Published in final edited form as:

Adv Chronic Kidney Dis. 2020 November ; 27(6): 455–460. doi:10.1053/j.ackd.2020.06.002.

Acute kidney injury in pregnancy

Elizabeth Taber-Hight¹, Silvi Shah²

¹Division of Nephrology and Hypertension, Indiana University, Indianapolis, Indiana, United States

²Division of Nephrology Kidney C.A.R.E. Program, University of Cincinnati, Cincinnati, Ohio, United States

Abstract

Acute kidney injury (AKI) in pregnancy is a public health problem and a significant cause of maternal and fetal morbidity and mortality. Pregnancy-related AKI is associated with worsening of kidney function resulting in chronic kidney disease and end-stage kidney disease, increased risk of adverse cardiovascular events, higher health care utilization, and longer hospital and intensive care unit stays. The incidence of pregnancy-related AKI has increased in the developed countries, theorized to be the result of an increase in pregnancies in advanced maternal age, and continues to remain higher in developing countries due to inadequate antenatal care and higher frequency of septic abortions. Causes of pregnancy-related AKI can be classified by pregnancy trimester. While hyperemesis gravidarum is a common cause of pregnancy-related AKI during the first trimester; complications like preeclampsia, hemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome, acute fatty liver disease of pregnancy, thrombotic thrombocytopenic purpura, and hemolytic uremic syndrome are important causes of AKI later in the pregnancy. Diagnosis of pregnancy-related AKI can be difficult due to lack of diagnostic criteria and overlapping clinical features between various causes. Kidney biopsy should be considered when the laboratory evaluation for AKI is non-diagnostic, and a definitive diagnosis will help to facilitate appropriate treatment outweighing the risks of biopsy. Management of AKI in pregnancy should be done by a multidisciplinary team consisting of nephrologists, obstetricians, and neonatologists to ensure best possible maternal and fetal outcomes. General measures to treat pregnancy-related AKI include identification of the underlying cause of kidney injury, intravenous fluid resuscitation, timely initiation of dialysis if needed, and prompt fetal delivery, if necessary. Specific treatment includes steroid and immunosuppressive therapy for glomerulonephritis, prompt delivery for severe preeclampsia, HELLP syndrome and acute fatty liver of pregnancy, and plasmapheresis and eculizumab for thrombotic microangiopathies like thrombotic thrombocytopenic purpura, and atypical hemolytic uremic syndrome. In this review, we discuss the various causes of AKI in pregnancy, diagnostic approaches, complications, and the specific treatment strategies of pregnancy-related AKI.

Corresponding Author: Silvi Shah, MD, MS, Assistant Professor of Medicine, Division of Nephrology, University of Cincinnati, 231 Albert Sabin Way, MSB 6112, Cincinnati, Ohio 45267, Phone: 513-558-0668, Fax: 513-5584309, shah2sv@ucmail.uc.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Disclosures: The Taber-Hight has no conflicts of interest. Dr. Shah is an associated editor for ACKD.

Introduction

Acute kidney injury (AKI) during pregnancy is a public health problem and is a significant cause of maternal and fetal morbidity and mortality.¹ Furthermore, AKI is associated with a decline in kidney function resulting in chronic kidney disease (CKD) and end-stage kidney disease (ESKD), increased risk for adverse cardiovascular events, higher health care utilization, and longer hospital stays.^{2,3} Therefore, early recognition and treatment for AKI in pregnancy are of paramount importance and a potentially life-saving measure.

Although the incidence in pregnancy-related AKI is low in developed countries due to improved prenatal care, the rates have increased almost three-fold in the recent decade in the United States possibly due to older maternal age with more comorbidities, higher detection rates of AKI, increase in the incidence of hypertensive disorders of pregnancy, and increase in obesity rates.^{4,5} A recent study identified 42,190,790 pregnancy-related hospitalizations in the United States in women aged 15–49 years old and showed an increase in the rate of AKI during pregnancy-related hospitalizations from 0.04% in 2006 to 0.12% in 2015.⁵ Similarly, Mehrabadi et al reported an increase in the incidence of AKI in pregnancy from 2.4 per 10,000 deliveries in 1999–2001 to 6.3 per 10,000 deliveries in 2010–2011.⁶ In contrast, although developing countries report an overall reduction in pregnancy-related AKI in the recent years, pregnancy-related AKI rates continue to remain higher than in the developed countries due to lack of antenatal care and higher frequency of septic abortions. For example, in India, there was a decline in pregnancy-related AKI from 15% in the 1980s to 1.5% in the 2010s among hospitalized women.¹ Similarly, a study from China showed a decline in the incidence of pregnancy-related AKI ranging from 0.2% to 1.8%.⁷ Significant racial differences have been reported in the occurrence of AKI during pregnancy in the United States with black women having a 52% higher likelihood of AKI during pregnancy and Native American women having a 45% higher likelihood of AKI during pregnancy, as compared to white women.⁵ These racial differences in pregnancy-related AKI are significant, and are likely attributed to the differential access to obstetric care and level of education.

