Kidney stones during pregnancy

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Abstract | Kidney stones affect 10% of people at some point in their lives and, for some unfortunate women, this happens during pregnancy. Pregnancy is a complex state and both physiological and mechanical changes alter risk factors for kidney stone formation. When a pregnant woman develops acute nephrolithiasis, the situation is more complicated than in nonpregnant women. Imaging limitations and treatment restrictions mean that special diagnostic and management algorithms are needed upon presentation. Ultrasonography remains the gold-standard first-line diagnostic imaging modality for kidney stones during pregnancy but several second-line alternatives exist. Acute renal colic during pregnancy is associated with risks to both mother and fetus. As such, these patients need to be handled with special attention. First-line management is generally conservative (trial of passage and pain management) and is associated with a high rate of stone passage. Presentation of obstructive nephrolithiasis with associated infection represents a unique and serious clinical situation requiring immediate drainage. If infection is not present and conservative management fails, ureteroscopy can be offered if clinically appropriate, but, in some circumstances, temporary drainage with ureteral stent or nephrostomy tube might be indicated. Shockwave lithotripsy and percutaneous nephrolithotomy are contraindicated during pregnancy.

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Introduction

Kidney stones affect about 10% of the population, an incidence rate that is steadily rising, with a 40% increase in outpatient hospital visits and a 50% increase in annual expenditure from 1992–2000 according to the Urologic Diseases in America Project.[1–3] Furthermore, stones are associated with a high recurrence rate of up to 50% within 5 years, and are now much more common in the female population.[1–3] A recent study of the National Health and Nutrition Examination Survey (NHANES) database revealed male prevalence to be 10.6% and female prevalence to be 7.1%, a ratio of 1.49:1, whereas it used to be predominantly a disease of middle-aged men.[4] A stone event occurs in 1 out of every 200–1,500 pregnancies, with 80–90% of patients presenting during the second and third trimesters.[5–13] Although the incidence of stones is no higher in pregnant women than in the general nonpregnant female population, a stone event during pregnancy represents a unique clinical situation that poses unique risks to both the mother and the fetus, with specific diagnostic challenges and management strategies.[14,15] In this Review, we discuss risk factors for stone development during pregnancy and consider the diagnostic challenges that acute renal colic poses for these patients. We also highlight potential stone-related complications for the mother and fetus, and specific management recommendations for this unique condition.

Risk factors for stone development

The incidence of nephrolithiasis is steadily increasing among the entire population, presumably owing to increased levels of obesity, environmental changes, and a rise in the incidence of comorbidities such as diabetes mellitus and metabolic syndrome. However, pregnancy has its own unique set of risk factors for kidney stone development. In fact, although the incidence of kidney stones continues to rise for the general population, a recent study from a tertiary care women's hospital suggests that rates of stone incidence have stabilized among the pregnant population.[16] This finding awaits confirmation in further studies, but suggests a unique pathophysiology of stone formation during pregnancy. Indeed, systemic, nephrological, and mechanical changes that occur during pregnancy combine to create an optimal environment for stone formation.

Glomerular filtration rate and renal plasma flow rate rise as a result of increased cardiac output and decreased systemic vascular resistance (which causes increased excretion of filtered loads).[17,18] Levels of calcium, oxalate, uric acid, and sodium are all increased in the urine of pregnant females.[5,17,19–23] This rise in lithogenic factors is joined by a rise in levels of urinary citrate, nephrocalcin, magnesium, glyscosaminoglycans, and uromodulin, all of which act as inhibitors of stone formation.[20,24,25] However, although citrate is an inhibitor of stone formation, it also causes a rise in urinary pH, which can alter the supersaturation point of calcium phosphate crystallization, increasing the risk of calcium phosphate kidney stones.

When combined with the alteration in urinary constituents, urinary stasis promotes stone formation. The static conditions result in longer contact time between the lithogenic factors, enhancing the crystallization process. Hydronephrosis during pregnancy, which occurs in up to 90% of pregnant women, is responsible for this stasis

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Key points

- Pregnancy is a complex physiological state that alters the risk factors for kidney stone formation
- Kidney stones that occur during pregnancy require special diagnostic and management algorithms upon presentation
- Ultrasonography remains the gold-standard first-line diagnostic imaging modality for kidney stones during pregnancy
- First-line management of a kidney stone during pregnancy is conservative, but ureteroscopy might be offered if clinically appropriate or when spontaneous passage fails

and, although it is more common later in pregnancy, can sometimes present in the first trimester.[26] Antenatal hydronephrosis and hydroureter both result from compression of the ureter at the pelvic brim by the growing uterus and smooth muscle relaxation induced by elevated progesterone levels.[27,28] Stasis also increases the risk of infection, which can increase the urinary pH, and 24 h urine studies show that hypercitraturia further elevates the urinary pH during pregnancy.[21] An increase in pH is important as calcium phosphate stone risk increases at an alkaline pH. Indeed, stone composition profiles are different in pregnant and nonpregnant women, with calcium phosphate being the predominant stone type (with an incidence rate of almost 75% in one study) in pregnant women, whereas calcium oxalate is the most common stone type in the general population.[8,14,29–34]

