Management of Urinary Calculi in Pregnancy: A Review

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ABSTRACT

Nephrolithiasis during pregnancy can represent a clinical dilemma because of potential risks to both mother and fetus. While the incidence of symptomatic nephrolithiasis during pregnancy varies between 1 in 244 to 1 in 2000 pregnancies, the actual incidence is likely to be higher. A significant proportion of patients with asymptomatic renal calculi are detected incidentally in the nonpregnant population compared with pregnant women. Factors that contribute to the diagnostic challenges include anatomic and physiologic changes to the female urinary tract during pregnancy and the limitations on the use of ionizing radiation. The treatment of such patients requires a multidisciplinary team approach involving the urologist, obstetrician, and radiologist. The potential hazards of intervention (either surgical or medical) and anesthesia need to be considered carefully.

INTRODUCTION

NEPHROLITHIASIS in the pregnant patient can be a clinical dilemma because of potential risks to both mother and fetus. The incidence of symptomatic nephrolithiasis during pregnancy varies between 1 in 244 and 1 in 2000 pregnancies. The actual incidence, however, is likely to be higher because a significant proportion of patients have asymptomatic renal calculi that are detected incidentally in the nonpregnant population when compared with pregnant women.¹⁻³

DIAGNOSIS

Diagnostic challenges occur because of such factors as anatomic and physiologic changes to the female urinary tract during pregnancy and the limitations on the use of ionizing radiation.

Anatomic alterations in the urinary tract during pregnancy

Normal anatomic changes within the urinary tract of the pregnant patient may not only predispose to calculi formation but may also pose a diagnostic challenge. Physiologic hydronephrosis can occur in 90% of right kidneys and up to 67% of left kidneys during pregnancy.⁴ The predominance of right

upper tract dilation compared with the left may be caused by a combination of various factors including preferential compression of the right ureter because of uterine dextrorotation and protection of the left ureter by the gas-filled sigmoid colon. It is not uncommon for some pregnant women to experience greater pain relief when placed in the left lateral position.⁵

The mechanical theory (compression of the ureters by the gravid uterus and ovarian vein plexus) is likely to be the most significant cause of dilation.⁶ This is supported by the fact that ureteral dilation is absent below the pelvic brim and also in patients with a pelvic kidney or those who have previously undergone urinary diversion.^{5,7,8} Nulliparous patients have demonstrated a higher incidence of hydronephrosis in some studies presumably because of a better preserved abdominal musculature tone, which results in a greater degree of ureteral compression.^{5,9}

The hormonal theory postulates that circulating progesterone may influence smooth muscle dilation and thereby result in reduced ureteral peristalsis and increased dilation.¹⁰ While hormonal factors may contribute to the early development of gestational hydronephrosis, which is usually evident between 6 and 10 weeks of gestation, mechanical factors remain the major cause. Therefore, ureteral obstruction, dilation, and urinary stasis may aid aggregation of stone microconstituents, ultimately resulting in stone formation. Furthermore, it may be difficult to distinguish typically asymptomatic physiologic hydronephrosis from pathologic hydronephrosis using radiologic techniques.

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Physiologic alterations in the urinary tract during pregnancy

An increase in cardiac output in combination with a decrease in renal vascular resistance results in significant elevations in both glomerular filtration rate (GFR) and renal plasma flow (RPF). By the second trimester, GFR and RPF can increase by 40% to 65% and 50% to 85%, respectively.¹¹ Subsequently, pregnancy is associated with an elevated creatinine clearance (by up to 50%); lowered serum creatinine and urea levels; and higher renal filtration rate of glucose, sodium, calcium, and uric acid (potential stone formation promoters), as well as citrate, magnesium, and glycosaminoglycans (stone formation inhibitors).¹² These physiologic changes may significantly alter the risk of stone formation and will need to be carefully considered in patients undergoing surgery under anesthesia, and affect those taking medications subjected to renal clearance.

Other nonrenal physiologic changes, while not directly influencing stone formation, may be relevant in the treatment of the pregnant patient, especially if invasive intervention is required: *Cardiac*—increased cardiac output by up to 50%; *respiratory*—decreased functional reserve capacity and increased oxygen consumption (therefore increased minute ventilation); *acid-base balance*—relative respiratory alkalosis and a compensatory increase in renal bicarbonate excretion; and *hematologic*—physiologic anemia of pregnancy and hypercoagulable state with increased risk of deep-vein thrombosis.