While AKI in the general population is well defined by the RIFLE (Risk, Injury, Failure, Loss and End stage) criteria, the KDIGO (Kidney Disease Improving Outcomes) guidelines and the AKI Network (AKIN) criteria, pregnancy-related AKI is difficult to determine due to non-validation of these AKI diagnostic criteria in the pregnant population.^{8,9} Pregnancy results in an increase in blood volume, a decrease in systemic vascular resistance, and an increase in cardiac output. In the setting of hyperfiltration, intrarenal vasodilation and an increase in effective plasma flow, glomerular filtration rate increases by 40–60%, resulting in a physiological reduction in serum creatinine.¹⁰ The normal level of serum creatinine in pregnancy is lower than the baseline usually ranging between 0.4 and 0.6 mg/dL range. Due to the lower baseline creatinine in pregnancy, the detection of AKI is further confounded.¹¹ Often, a serum creatinine value is unavailable prior to pregnancy. This, along with limited accuracy of the current AKI diagnostic criteria in the general population, makes the early and accurate diagnosis of AKI in pregnancy challenging. Since routine monitoring of kidney function is not a standard of care in pregnant women, a comprehensive assessment of AKI, including differentials, is warranted.

Causes of acute kidney injury during pregnancy

Like the general population, the causes of AKI in pregnant women can be divided into three groups: prerenal, intrarenal, and postrenal causes. Age of gestation and clinical presentation are important determinants of AKI in a pregnant woman (Table 1). In the first trimester, due to hormonal variations, women commonly experience “morning sickness” with an increase in nausea and vomiting as well as poor appetite. Hyperemesis gravidarum, with the associated volume depletion, can result in AKI. Septic abortion is another common cause of AKI, especially in developing countries, and can lead to acute tubular necrosis. Although rare, women may experience a *denovo* or a flare of glomerulonephritis such as lupus nephritis during pregnancy. Placental rupture and hemorrhage are other causes of prerenal AKI, while posing a considerable risk for maternal mortality. Due to the hypercoagulable nature of pregnancy, women have a high risk of acute cortical necrosis in the setting of severe hypotension. During the second and third trimesters, the causes of AKI are more specific to an isolated pregnancy-related complication. These include preeclampsia, hemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome, acute fatty liver of pregnancy (AFLP), thrombotic microangiopathies like thrombotic thrombocytopenic purpura (TTP) and atypical hemolytic uremic syndrome (aHUS), and urinary tract infection and pyelonephritis. Post-obstructive AKI is more common in the second and third trimester due to the growing uterus directly compressing the nearby ureters.^{1,11} We describe below the important causes of AKI during pregnancy.

Preeclampsia

Preeclampsia affects 5–8% of pregnancies and accounts for 15–20% of pregnancy-related AKI. Diagnosis of preeclampsia is made by the new onset of hypertension after 20 weeks of gestation in a previously normotensive woman. Hypertension is defined by blood pressure 140/90 mm Hg on two occasions 4 hours apart, or 160/110 mm Hg within a shorter interval, and proteinuria 300-mg/24-hour urine or spot urine protein creatinine ratio 0.3g (dipstick 1+). Of note, preeclampsia can be diagnosed in the absence of proteinuria if any of the following signs of end-organ dysfunction are present: elevated serum creatinine > 1.1 mg/dl or doubling of serum creatinine in the absence of other kidney disease, thrombocytopenia (< 100,000/microliter), elevated liver transaminases two times normal, pulmonary edema or, cerebral/visual symptoms. A subset of patients, about 40–50% will experience preeclampsia with severe features, which is defined as systolic blood 160 mmHg or diastolic blood pressure 110 mmHg and proteinuria or systolic blood pressure 140 mm Hg systolic or diastolic blood pressure of 90 mmHg with or without proteinuria but with the presence of end-organ dysfunction.^{12–14}