In addition to increased filtration, women also experience increased gastrointestinal absorption and bone mobilization during pregnancy as a result of rising circulating levels of 1,25-dihydroxycholecalciferol (produced by the placenta), further contributing to a state of hypercalciuria.[19,20,35] The kidney also reabsorbs less filtered calcium owing to parathyroid hormone suppression caused by a rise in vitamin D levels.[15,19,20] Two Cochrane analyses, published in 2010 and 2011, demonstrated that calcium supplementation during pregnancy might be beneficial for women who are at risk of developing gestational hypertension and experiencing preeclampsia.[36,37] For women taking ≥1 g of calcium supplementation, this analysis demonstrated a reduction in the risk of hypertension (risk ratio of 0.65) and a twofold decrease in the risk of preeclampsia compared with women taking <1 g calcium supplements, but no significant difference in the risk of preterm birth.

One recent review of the effects of calcium supplementation on hypertension reported a significantly reduced risk of preeclampsia (a major cause of death during pregnancy for both mothers and newborn babies), maternal morbidity and mortality, and preterm birth in the intervention group compared with controls.[38] The investigators also found an increased risk of urolithiasis in the intervention group, although this was not statistically significant. Patients might be taking extra calcium during pregnancy because of these findings, which could be contributing to an increased risk of stones. Furthermore, calcium carbonate is given routinely during pregnancy to relieve the symptoms of reflux, further exacerbating hypercalciuria. The risk of calcium supplementation with respect to kidney stone formation needs to be balanced against the benefits of decreased risk of preeclampsia and hypertension, particularly in pregnant women at high risk of nephrolithiasis, such as those with a personal or family history of kidney stones.

Diagnostic imaging

Noncontrast CT is the gold-standard imaging modality for the evaluation of renal colic in the general population. However, CT emits radiation and is generally avoided during pregnancy because of the potential teratogenic risk associated with exposure, which is particularly high during the first trimester. According to guidelines issued by the American College of Obstetricians and Gynecologists, radiation doses of <50 mGy are safe, with no increased risk of pregnancy loss or fetal anomalies.[15,31] As mean fetal dose of an abdominal and pelvic CT scan is 8 mGy, the judicious use of CT during pregnancy is likely to be safe; however, every effort should be made to minimize radiation exposure in this population. The use of low-dose CT techniques minimizes radiation to the fetus (4 mGy versus 25 mGy) while maintaining high rates of sensitivity and specificity.[39–41] Although this imaging modality is now being used in certain settings, other techniques that do not involve radiation are preferable.

Renal and bladder ultrasonography remains the initial diagnostic modality of choice when a pregnant woman presents with renal colic (Figure 1). Although ultrasonography has a reported specificity of 86%, it has a sensitivity of just 34%.[42,43] In one study of renal colic in pregnant patients, only 60% of stones were identified using ultrasonography.[44] Physiological hydronephrosis during pregnancy, which occurs in up to 90% of patients, often confuses the clinical situation as it can be quite difficult to establish a firm diagnosis if the stone is not visible on ultrasonography.[26–28] Transvaginal ultrasonography can sometimes be used to visualize a distal stone or establish dilation only to the pelvic brim, and might be useful if the diagnosis remains unclear. Plain radiography and intravenous urography can also be used in the evaluation of renal colic and might be more useful when used in conjunction with ultrasonography.[34,45] However, obstruction by the bowel or fetal skeleton (which can obstruct visualization of the urinary tract), radiation exposure, and intravenous contrast limit the usefulness of these diagnostic modalities.[46]

T2-weighted half-fourier single-shot turbo-spin echo (HASTE) magnetic resonance urography (MRU) without contrast has been used for diagnostic imaging of both pregnant and nonpregnant patients with suspected nephrolithiasis.[47–50] MRU, which has a fast acquisition time of about 15 mins (compared with >45 min for traditional MRI), can also be used to evaluate nonurological differential diagnoses (obstetric and gastrointestinal). MRU has similar diagnostic capabilities to CT when evaluating secondary findings of acute obstruction combined with the presence of a stone (seen as a signal void), and can better distinguish between hydronephrosis of pregnancy and obstruction, with presence of dilation only to the pelvic brim suggesting the former. The use of contrast with MRU is unnecessary, although this has been