Excretion of stone-related substrates during pregnancy

Gestational hypercalciuria is secondary to a combination of an increased GFR and therefore increased filtered load of calcium, suppression of parathyroid hormone (causing suppression of tubular calcium resorption), and increased levels of placental 1,25-dihydroxycholecalciferol (which promotes intestinal reabsorption of calcium as well as release of calcium from bone). Serum calcium levels, however, remain unaltered. Similarly, urinary excretion of uric acid and oxalate (both agents known to encourage stone formation) increases in pregnant patients. The cause is not accurately known but is likely to be multifactorial, including increased renal filtration, and dietary and fetal factors.^{13,14}

Even in the presence of conditions that facilitate crystal precipitation and growth, pregnancy is not associated with an increased incidence of urolithiasis.^{15,16} This is most likely because of the limited duration of pregnancy and the significantly increased urinary excretion of substances known to retard stone formation by inhibition of crystal growth and aggregation, such as citrate, magnesium, and glycosaminoglycans.^{12–14}

Demographics

Urolithiasis in pregnant women has a similar incidence to that in nonpregnant women of a comparable age.^{16,17} The average age at presentation is 27 years.^{1,18} Between 80% and 90% of these pregnant women are in their second or third trimester. Stone formation risk is roughly three times higher in multiparous compared with primiparous women.^{16–19} In addition, patients are more likely to be white and have a history of renal disease and hypertension.²

While previously known stone formers have a generally higher chance of recurrent stones, this risk does not appear to manifest itself during pregnancy. Residents in the “stone belt” formed by the southern United States still have a higher incidence of urolithiasis during pregnancy.²⁰ Either side may be affected equally, although gestational hydronephrosis is more common on the right side. Ureteral stones are encountered twice as often as renal calculi.^{18,21} Between 24% and 30% of women have a previous history of stone disease.^{18,22}

Clinical presentation

Two points are worth noting when considering presenting symptoms in the pregnant woman with stones. First, while a patient may complain of classic and unmistakable symptoms of ureteral calculi, concomitant nebulous complaints such as abdominal and visceral discomfort may confuse the clinical picture. Second, the anatomic and physiologic changes occurring within pregnancy may, of themselves, give rise to abdominal/flank pain, nausea, and lower urinary-tract symptoms. A high index of suspicion is mandatory to effect a prompt and correct diagnosis of urolithiasis.

Flank or abdominal pain is the most common symptom; it occurs in 85% to 100% of patients.^{1,7,16,18,20,21,23,24} Patients with stone disease often complain of more severe pain, necessitating more analgesia compared with those with noncalculous pyelonephritis. Inflammatory pathologies that affect the peritoneal contents, such as appendicitis and diverticulitis, may mimic pain secondary to stone disease. In one series, 28% of patients initially received an incorrect diagnosis, with appendicitis, diverticulitis, and placental abruption the most common incorrect diagnoses.¹⁸

Frank hematuria is reported in 15% to 30% of proven cases, and microscopic hematuria can be detected in 95% to 100% of cases, although urinalysis may need to be repeated up to three times.^{18,22} Hematuria may also be secondary to congenital anomalies, tumors, renovascular complications, and endometriosis.²⁵

Lower urinary-tract symptoms may suggest a lower ureteral stone or infection. Nonspecific symptoms, including nausea and vomiting, are present to a varying degree. Other modes of presentation include urinary-tract infection (UTI), pre-eclampsia, and premature onset or arrest of labor.^{2,7,24,26} Effective treatment or spontaneous passage of stone usually results in alleviation of the obstetric emergency.

Laboratory tests

Dipstick analysis of a midstream specimen of urine is mandatory to assess hematuria (almost invariably present in urolithiasis), pyuria (may suggest concomitant infection), and pH (if greater than 7, it may signal the presence of infection stones with an urea-splitting organism; if less than 5, it may be associated with a uric acid stone).

Urine culture and sensitivity may identify the underlying pathogen. Standard serum tests should include complete blood count (to assess anemia and existence of systemic infection); potassium (decreased in renal tubular acidosis, increased in renal failure); urea and creatinine (usually the same or 25% less than in nonpregnant women but may be elevated in renal failure); bicarbonate (decreased in renal tubular acidosis); calcium

(if elevated, may increase stone formation risk); and uric acid (increased levels predispose to both uric acid and calcium stones).