Among women with preeclampsia, the glomerular filtration rate decreases by only 30% to 40%, which causes a small increase in serum creatinine.¹⁵ A prospective observational multicenter study of 157 women admitted with preeclampsia in South Africa showed AKI was common in women with preeclampsia and was associated with higher maternal and perinatal mortality. Of the study cohort, 15.3% met AKI criteria: 6.9% stage 1, 4.3% stage 2, and 4.1% stage 3, and only two-thirds of women with AKI recovered their kidney recovery. Hypertension in a previous pregnancy had a 2.2 fold higher odds of AKI stage 2 or 3.¹⁶

Preeclampsia can be difficult to distinguish from progression of CKD in patients with preexisting kidney disease due to overlapping clinical features. The rate of decline of kidney function, as well as worsening of proteinuria, may prove to be helpful for the diagnosis of preeclampsia. Additionally, maternal serum levels of soluble angiogenic factors soluble fms-like tyrosine kinase-1 and placental growth factor may be utilized to distinguish between preeclampsia and CKD. Rolfo et al showed that women with preeclampsia had a significant increase in soluble fms-like tyrosine kinase-1 levels, increase in serum levels of placental growth factor, and an increase in soluble fms-like tyrosine kinase-1 to placental growth factor ratio (median 436) as compared to women with CKD (median 4).¹⁷

HELLP syndrome

HELLP syndrome is defined by the acronym: hemolysis, elevated liver enzymes, and low platelets. Hypertension and proteinuria are frequently, although not exclusively, associated with HELLP syndrome. AKI occurs in 3–15% of patients with HELLP syndrome. Typically, even severe AKI in HELLP syndrome has a high likelihood of kidney recovery of up to 80%.¹⁸ AKI is often multifactorial and, in addition to the kidney changes characteristic of preeclampsia, there is associated coagulopathy, resulting in bleeding and acute tubular necrosis. HELLP syndrome is considered a thrombotic microangiopathy like syndrome due to occurrence of thrombocytopenia, hemolysis, and AKI. Like TTP and HUS, kidney biopsies of women with HELLP syndrome may occasionally display findings of thrombotic microangiopathy, but commonly show manifestations consistent with acute tubular necrosis.¹⁵

Acute fatty liver of pregnancy

Acute fatty liver of pregnancy (AFLP) as a cause of AKI in pregnancy is on the rise. AFLP is diagnosed later in the pregnancy, mostly after 30 weeks. The pathogenesis in 20% of cases of AFLP is secondary to fetal long-chain 3-hydroxyacyl CoA dehydrogenase deficiency which leads to accumulation of fetal free fatty acids that crosses the placenta and results in hepatotoxicity to the mother. Women usually present in the third trimester with nonspecific symptoms of nausea, vomiting, and abdominal pain. Many laboratory findings of AFLP overlap with HELLP syndrome and preeclampsia such as hepatic derangements, but AKI is more common in AFLP, being present in 20–100% of women. AKI in AFLP usually manifests similarly to hepatorenal syndrome, due to presence of liver failure, ascites and peripheral vasodilation. Elevated creatinine has shown to be an independent predictor of maternal mortality in HELLP syndrome. Swanson Criteria, defined by clinical symptoms and laboratory derangements of encephalopathy, hyperbilirubinemia, abdominal ascites, hypoglycemia, and micro vesicular steatosis on liver biopsy, can differentiate AFLP from HELLP syndrome/preeclampsia. Management is expectant delivery, platelet transfusion prior to delivery if platelet count less than 40,000 per microliter, and evaluation for liver transplant in severe cases.^{18–20}