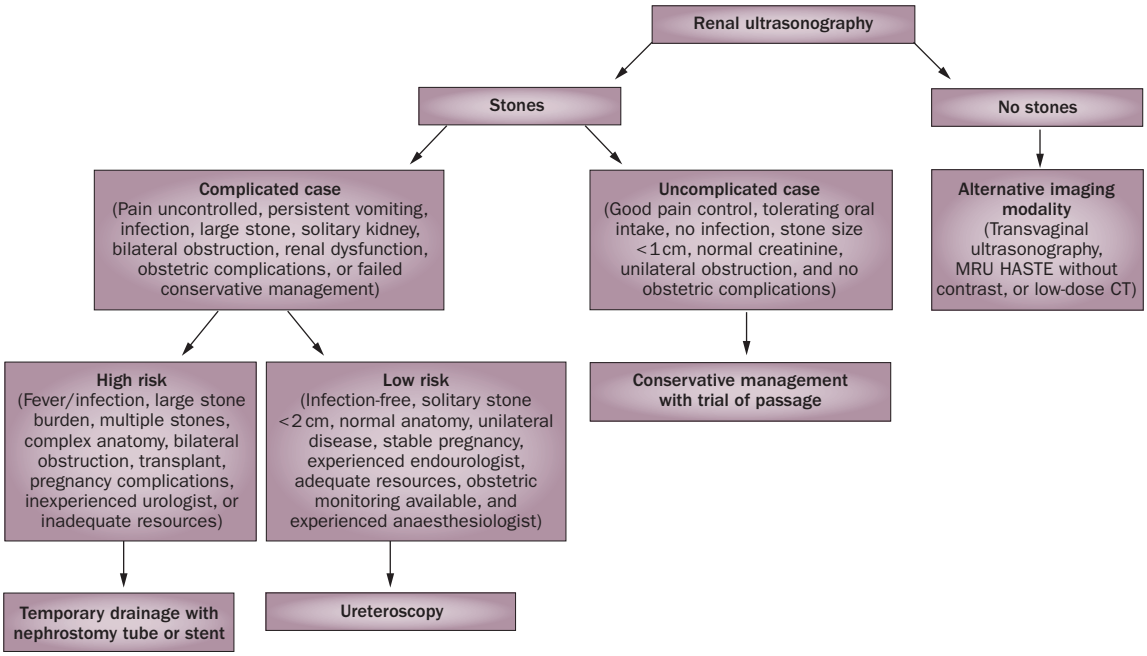

Figure 1 | Algorithm for the diagnosis and management of nephrolithiasis during pregnancy. Renal ultrasonography is the first-line diagnostic modality when a pregnant patient presents with renal colic. If this is nondiagnostic, alternative imaging can be performed, including transvaginal ultrasonography, MRU HASTE, or low-dose CT. Once a pregnant patient is diagnosed with a kidney stone, initial options are conservative management or intervention. Once intervention is deemed necessary, several clinical variables are considered before deciding upon temporary drainage with a stent or nephrostomy tube versus definitive management. Abbreviations: HASTE, half-fourier single-shot turbo-spin echo; MRU, magnetic resonance urography.

reported in some studies.[51–53] The widespread use of MRU is limited by its availability, cost, and the fact that it cannot be used in patients with metallic implants. Claustrophobia is also a limiting factor for some patients. If ultrasonography findings are unclear, MRU is generally used as a second-line imaging modality, as it still avoids radiation and, as discussed above, is reliable for stone evaluation.

As illustration of the diagnostic challenges that present during pregnancy, one recent group reported a total rate of negative ureteroscopy for renal colic to be 14% during pregnancy,[54] but the negative ureteroscopy rate increased to 23% when ultrasonography was used alone to prompt intervention. Rates of negative ureteroscopy for ultrasonography alone, ultrasonography plus low-dose CT, and ultrasonography plus MRU were 23%, 4.2%, and 20%, respectively. By contrast, low-dose CT had the highest positive predictive value (PPV); PPVs for CT, MRU, and ultrasonography were 95.8%, 80%, and 77%, respectively. For all imaging modalities, better diagnostic algorithms are needed to prevent unnecessary intervention. For example, renal ultrasonography should be used as the first-line imaging modality when a pregnant patient presents with renal colic. If findings are nondiagnostic, an alternative imaging modality, such as MRU HASTE or low-dose CT, should be performed before surgery.