In the report by Stothers and Lee,¹⁸ dipstick or frank hematuria was noted in more than 95% of patients, pyuria in 42%, and uropathogens-positive urine culture in 24%.

Stones passed spontaneously or surgically retrieved should be retained and sent for stone analysis. Metabolic studies in the form of 24-hour urine collection (for measurement of urine volume and urinary concentrations of sodium, potassium, calcium, oxalate, phosphate, uric acid, citrate, and magnesium) are recommended before pregnancy in any patient at high risk of stone recurrence. Because of the physiologic and dietary alterations that accompany pregnancy, however, such investigations ought to be postponed until after delivery.

RADIOLOGIC DIAGNOSIS

The accurate diagnosis of urinary stone disease ideally necessitates radiologic evaluation using ionizing radiation. The most important factor remains the risk of radiation exposure to the fetus, but often the perception of risk is greater than the risk itself.²⁷ Furthermore, inaccurate, missed, or delayed diagnosis may represent a more significant risk to the patient than the radiation risk.

A basic understanding of theoretical effects of ionizing radiation to the fetus is essential when counseling pregnant patients. Studies that involve the survivors of the Nagasaki and Hiroshima atomic bombs, as well as the Chernobyl nuclear reactor accident, have resulted in the classification of fetal effects into four categories.^{28,29} The categories are: intrauterine fetal death, fetal malformation, disturbance of growth and development, and mutagenic and carcinogenic effects.

The risk was also critically dependent on fetal gestational age and radiation dosage.³⁰ Radiation effects can be considered as:

1. Deterministic. Effects become more severe with radiation dose increases. There is a dose threshold for an observed clinical effect (eg, death, growth retardation, and malformations):
 - Preimplantation to week 3 gestation: Embryo most sensitive and likely to result in fetal death.

- Week 3 to week 10: Period of organogenesis and therefore growth malformations most likely.
 - Week 8 to week 15: Risk of fetal mental retardation. Fortunately, first-trimester presentation of urolithiasis is rare.
2. Stochastic. The probability, not the severity, of the effect increases with dose, and no threshold is believed to exist. These effects are commonly believed to affect the fetus in later pregnancy (eg, cancer and genetic effects).
 - Previous reports have suggested that radiation exposure *in utero* may result in a 1.3- to 2-fold increased risk of the development of childhood cancers, such as leukemia and other solid tumors.³⁰⁻³³ Other studies, however, have contradicted these findings, demonstrating no significantly elevated risk after exposure to either diagnostic radiation or the Hiroshima atomic bomb.^{34,35} Heritable genetic effects caused by ionizing radiation are difficult to quantify, given the high background rate of spontaneous mutations. At the low-level radiation doses involved in diagnostic radiology, however, it is unlikely that these result in significant inheritable genetic mutations.³⁶ The National Radiological Protection Board (NRPB) concludes that the majority of radiologic and nuclear medicine procedures in an individual pregnancy present no substantial hazard and carry a risk of less than about 1 in 5000 for fatal childhood cancers (1 in 33,000 per mGy) and less than 1 in 10,000 for induced inheritable diseases (1 in 40,000 per mGy).³⁷

The delivered fetal dose for each procedure does not remain constant but varies according to the precise technique used and maternal body configuration. Fetal exposures of less than 50 mGy have not been reported to cause fetal growth or congenital defects (although this is by no means impossible), and most diagnostic procedures use doses well below this threshold.³⁸ Fetal doses for common diagnostic procedures are given in Table 1.

The American College of Obstetricians and Gynecologists recommends that "Women should be counseled that the X-ray exposure from a single diagnostic procedure does not result in harmful effects." Specifically, exposure to less than 50 mGy has not been associated with an increase in fetal anomalies or pregnancy loss.³⁹

TABLE 1. FETAL DOSES FOR COMMON DIAGNOSTIC PROCEDURES

Procedure	Fetal dose (mGy)	
	Mean	Maximum
Ultrasonography	No known biologic effects	
MRI (<1.5 Tesla)	No known biologic effects	
Abdominal or KUB radiography	1.4	4.2
Intravenous urography	1.7	10
Renal tract CT	8.0	49
^{99m} Tc renal scan (MAG3 or DTPA)	0.2	4.0

MRI = magnetic resonance imaging; KUB = kidneys, ureters, bladder; CT = computed tomography; Tc = technetium; MAG = mercaptoacetyl triglycine; DTPA = diethyl triamine pentaacetic acid.