Thrombotic microangiopathies

Thrombotic microangiopathies like TTP and atypical HUS (aHUS) are rare causes of AKI in pregnancy and are associated with high morbidity. Most commonly, TTP is associated with ADAMTS13 (von Willebrand factor protease) deficiency. ADAMTS13 levels tend to decline as the pregnancy progresses, and as such, TTP is usually seen in the second and third trimesters. Diagnostic criteria for TTP includes thrombocytopenia, schistocytosis, neurologic manifestations and absence of coagulation abnormalities typically found in disseminated intravascular coagulation. Severe AKI is seen in up to 10% of patients with TTP during pregnancy. Further along the spectrum of pregnancy is aHUS as a cause of pregnancy-related AKI. aHUS is typically diagnosed in the postpartum period and is more common in multiparous women. Thrombotic microangiopathy of aHUS is commonly associated with a complement dysregulation and uncontrolled activation which results in complement induced endothelial damage. aHUS is characterized by microangiopathic hemolytic anemia, thrombocytopenia, and decreased kidney function. The diagnosis of pregnancy-associated aHUS may be challenging and can have overlapping features with TTP and severe preeclampsia with HELLP syndrome. While TTP is seen mostly in the third trimester, aHUS commonly present during the postpartum period. Plasma exchange should be started when TTP or aHUS is suspected while waiting for the ADAMTS13 levels. Additionally, eculizumab for the treatment of aHUS has been beneficial. A kidney biopsy can be considered if the AKI is not resolving despite appropriate treatment.^{7,21}

Risk of maternal and fetal complications with pregnancy-related AKI

AKI in pregnancy is associated with adverse maternal and fetal outcomes. A metanalysis by Liu et al examined 845 pregnancies in 834 women with pregnancy-related AKI and 5387 pregnancies in 5334 women without AKI and showed women with pregnancy-related AKI had higher rates of maternal deaths (13.3% vs. 4.2%), and a longer intensive care unit stay of 2.1 days than did women without pregnancy-related AKI. Pregnancy-related AKI was also associated with a 1.5-fold higher likelihood of cesarean deliveries, a 1.3-fold high likelihood of hemorrhage, a 1.9-fold higher likelihood of HELLP syndrome, and a 2.0-fold higher likelihood of placental abruption.²² A recent study from the United States reported a 13.5-fold higher likelihood of inpatient mortality and a 10-fold higher likelihood of cardiovascular events with pregnancy-related AKI hospitalizations as compared to hospitalizations with no AKI. Of all pregnancy-related AKI hospitalizations, 8.9% required acute dialysis. As compared to non-AKI pregnancy-related hospitalizations, pregnancy-related AKI requiring acute dialysis was associated with a 32-fold higher adjusted odds.⁵ AKI during pregnancy increases the risk of progression to chronic kidney disease and ESKD. About 2.4% of women with pregnancy-related AKI progress to ESKD needing dialysis.²² A Canadian study showed that 1 in 10000 pregnancies were complicated by AKI needing dialysis and 3.9% remained on dialysis four months after delivery. Women with pregnancy-related AKI needing dialysis initiation had a 3.4 fold higher risk of low birth weight, small for gestational age, or preterm birth as compared to the general population.²³ Pregnancy-related AKI is associated with a lower mean gestational age at delivery (−0.70 week), lower mean birth weight (−740 grams), and a 3.4-fold higher likelihood of stillbirths and perinatal deaths as compared to women without pregnancy-related AKI.²² Since routine

monitoring of serum creatinine is not done prior to or during pregnancy, there is a need for continued research on early recognition and treatment of AKI. Early identification of AKI in pregnancy may reduce fetal and maternal mortality and lessen the risk of developing ESKD later in life.