Potential complications

Acute renal colic from a kidney stone during pregnancy carries several potential complication risks and is the most common admitting diagnosis that is not related directly to pregnancy.[33,55] Among these potential complications, which have been noted in several small case series and large datasets, are preterm labour, premature rupture of membranes, preterm delivery, pregnancy loss, hypertension, preeclampsia, and infection.[7,9,11,56,57] However, several studies have found no association between stone-related acute renal colic and many of these potential complications including adverse perinatal outcomes.[7,57,58] Reported complication rates range widely (from 0–67%), possibly owing to advances in both obstetric and endourological care, the analysis of data from small case series, and a greater focus on urological data than obstetric data.[34,56,59]

The pregnant state causes several physiological changes that complicate patient care and can result in complications; for example, anaemia is often present during pregnancy. A pregnant patient is also at greater risk for thromboembolic events, as pregnancy is a hypercoagulable state.[15] In addition, pregnancy results in several cardiopulmonary changes, including increased cardiac output, increased oxygen consumption from decreased functional reserve lung capacity, respiratory alkalosis, and increased bicarbonate excretion.[15] These changes need to be considered when caring for the patient, particularly if anaesthesia is necessary.

Management recommendations

As a result of the potential complications associated with kidney stones and the altered physiology that occurs during pregnancy, management of the pregnant patient during an acute stone episode is complex and requires special attention (Figure 1). We recommend a multidisciplinary approach with involvement of a

urologist, obstetrician, radiologist, and neonatologist if necessary. If the patient requires surgical management, an experienced anaesthesiologist should also be involved. As is the case for the general population, expectant management is generally first-line treatment for the pregnant patient passing a stone. Spontaneous passage rates for kidney stones <1 cm range from 70–80%, which is possibly a little higher than in the general population, perhaps owing to increased dilation of the ureter secondary to increased progesterone levels and mechanical compression of the ureters from the enlarged uterus.[8,9,11,34,57,60–62] Of the stones that do not pass during pregnancy, half of them will pass after delivery (usually within the first month).[34] However, data from one recent study suggest that these rates might be an overestimate of the true rates of stone passage owing to erroneous diagnosis and incomplete follow-up data.[63] Additionally, bias might exist in some studies because surgeons are more reluctant to operate on pregnant patients, preferring to wait for spontaneous passage. Regardless of the exact rates, a trial of passage is appropriate provided there are no contraindications such as infection.

Trial of passage should be carried out with adequate pain management and aggressive hydration, as many pregnant patients with stones experience dehydration from nausea and vomiting. As such, narcotics and antiemetics are important components of conservative management. Nonsteroidal anti-inflammatory drugs are generally avoided because of potential teratogenic effects. α-blockers, such as silodosin, tamsulosin, and uroxatral, and calcium channel blockers are classed as category B drugs in pregnancy and are, therefore, thought to be safe, so medical expulsive therapy can also be used.[64] However, pregnant patients should be counselled regarding the use of these medications, as medical expulsive therapy is an off-label indication for these patients (not currently FDA approved for this use). Routine laboratory investigations, ultrasonography, and close observation are required for those who choose this management option.

If the pregnant patient fails conservative management, then intervention is needed. Other reasons for intervention include symptoms of infection such as fever, uncontrolled pain, solitary kidney, bilateral obstructing stones, renal dysfunction, preterm labour, preeclampsia, other obstetric complications, persistent nausea and vomiting, worsening obstruction, stone size of >1 cm, or inability to diagnose the clinical condition.[65] Surgical intervention has only recently become a widely acceptable option for pregnant women within the past 1–2 decades, as this approach was previously thought to involve too much risk to the fetus. Prior to this shift in management approach, drainage with a nephrostomy tube or stent placement was the mainstay of temporary management, with definitive surgical management deferred until after delivery. However, definitive surgical management with ureteroscopy is now an acceptable option and might even be preferable in some situations, including patients who require multiple tube changes before delivery and those who cannot tolerate a stent or nephrostomy tube owing to discomfort.[15,66] Ureteroscopy during pregnancy has been made possible because of the substantial endourological and obstetric advances that have occurred over the past two decades.

It is worth noting that shockwave lithotripsy and percutaneous nephrolithotomy are contraindicated during pregnancy.[67–69] Shockwave lithotripsy can cause miscarriage, congenital malformation, intrauterine growth retardation, and placental displacement.[67,68] Percutaneous nephrolithotomy (PCNL) generally requires longer operative times, is usually performed with the patient in the prone position, is more invasive, and has higher overall complication rates. Also, if fluoroscopy is used, it involves the use of radiation, which is generally avoided during pregnancy, although PCNL can also be performed using ultrasonography guidance alone.