Ultrasonography

Ultrasonographic assessment of the urinary tract is the first investigation for all pregnant women when there is a suspicion of stone disease. The imaging mode operates at acoustic outputs, without any considerable rise in tissue temperature, and no harmful effects have been documented after years of use. Doppler ultrasonography (US) does have the theoretical potential to induce temperature rises, but this has not been a significant clinical finding. Real-time US demonstrates the renal parenchyma, pelvicaliceal system, dilated ureter, and, occasionally, the offending calculus without fetal radiation exposure and is therefore the primary diagnostic modality of choice.

US does, however, have a number of important disadvantages. First, the sensitivity of standard US in confirming urolithiasis varies considerably between 34% and 86%.^{18,19,40} Second, it is highly nonspecific and may be unable to differentiate between ureteral obstruction secondary to calculi and physiologic hydronephrosis. Ureteral dilation below the level of the pelvic brim/iliac artery is, however, not seen in the latter, and its presence must alert the investigator to the possibility of a lower ureteral stone.⁴¹

Transvaginal US is well tolerated and quick and has been shown to be effective in the detection of distal ureteral stones.⁴² Other modifications have been investigated to increase the accuracy of standard US. Doppler-assisted measurement of the resistive index (RI) (peak systolic velocity of intrarenal blood flow minus the end-diastolic velocity divided by the peak systolic velocity) has shown some promise in pregnancy. The RI does not appear to be affected by the nonobstructive physiologic obstruction of pregnancy.

Shokeir and colleagues^{43,44} have shown that an RI of 0.70 (sensitivity 45%; specificity 91%; accuracy 87%) and, more importantly, a change in RI (Δ RI) of 0.06 (sensitivity 95%; specificity 100%; accuracy 99%) may have a valuable role in the diagnosis of acute unilateral ureteral obstruction. As a single modality, RI may have certain limitations, and larger studies are needed. Renal disease, nonsteroidal anti-inflammatory drugs (NSAIDs), and early (less than 6 hours) and delayed (more than 48 hours) measurement may result in decreased sensitivity of RI in the diagnosis of obstruction.⁴⁴

In a study that compared the value of US and renography in pregnant women with hydronephrosis, a renal pelvic diameter of less than 17 mm in asymptomatic patients effectively excluded the diagnosis of ureteral calculi.⁴⁵ The presence of ureteral jets on real-time US or Doppler US can exclude complete ureteral obstruction in 80.4% to 100% of cases but requires a skilled sonographer.^{46–48}

Intravenous urography (IVU)

Lee and Stothers¹⁸ reported that an IVU demonstrated calculi in 16 of 17 patients using a limited protocol. Irving and Burgess⁴⁹ reported 14 of 15 cases of correct diagnosis and concluded that IVU was safe and accurate in pregnancy. Urography should be considered after adequate time has elapsed to allow spontaneous elimination of calculi. Persistent fever after 48 hours of antibiotic therapy, rising serum urea and creatinine levels, US hydronephrosis, and persistent vomiting that results in dehydration are all indications for a limited IVU.²³

The IVU is effective in providing anatomic and functional/excretory information and will verify site and extent of obstruction. The main concern related to IVU, however, is the potential adverse effects on the fetus of intravenous contrast media and ionizing radiation. Although a small proportion of iodinated contrast material is known to cross the placenta, no significant teratogenic or mutagenic effects have been demonstrated.⁵⁰ Iodinated contrast exposure in later pregnancy has been shown to suppress fetal thyroid function, and neonates must be screened for hypothyroidism within the first week of life.⁵⁰

If IVU is used, we suggest a limited sequence IVU (scout, 30 minutes after contrast injection, with or without delayed film at 2 hours), which results in a fetal radiation dose delivery of 0.5 mGy, far below the 5 mGy safety margin. Fetal radiation can be further reduced by decreasing exposure times, using tight collimation, low voltages (60–70 kV), maximal fetal shielding, and prone patient position.¹⁶ While ionizing radiation is best avoided, the maternal risk from delayed diagnosis must be balanced against potential risks to the fetus.

Isotope renography

Some investigators have advocated the use of nuclear medicine renography, rather than IVU, because the fetal radiation dose is one tenth the dosage delivered in IVU.^{21,51,52} Isotope renography will demonstrate drainage or confirm ureteral obstruction, but it lacks the anatomic information provided by IVU. The fetal dose can be further decreased by maintaining a high maternal oral fluid intake and encouraging frequent voiding to reduce isotope dwell time within the maternal bladder.