Diagnosis of AKI in pregnancy

The diagnosis of AKI in pregnancy is not standardized in clinical practice due to inconsistency in the definition of pregnancy-related AKI and non-validation of the KDIGO (Kidney Disease Improving Outcomes) guidelines, RIFLE (Risk, Injury, Failure, Loss and End-stage) and the AKIN (Acute Kidney Injury Network) criteria for the non-pregnant population in pregnant women.^{8,9} Furthermore, detection AKI is confounded by the physiological lowering of serum creatinine due to glomerular hyperfiltration in pregnancy. For instance, an increase in serum creatinine concentration by 0.4 mg/dl, consistent with stage 1 in the AKIN criteria, may point towards significant kidney injury. Currently, there are no distinct criteria for the diagnosis of AKI in pregnancy. Attention should be paid to trends in serum creatinine levels in pregnancy, and even small changes in creatinine are sensitive in picking up early kidney injury in specific clinical settings. For example, in a woman with new onset hypertension, concomitant increase in serum creatinine by 0.3 mg/dl with increases in liver enzymes and thrombocytopenia, represents AKI and requires close follow of kidney function.²⁴ Initial evaluation for AKI should start with a comprehensive review of the patient's history of CKD, chronic hypertension, diabetes, preeclampsia in prior pregnancies, systemic lupus erythematosus, and preexisting glomerular diseases. The onset of AKI during pregnancy by trimester can point towards the underlying etiology. While hyperemesis gravidarum and septic abortions are common causes of AKI in the first trimester, majority of AKI occurring in the second and trimester are specific to a pregnancy complication of preeclampsia, HELLP syndrome, AFLP, thrombotic microangiopathies like TTP, and placental abruption. Atypical HUS and NSAID's induced kidney injury are common causes of AKI in the postpartum period. Diagnostic evaluation should include urinalysis, urine microscopy, comprehensive metabolic panel, coagulation panel, and appropriate serological workup along with a thorough review of medications. Serum complement levels can be elevated in pregnancy due to increased synthesis by the liver and can complicate the diagnosis of lupus nephritis. Kidney ultrasound should be performed to rule out post-obstructive causes of AKI, such as pathological hydronephrosis. Pathological hydronephrosis should be differentiated from physiological hydronephrosis. Due to the hypercoagulable state of pregnancy, ultrasound with doppler should be performed if there is a high suspicion for the embolic disease. Common causes of AKI in the second and third trimester like preeclampsia, HELLP syndrome, TTP, aHUS, AFLP, and lupus nephritis can have overlapping features and requires detailed evaluation.²⁴ Kidney biopsy should be considered when the laboratory evaluation for AKI is non-diagnostic, and a definitive diagnosis will help facilitate appropriate treatment outweighing the risks of biopsy. The decision to perform a kidney biopsy is based on gestation age, available treatment options, and viability of pregnancy. Since late-term pregnancy biopsies have a higher risk of complication, notably after 25 weeks, it is recommended to biopsy in the first and second trimesters, and best to avoid in the third trimester unless treatment of AKI leads to

improvement in maternal and fetal outcomes.²⁵ Depending on fetal maturity, and the impact of declining kidney function on fetus and mother, early delivery should be weighed and offered when feasible. Delivery prior to biopsy may be a more prudent option for the late-term pregnancies, especially if the fetus has reached viability. Complications and risks should be thoroughly discussed with the patient, including the risk of major bleeding requiring transfusion, embolization, severe obstetric complications, early preterm delivery, and fetal death.^{4,26} Women at high risk for developing an AKI should be evaluated in the postpartum period with regular monitoring of blood pressure, kidney function, and proteinuria. This includes women with CKD prior to pregnancy, as well as those who developed preeclampsia during pregnancy. aHUS is usually diagnosed postpartum, and when suspected, laboratory work including complement levels should be completed during hospitalization. Hemodynamic monitoring in high-risk pregnancies should be performed during follow-up visit as postpartum derangements may be associated with developing postpartum cardiomyopathy or HUS.¹⁵

Management of AKI in pregnancy

Management of AKI in pregnancy should be done by a multidisciplinary team consisting of nephrologists, obstetricians, and neonatologists. General measures to treat pregnancy-related AKI include identification of the underlying cause of kidney injury, intravenous fluid resuscitation, timely initiation of dialysis if needed, and prompt delivery of fetus, if necessary. Intravenous fluid resuscitation is critical with prerenal causes of AKI but should be performed with caution due to the risk of developing pulmonary edema in women with preeclampsia or endotoxin-mediated injury. The treatment for other complications of kidney injury is similar to non-pregnant patients, for instance, use of alkali therapy for metabolic acidosis, loop diuretics for volume overload, blood transfusion for anemia, and potassium binders for hyperkalemia. Since pregnancy is a state of physiological respiratory alkalosis, arterial or venous blood gas should be used to diagnose metabolic acidosis along with a comprehensive metabolic panel. The specific treatment of AKI depends on the underlying cause of the injury. Treatment for glomerulonephritis includes steroid and immunosuppressive therapy, and risk and benefits should be weighted when therapy is initiated in a pregnant woman.⁴ Antimetabolites, such as mycophenolate mofetil are contraindicated during pregnancy due to teratogenicity. Low dose steroids may be used during pregnancy but warrant monitoring for the development of gestational diabetes. Azathioprine and calcineurin inhibitors (cyclosporine and tacrolimus) are not teratogenic and commonly used immunosuppressive drugs in pregnancy. During pregnancy, higher doses of tacrolimus and cyclosporine are needed to achieve therapeutic targets, and therefore frequent monitoring of drug trough levels should be done.²⁷

