disorder. Volume and electrolytes should be optimally controlled, and medications should be adjusted to estimated levels of renal function. General measures such as maintaining nutrition and physical conditioning may also be important. The immediate indications for dialysis are the same as for the nonpregnant patient in terms of fluids and electrolyte control and preventing complications of uremia. However, there is some controversy regarding the best time to begin prophylactic dialysis. Registries, at least for chronic kidney disease, suggest that aggressive control of azotemia results in better fetal and maternal outcomes. Experts suggest starting dialysis when the urea levels are only modestly elevated and maintaining them at less than 60 mg/dL (3). No controlled trial is available, to our knowledge, but the physician should likely be prepared to start dialysis early and maintain effective doses when pregnancy continues (4). For postpartum patients, there is no evidence to support dosing their dialysis differently than for other patients with AKI.

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**Table 1. Differential of acute kidney injury in pregnancy based on physiology and timing**

| EARLY | LATE | POSTPARTUM |
|---|---|---|
| **Prerenal** | **Prerenal** | **Prerenal** |
| Hyperemesis gravidum | Bleeding | Bleeding |
| **Postrenal** | Acute fatty liver of pregnancy | Medication side effects |
| Rare | **Postrenal** | **Postrenal** |
| **Intrarenal** | Obstruction from stones | Retained clots |
| Chronic kidney disease progression | Obstruction from uterus | **Intrarenal** |
| Autoimmune disease, glomerulonephritis | **Intrarenal** | Hemolytic uremic syndrome |
| Complications of hemorrhage, sepsis, urinary tract infection, stones | Chronic kidney disease progression | Severe pre-eclampsia |
| Familial hemolytic uremic syndrome/TTP | Severe pre-eclampsia/ hemolysis, elevated liver enzymes, low platelets syndrome | Chronic kidney disease progression |
| Anticardiolipin antibody syndrome | Acute fatty liver of pregnancy | Acute tubular necrosis from sepsis, hemorrhage |
| | Hemolytic uremic syndrome/TTP | |
| | Autoimmune glomerulonephritis, postinfectious glomerulonephritis | |
| | Pyelonephritis | |