MRI

A heavily T2-weighted pulse sequence MRI with intravenous gadolinium has emerged as an attractive alternative to IVU, with many investigators reporting a comparable accuracy rate of 93% to 100% in the detection of pathologic ureteral obstruction.^{52–54} MRI uses electromagnetic radio waves rather than ionizing radiation, and no harmful effects to the patient or fetus have been reported.^{55,56} Because the experience with gadolinium is limited, especially during the first trimester, the NRPB recommends avoiding MRI in the first trimester. No adverse effects of gadolinium to the fetus, however, have been reported in pregnancy, and its use may be considered after full discussions with the patient.⁵⁰

Although MRI does not visualize ureteral calculi, many salient features may suggest the presence of obstructing calculi. Stones appear as signal voids overlying the high signal of urine within a dilated ureter.⁵⁴ The presence of a standing column of urine below the level of the pelvic brim, in addition to proximal ureteral dilation, is suggestive of an obstructing distal ureteral calculus (“double kink sign”).⁵⁴ Other MRI features that suggest pathologic rather than physiologic hydronephrosis include an “unusual” site of obstruction (such as the pelvoureteral junction or vesicoureteral junction), an abrupt ending of the ureter (rather than a smooth taper at the level of the pelvic brim), and perinephric or periureteral edema.

Other benefits of MRI include the ability to detect nonurinary tract pathology (eg, appendicitis, ovarian torsion), characterize renal masses, and produce good image quality in spite of

coexisting renal impairment. Drawbacks of MRI include a lack of a distinct signal from the calculi, limited availability, and interference with metal objects. In addition, MRI is time consuming and expensive and can produce a sense of claustrophobia. In spite of this, it is our belief that MRI is a useful, safe, and effective tool to aid the second-line assessment of the pregnant patient with suspected urolithiasis.

CT

Unenhanced CT has a detection rate approaching 100% for urinary-tract calculi, but at the expense of higher fetal radiation. Fetal exposure may be reduced by using narrow collimation and faster image acquisition, but CT is best avoided in routine use. It may have a limited role in the clarification of a suspected renal mass.⁵⁷

TREATMENT

Although randomized studies in this field do not exist, the majority of symptomatic ureteral stones in pregnancy pass spontaneously, caused in part by the normally dilated upper urinary tract during pregnancy. Many series have constantly demonstrated a 64% to 84% spontaneous stone passage rate with conservative therapy.^{1,18,58} Of the remaining stones, Stothers¹⁸ reported that nearly half of these were passed in the postpartum period. Horowitz and Schmidt²³ coined the phrase “expectant therapy for the expectant mother,” because the guiding principle remains to minimize risk to the patient and fetus. Conservative treatment, which requires close communication between the urologist and obstetrician, includes hydration (oral or intravenous), analgesia, antibiotics (if infection present), antiemetics, rest, and routine sieving of urine. Approximately one third of patients treated in this way will have multiple admissions for fetal monitoring and intravenous hydration, although this is not an indication for surgery. The indications for active intervention will be discussed.

Medical treatment

Pharmacotherapy, in conjunction with expectant therapy, has a restricted role because most drugs used in the management of renal colic are contraindicated in gestation. Effective drugs that have been used for long periods are preferable to new, less-studied alternatives. To minimize fetal risk, drug doses at the lower end of the therapeutic range should be used.⁵⁹

Analgesia. Opiates are the first-line choice during pregnancy, because most other analgesics have a teratogenic potential. Morphine and meperidine are considered safe in pregnancy as are oral agents such as codeine or oxycodone.⁶⁰ The use of NSAIDs is contraindicated because of concern about increased risk of oligohydramnios, early spontaneous abortion, and cardiac malformations. Other studies have not confirmed these findings.⁶¹ While uncertainty exists, NSAIDs are discouraged throughout pregnancy.

For severe pain, patients should receive either a patient-controlled analgesia pump or epidural administration of narcotics.⁶² The use of continuous segmental block (T11 and L2) has been recommended and may influence spontaneous passage of stones.²⁰ An epidural block may also reduce distal ureteral

smooth muscle tone and aid stone passage.^{20,62} This is rarely used but can be administered if patients refuse intervention or if there is a lack of endourologic expertise or equipment.