Treatment of severe preeclampsia, HELLP syndrome and AFLP, require prompt delivery of the fetus. Glucocorticoids are administered if delivery is performed prior to 34 weeks of gestation to decrease the risk of neonatal respiratory distress syndrome. Treatment of the thrombotic microangiopathies, including TTP, and atypical HUS, includes plasmapheresis and eculizumab (for aHUS). In ADAMTS13-deficient TMA, the goal is to regain enzymatic activity through plasma exchange, and if plasma exchange is unsuccessful, rituximab is an option for treatment. Rituximab is a B-cell depleting monoclonal antibody and provides

short-term benefits with a reduced hospital stay, decreased plasma exchange requirements, and lower rates of relapse. Rituximab in pregnancy-related TMA should be used with caution. While fetal toxicity (thrombocytopenia, neutropenia, and B-cell depletion) was seen in <10% of neonates and short-term outcomes were promising, no long-term assessment of rituximab safety in neonates is available.¹⁵

Conclusion

The rates of pregnancy-related AKI have increased in the recent decade in the United States and AKI continues to remain a frequent complication of pregnancy. Pregnancy-related AKI is associated with high maternal mortality and adverse maternal and fetal outcomes.

Regular monitoring of kidney function should be done by kidney health providers during pregnancy, especially in women who are at higher risk. Since, diagnosis of AKI during pregnancy may not be straight-forward, clinical judgment should be used to identify AKI promptly and initiate appropriate therapy to optimize recovery. Pregnancy-related AKI require a multidisciplinary team for best practices and management of pregnant women and to improve maternal and fetal outcomes. Pregnancy-related AKI continues to remain underrecognized and therefore needs continued exploration to ensure that long-lasting effects, including development of chronic kidney disease and need for kidney replacement therapy, are minimized.

Funding

Silvi Shah is supported by the by the National Center for Advancing Translational Sciences of the National Institutes of Health CT2 grant, under Award Number 2UL1TR001425-05A1, intramural funds from the Division of Nephrology, University of Cincinnati and the Dialysis Clinic, Inc. (DCI) grant S-2719. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

References

1. Rao S, Jim B. Acute Kidney Injury in Pregnancy: The Changing Landscape for the 21st Century. *Kidney international reports*. 2018;3(2):247–257. [PubMed: 29725629]
2. Chawla LS, Amdur RL, Shaw AD, Faselis C, Palant CE, Kimmel PL. Association between AKI and long-term renal and cardiovascular outcomes in United States veterans. *Clinical journal of the American Society of Nephrology : CJASN*. 2014;9(3):448–456. [PubMed: 24311708]
3. Thakar CV, Christianson A, Himmelfarb J, Leonard AC. Acute kidney injury episodes and chronic kidney disease risk in diabetes mellitus. *Clinical journal of the American Society of Nephrology : CJASN*. 2011;6(11):2567–2572. [PubMed: 21903988]
4. Gonzalez Suarez ML, Kattah A, Grande JP, Garovic V. Renal Disorders in Pregnancy: Core Curriculum 2019. *American journal of kidney diseases : the official journal of the National Kidney Foundation*. 2019;73(1):119–130. [PubMed: 30122546]
5. Shah S, Meganathan K, Christianson AL, Harrison K, Leonard AC, Thakar CV. Pregnancy-Related Acute Kidney Injury in the United States: Clinical Outcomes and Health Care Utilization. *Am J Nephrol*. 2020;51(3):216–226. [PubMed: 32045905]
6. Mehrabadi A, Dahhou M, Joseph KS, Kramer MS. Investigation of a Rise in Obstetric Acute Renal Failure in the United States, 1999–2011. *Obstetrics and gynecology*. 2016;127(5):899–906. [PubMed: 27054929]
7. Liu YM, Bao HD, Jiang ZZ, Huang YJ, Wang NS. Pregnancy-related Acute Kidney Injury and a Review of the Literature in China. *Internal medicine (Tokyo, Japan)*. 2015;54(14):1695–1703.

8. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P. Acute renal failure - definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. *Crit Care*. 2004;8(4):R204–212. [PubMed: 15312219]
9. Mehta RL, Kellum JA, Shah SV, et al. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. *Crit Care*. 2007;11(2):R31. [PubMed: 17331245]
10. Davison JM, Dunlop W. Renal hemodynamics and tubular function normal human pregnancy. *Kidney Int*. 1980;18(2):152–161. [PubMed: 7003196]
11. Vijayan M, Avendano M, Chinchilla KA, Jim B. Acute kidney injury in pregnancy. Current opinion in critical care. 2019;25(6):580–590. [PubMed: 31524717]
12. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. *Obstetrics and gynecology*. 2013;122(5):1122–1131. [PubMed: 24150027]
13. Mustafa R, Ahmed S, Gupta A, Venuto RC. A comprehensive review of hypertension in pregnancy. *Journal of pregnancy*. 2012;2012:105918. [PubMed: 22685661]
14. Shah S, Gupta A. Hypertensive Disorders of Pregnancy. *Cardiology clinics*. 2019;37(3):345–354. [PubMed: 31279428]
15. Fakhouri F, Vercel C, Fremeaux-Bacchi V. Obstetric nephrology: AKI and thrombotic microangiopathies in pregnancy. *Clinical journal of the American Society of Nephrology : CJASN*. 2012;7(12):2100–2106. [PubMed: 22879435]
16. Conti-Ramsden FI, Nathan HL, De Greeff A, et al. Pregnancy-Related Acute Kidney Injury in Preeclampsia: Risk Factors and Renal Outcomes. *Hypertension (Dallas, Tex : 1979)*. 2019;74(5):1144–1151.
17. Rolfo A, Attini R, Nuzzo AM, et al. Chronic kidney disease may be differentially diagnosed from preeclampsia by serum biomarkers. *Kidney Int*. 2013;83(1):177–181. [PubMed: 23014459]
18. Ye W, Shu H, Yu Y, et al. Acute kidney injury in patients with HELLP syndrome. *Int Urol Nephrol*. 2019;51(7):1199–1206. [PubMed: 30989565]
19. Vigil-De Gracia P. Acute fatty liver and HELLP syndrome: two distinct pregnancy disorders. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*. 2001;73(3):215–220.
20. Tran TT, Ahn J, Reau NS. ACG Clinical Guideline: Liver Disease and Pregnancy. *Am J Gastroenterol*. 2016;111(2):176–194; quiz 196. [PubMed: 26832651]
21. Fakhouri F, Roumenina L, Provot F, et al. Pregnancy-associated hemolytic uremic syndrome revisited in the era of complement gene mutations. *Journal of the American Society of Nephrology : JASN*. 2010;21(5):859–867. [PubMed: 20203157]
22. Liu Y, Ma X, Zheng J, Liu X, Yan T. Pregnancy outcomes in patients with acute kidney injury during pregnancy: a systematic review and meta-analysis. *BMC pregnancy and childbirth*. 2017;17(1):235. [PubMed: 28720086]
23. Hildebrand AM, Liu K, Shariff SZ, et al. Characteristics and Outcomes of AKI Treated with Dialysis during Pregnancy and the Postpartum Period. *Journal of the American Society of Nephrology : JASN*. 2015;26(12):3085–3091. [PubMed: 25977311]
24. Jim B, Garovic VD. Acute Kidney Injury in Pregnancy. *Seminars in nephrology*. 2017;37(4):378–385. [PubMed: 28711077]
25. Day C, Hewins P, Hildebrand S, et al. The role of renal biopsy in women with kidney disease identified in pregnancy. *Nephrol Dial Transplant*. 2008;23(1):201–206. [PubMed: 17720987]
26. Piccoli GB, Daidola G, Attini R, et al. Kidney biopsy in pregnancy: evidence for counselling? A systematic narrative review. *BJOG : an international journal of obstetrics and gynaecology*. 2013;120(4):412–427. [PubMed: 23320849]
27. Shah S, Verma P. Overview of Pregnancy in Renal Transplant Patients. *International journal of nephrology*. 2016;2016:4539342. [PubMed: 28042483]