When temporary drainage is indicated or selected, ureteral stent or nephrostomy tube placement are both options. Drainage type will depend on surgeon and patient preference, availability of resources, and clinical scenario. Both require frequent changes (every 4–6 weeks) to minimize the risk of encrustation because of the metabolic changes that occur during pregnancy (increased calcium and uric acid excretion and elevated urine pH). Both stents and tubes can become infected or dislodged, and each cause unique pain symptoms.[70–72] External drainage tubes can be quite bothersome to the patient as it can be quite uncomfortable in the flank region to have an external tube. Additionally, they can be hard to care for, and the patient might have difficulty lying on that side of their body. Stents can cause lower urinary tract symptoms such as frequency, urgency, suprapubic discomfort, and dysuria, as well as flank pressure with voiding. Additionally, temporary drainage prolongs the condition throughout the pregnancy and requires definitive management postpartum at a time when the parent would like to focus on their newborn child. Although these are all disadvantages of temporary decompression over definitive management, there are potential advantages as well. Both stents and tubes can be inserted with minimal anaesthesia under ultrasonography guidance. A nephrostomy tube is almost always successful, results in rapid decompression, avoids ureteral manipulation, and has traditionally been preferred when sepsis is present, although current evidence suggests that ureteral stents are probably equivalent to nephrostomy tubes with respect to outcomes.[15,73,74] A nephrostomy tube can also provide future access for antegrade treatment after delivery if the patient has a large stone burden.

Temporary drainage is preferred and definitive management is contraindicated when the patient has active infection, large stone burden, abnormal anatomy, bilateral stones, transplant kidney, or obstetric complications, or when there are inadequate obstetric, endourological, or anaesthetic resources available to the patient.[66] For all other patients (who are beyond the first trimester), definitive management is a reasonable option. Teratogenic effects and risks of anaesthesia are higher in the first trimester so tubes are generally only placed once the patient has entered the second trimester. A meta-analysis published in 2009 of over 100 patients undergoing ureteroscopy during pregnancy showed it to be safe

and effective approach that offers equivalent complication rates to the nonpregnant female population.[75] Since this meta-analysis was published, several other case series have published supportive findings,[13,14,76–79] all of them retrospective reports with strict patient selection criteria of ureteroscopies performed by experienced surgeons with specialist training.

This shift in patient care is a direct result of advances in the fields of endourology and obstetrics. Urology equipment has become more sophisticated and the urologist's armamentarium has expanded, resulting in lower overall complication rates, increased efficacy, and decreased treatment time. For example, ureteroscopes are now smaller and more flexible, fragmentation and extraction devices are more effective, and visualization systems are more accurate. Ureteroscopy can be performed using ultrasonography alone, or using limited fluoroscopy with the pelvis covered, under spinal, general, or local anaesthesia.[80] Risk of preterm labour is a unique complication that has been reported in several of the above studies; however, this risk is actually very low (0–1% in most studies). Obstetric care has also advanced (for example, with improvements to fetal monitoring), facilitating the treatment of stones during pregnancy. Fetal monitoring throughout the procedure and postoperatively is recommended, and intraoperative and postoperative dynamic decision-making is also important. Careful patient selection, multidisciplinary care by experienced physicians, and resource availability is critical to achieving good outcomes for patients.[15,66,81]

Conclusions

In summary, kidney stones during pregnancy are not uncommon and might occur because of changes in the physiological state of the patient. A kidney stone event in the pregnant state represents a complex clinical scenario that requires careful attention as there are unique risks to mother and fetus. Additionally, evaluation can be challenging as the gold-standard approach for kidney stone diagnosis in the nonpregnant state involves the use of radiation. As such, ultrasonography is the first-line diagnostic modality in pregnant patient but might be inconclusive and secondary alternatives such as MRU HASTE and low-dose CT are often required. First-line management is conservative, with pain control and trial of passage. If this fails, or if there are signs of infection, intervention is necessary. Options for intervention include temporary drainage with delayed stone treatment or definitive management with ureteroscopy, depending on the clinical scenario. If infection is present, definitive management is contraindicated and temporary drainage is required. A multidisciplinary approach is critical for an optimal outcome.

Review criteria

The PubMed and MEDLINE databases were searched for articles published from 1985 to 2013 relating to either kidney stones and pregnancy, or ureteroscopy and pregnancy. Other articles were found by reviewing the reference lists of selected papers.

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Author contributions

Both authors contributed towards researching, writing, editing, reviewing, and discussing this article with colleagues.