Antibiotics. Approximately 50% of pregnant women who have stones have associated infection, and vigorous antibiotic treatment is indicated.⁶¹ Most trials of antibiotics in pregnancy involve patients with pyelonephritis (without the presence of stones). Enterobacteriaceae (*Escherichia coli*, *Klebsiella*, *Enterobacter*) make up 90% of causative pathogens seen on urinalysis.⁶³ Most antibiotics cross the placenta, and both maternal and fetal safety must be considered.

Antimicrobials considered safe in pregnancy with good long-term data include cephalosporins, penicillins, macrolides, and nitrofurantoin, and these will form the mainstay of treatment in women with urolithiasis and infection. All patients should be treated individually, with treatment based on culture results and microbiologist advice.

Expulsive therapy. While alpha-adrenoceptor blockers, calcium channel blockers, and, to a lesser extent, corticosteroids significantly enhance spontaneous stone passage, there are no data for their use in pregnant women because these drugs are contraindicated in pregnancy.^{64,65} Their routine use cannot be recommended.

Active management

Unfortunately, 15% to 30% of patients' stones will ultimately necessitate some form of active invasive intervention. Indications for intervention are largely based on individual patient factors but include uncontrolled pain, sepsis, obstruction of a solitary kidney, bilateral obstruction, obstetric complications (premature onset of labor, pre-eclampsia), and poor access to urology care/equipment.⁶⁶

Preintervention counseling must make the patient aware of the nature of the proposed intervention, the potential risks to patient and fetus, alternative therapies, and local available expertise. The counseling must take into consideration patient wishes and the gestational age. It is also imperative that a multidisciplinary team approach be adopted, including urologist, obstetrician, anesthesiologist, and radiologist.

Percutaneous nephrostomy (PCN) drainage. Temporary diversion of urine via a PCN tube remains a tested option, especially if the patient presents with sepsis because of an obstructing stone and when excessive ureteral manipulation is best avoided.^{67–69} Insertion is usually performed by a radiologist under local anesthesia using US guidance and is successful in more than 90% of patients.^{70,71} PCN tube insertion in pregnancy has a number of desirable advantages.^{24,66,69} It is minimally invasive, provides immediate and effective decompression of the obstructed system, can be performed in patients with acute sepsis, and can be accomplished under local anesthesia without ionizing radiation. The procedure allows urine collection for culture and sensitivities, avoids ureteral manipulation and associated complications, establishes access for future percutaneous nephrolithotomy or stone dissolution therapy, and produces minimal lower urinary-tract symptoms. In addition, straightforward tube exchanges can be effected over a guidewire, and the procedure is more cost-effective than placement of ureteral stents.

In comparison with internal ureteral stents, however, complications of PCN tube insertion include discomfort or bleed-

ing during insertion, bacterial colonization, dislodgement, tube blockage requiring intervention or changes, and physical and social aspects of dealing with an external apparatus.⁷¹ PCN, therefore, is an effective option that will stabilize the clinical situation and permit definitive treatment of stones in the postpartum period. To minimize the occurrence of adverse effects of an indwelling PCN tube, however, it is advisable to change the tube at 6- to 8-week intervals.

Ureteral stent insertion. Effective and rapid ureteral decompression by the retrograde (via cystoscopy) or antegrade (after percutaneous renal puncture) insertion of an indwelling ureteral Double-J stent has been the traditional method of treating pregnant women with obstructed renal systems.^{19,72,73} It is also possible to insert such retrograde stents under local anesthesia using US guidance rather than fluoroscopy.⁷⁴ Limited fluoroscopy may only be used if an inability to advance the guidewire up the ureter is encountered. The stone can be dealt with definitively after delivery.

In comparison with PCN, nonpregnant patients with indwelling ureteral stents are significantly more likely to complain of irritative lower urinary-tract symptoms (LUTS), stent-related pain, and decreased quality of life, although this has not been studied in pregnant patients.⁷⁵ Other well-recognized potential complications of stents include manipulation of the urinary tract causing possible trauma to the ureter, a higher incidence of LUTS including hematuria, an increased risk of ascending UTIs, and stent encrustation causing blockage.