Clinical Summary

1. Acute kidney injury (AKI) during pregnancy is an important cause of maternal and fetal morbidity and mortality. Hyperemesis gravidarum is a common cause of pregnancy-related AKI during the first trimester, and complications like preeclampsia, hemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome, acute fatty liver disease of pregnancy, thrombotic thrombocytopenic purpura, and hemolytic uremic syndrome are causes of AKI later in the pregnancy.
2. Diagnosis of pregnancy-related AKI is challenging due to lack of diagnostic criteria and a kidney biopsy should be considered when the laboratory evaluation for AKI is non-diagnostic, and a definitive diagnosis will help to facilitate appropriate treatment outweighing the risks of biopsy.
3. General measures to treat AKI during pregnancy include identification of the underlying cause of kidney injury, intravenous fluid resuscitation, timely initiation of dialysis if needed, and prompt delivery of fetus, if necessary. We recommend the management of AKI in pregnancy by a multidisciplinary team consisting of nephrologists, obstetricians, and neonatologists.

Table 1.

Differential causes for acute kidney injury in pregnancy

Causes of AKI in pregnancy	Timing in pregnancy	Signs and symptoms	Cause of AKI	Treatment options
Hyperemesis gravidarum	First trimester	Intractable nausea, vomiting	Volume depletion, possible acute tubular necrosis	Oral hydration, intravenous hydration if necessary
Septic abortion	First trimester	Fever, abdominal pain	Septic acute tubular necrosis	Broad spectrum antibiotics, surgical removal of products of conception
Preeclampsia/eclampsia	After 20 weeks	New onset hypertension (SBP 140 mmHg and DBP 90 mmHg) and proteinuria	Endothelial damage, coagulopathy/thrombotic microangiopathy, possible acute tubular necrosis	Supportive care, delivery when able, expectant management for preterm pregnancies
Urinary tract infection/acute pyelonephritis	More common after 20 weeks	Flank pain, dysuria, fever, chills	Prerenal AKI secondary to infection, possible acute tubular necrosis	Directed antibiotic therapy
HELLP syndrome	Late second or third trimester	Hemolysis, elevated liver enzymes, low platelets. Can be seen concomitantly with preeclampsia	Endothelial damage, coagulopathy/thrombotic microangiopathy, possible acute tubular necrosis	Delivery when able, imaging for right upper quadrant to rule out hepatic bleeding, hypertension control if severe
Thrombotic thrombocytopenic purpura (TTP)/hemolytic uremic syndrome (HUS)	Usually late second trimester or third trimester for TTP, commonly postpartum for HUS	Hemolytic anemia, thrombocytopenia, neurologic abnormalities	Thrombotic microangiopathy	Plasma exchange +/- rituximab
Acute fatty liver disease of pregnancy	Third trimester	Nonspecific-nausea, vomiting, abdominal pain, hypoglycemia, elevated liver enzymes	Prerenal AKI, possible hepatorenal syndrome appearing picture	Delivery when able, liver transplant if warranted
Lupus nephritis	Delay in pregnancy recommended after 6 months of disease quiescence, kidney manifestations more common postpartum, extrarenal manifestations are more common in second and third trimester	Lupus flare diagnosed with markers of disease activity such as low complement levels, presence of double stranded DNA, and proteinuria	Increased disease activity worsening kidney function	Immunosuppression, continue hydroxychloroquine during pregnancy
Obstructive uropathy	Second and third trimester	Worsening abdominal pain, oliguria	Reflux and obstruction can cause hydronephrosis	Analgesics, increase in fluid intake, stent or percutaneous nephrostomy tube if conservative management unsuccessful
Placental abruption and placental hemorrhage	Third trimester	Increased vaginal bleeding, abdominal pain	Can cause renal cortical necrosis (rare), prerenal AKI from acute blood loss anemia	Control bleeding, supportive care, delivery of infant
Postpartum non-steroidal anti-inflammatory drugs (NSAIDs) use	Postpartum	No specific symptoms, elevated creatinine and bland urine analysis	Worsening prerenal AKI in setting of hypovolemia and NSAIDs induced vasoconstriction	Stop NSAIDs, increase hydration, supportive care

Terms: SBP - systolic blood pressure, DBP - diastolic blood pressure