A potent combination of gestational hypercalciuria, hyperuricosuria, and infection results in a tendency toward rapid stent encrustation.^{19,72} Patients are advised to maintain a high oral fluid intake and restrict dietary calcium intake to minimize oc-

currence of encrustation; ultimately, stents may have to be replaced every 6 to 8 weeks, resulting in further inconvenience and potential risks for the patient.^{19,66} For this reason, investigators have suggested that the preferred technique of choice remain PCN before 22 weeks' gestation and a ureteral stent in later pregnancy.^{19,76}

Ureteroscopy. In the event of failure of conservative treatment, ureteroscopy with stone retrieval is now considered the procedure of choice, provided that the appropriate endourologic expertise and equipment are available. It is associated with a significant decrease in the length of hospital stay when compared with ureteral stenting.⁷⁷ Smaller endoscopes (7.5F, 9F, or 11.5F) allow complete visualization of the ureter and renal pelvis, enabling accurate diagnosis and definitive management for urolithiasis.

Numerous small series have demonstrated ureteroscopy to be safe and effective in all stages of pregnancy with stone-free rates between 70% and 100%.⁷⁷⁻⁸³ Concerns had previously persisted regarding technical difficulties because of the tortuous nature of the lower ureter from uterine compression, but the physiologic ureterohydronephrosis makes manipulation easier. Ureteral dilatation is therefore avoided.

Ureteroscopy (both rigid and flexible) may be performed under a general or spinal anesthesia or even sedation, with the patient in the modified dorsal lithotomy position.^{77,81,83} The majority of procedures can be performed without ionizing radiation under US guidance, with fluoroscopy only used in the event of failure to advance the guidewire.^{77,83}

Stone fragmentation/retrieval via ureteroscopy has been performed using the holmium:yttrium-aluminum-garnet (YAG) laser, pulsed-dye laser, ballistic lithotripter, ultrasonic lithotrip-

TABLE 2. SUMMARY OF STUDIES USING URETEROSCOPY IN PREGNANCY

	Number of patients	Fluoroscopy used?	Intracorporeal lithotripsy	Stone retrieval	Stent inserted?	Which trimester?	Obstetric complications	Stone free?
Juan 2007 ⁷⁸	3	No	None	Basket	No	3	None	3/3
Akpinar 2006 ⁸⁴	7	No	Ho: YAG (6)	Basket	5/7	1,2,3	None	6/7
Khoo 2002 ⁷⁰	2	N/S	N/S	N/S	No	3	None	2/2
Yang 2002 ⁹²	3	No	EHL (1)	Basket (2)	No	1,2	None	3/3
Lemos 2002 ⁷⁹	14	1/14	USL (2)	Basket (11)	8/14	2,3	None	13/13
Lifshitz 2002 ⁸⁰	6	Yes	None	Basket (4)	3/6	2,3	None	4/4
Watterson 2002 ⁸¹	8	Yes	Ho: YAG	No	4/9	1,2,3	None	7/9
Butler 2000 ⁴⁰	2	N/S	Laser	N/S	No	N/S	None	2/2
Shokeir 1998 ⁸²	10	No	USL (2)	Basket (3)	10/10	N/S	None	5/8
Parulkar 1998 ⁵⁸	4	Yes	None	Basket (4)	No	2	None	4/4
Lee 1997 ⁹³	1	N/S	None	Basket	No	N/S	None	1/1
Scarpa 1996 ⁸³	15	No	Pulsed dye (3) Ho: YAG (3) Pneumatic (2)	Basket (2)	15/15	2,3	None	10/13
Carringer 1996 ⁹⁴	4	No	Pulsed dye (4)	No	No	3	None	4/4
Ulvik 1995 ⁷⁷	24	No	USL (2) Forceps x1	Basket (13)	7/24	1,2,3	PUC	13/13
Denstedt 1992 ¹⁹	3	Yes	None	Basket (3)	No	3	None	3/3
Vest 1990 ⁹⁵	2	N/S	None	Basket (2)	2/2	2	None	2/2
Rodriguez 1988 ⁹⁶	1	No	None	Basket (1)	1/1	2	None	1/1
Rittenberg 1988 ⁹⁷	2	No	None	Basket (1)	1/1	2,3	None	1/1

Ho: YAG = holmium:yttrium-aluminum-garnet; N/S = not specified; USL = ultrasound lithotripsy; EHL = electrohydraulic lithotripsy; PUC = premature uterine contractions.

tor, basket retrieval, and forceps crush. Although all have been shown to be safe and successful without any known complications, it is our belief that the holmium:YAG laser represents the safest modality for intracorporeal lithotripsy.^{81,84} The holmium:YAG laser has a large safety margin (penetration of less than 0.5 mm from tip of probe), is effective against all stone types, can be used in the rigid as well as flexible instrument, has very little periureteral thermal effect, and its use does not result in any energy transmission through the patient or fetus.^{81,84}

Sound intensities generated by holmium:YAG lasers are greatly reduced compared with those produced by US and electrohydraulic probes, thus potentially reducing the risk of damage to the developing fetal hearing.⁸⁵ Although there remains the theoretical risk of cyanide formation by the action of laser on uric acid stones, this has not been reported as a clinical problem and it is likely that any cyanide produced is removed by the irrigation fluid.¹³

Most stones may be removed using a tipless stone basket with minimal trauma to the already dilated ureter. Many other modalities of intracorporeal lithotripsy have been used, but there remain legitimate concerns regarding unrecognized fetal hazards. Because of the high peak pressures generated by electrohydraulic lithotripsy, there is a risk of injury to the fetus or premature labor.⁸⁶

It is postulated that US-generated high-pitched noise may result in hearing injury to the fetus, but Karlsen and associates⁸⁵ concluded that peak pressures emitted by intracorporeal lithotriptors are unlikely to damage fetal hearing. The rigid nature of the pneumatic probe restricts its use to the semirigid ureteroscope and may limit its usefulness in pregnancy. Unlike the holmium:YAG laser, which fragments all types of calculi, the pulsed-dye laser is ineffective against harder stones (eg, cystine). Fetal complications related to intracorporeal lithotripsy are theoretical and have not been reported in the medical literature, except in a few case reports.

Akpinar and colleagues⁸⁴ recommend routine stent placement with a string for 72 hours after ureteroscopy to reduce pain and analgesic requirements. Routine ureteral stenting (Double-J stent or ureteral catheter) beyond a few days after surgery may be advisable in the presence of ureteral trauma, edema, confirmed preexisting infection/sepsis, bleeding, or the presence of residual stones/fragments.

Contraindications to ureteroscopy according to Biyani and Joyce⁶⁶ include stones larger than 1 cm, multiple calculi, sepsis, transplanted kidney, inadequacy of ureteroscopic experience or instruments, and solitary kidney (relative contraindication).

All reports that investigated the role (effectiveness and safety) of ureteroscopy in pregnancy in the English medical literature during the last 20 years are summarized in Table 2.

Percutaneous nephrolithotomy (PCNL). Patients with an indwelling nephrostomy tube may proceed to PCNL after delivery, but PCNL is not advised during pregnancy. Although two case reports have described successful PCNL in early pregnancy, the necessity for general anesthesia, need for fluoroscopy, and prone position of the patient make this a hazardous procedure.^{87,88}

Extracorporeal shockwave lithotripsy (SWL). SWL is contraindicated in pregnancy because of the effects of the

shockwave on the fetus, potentially resulting in fetal death.⁸⁹ There have, however, been reports of SWL treatment in young women with unrecognized early pregnancies, who went on to have an uncomplicated pregnancy and healthy babies.^{90,91} Mandatory termination of pregnancy must therefore not be recommended in such instances.

Open surgery. Open surgery is not advised, except in the treatment of a symptomatic patient with sepsis who is not responding to other therapeutics options and when endourology expertise or equipment is not available.^{66,67} This is a rare occurrence.

CONCLUSION

Although uncommon, urolithiasis that occurs during pregnancy can pose a challenge to urologists, obstetricians, and radiologists. A high index of suspicion is required for a prompt and correct diagnosis. The health of the patient and the developing fetus is paramount when considering investigations and therapeutic options. In the absence of prospective studies, this remains an area of much debate. US is the primary radiologic investigation of choice, followed by either an MRI or limited IVU. Fortunately, conservative, supportive management will result in spontaneous stone passage in the majority of patients. Where intervention is necessary, advances in endourologic equipment and techniques suggest that ureteroscopy, with holmium:YAG laser lithotripsy, is likely to be the safest and most effective management choice.

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ABBREVIATIONS USED

CT	=	computed tomography
GFR	=	glomerular filtration rate
LUTS	=	lower urinary-tract symptoms
MRI	=	magnetic resonance imaging
NRPB	=	National Radiological Protection Board
NSAIDs	=	nonsteroidal anti-inflammatory drugs
PCN	=	percutaneous nephrostomy
PCNL	=	percutaneous nephrolithotomy
RI	=	resistive index
RPF	=	renal plasma flow
SWL	=	shockwave lithotripsy
US	=	ultrasonography
UTI	=	urinary-tract infection
YAG	=	yttrium-aluminum-garnet