ClinicalPractice

Managing stones in pregnancy: an update

Practice points

- Stone formation is a multifactorial process, and the incidence appears to be increasing among women.
- Overall, the risk of stone formation during pregnancy does not appear to be increased.
- Common presentations of stones in pregnancy include nonspecific flank or abdominal pain, fever, recurrent or persistent urinary tract infections, or microscopic hematuria.
- Imaging investigations of a pregnant woman with a suspected stone include ultrasound as the initial evaluation with an evolving second line role for MRI and low-dose CT depending on the stage of pregnancy.
- A multidisciplinary management strategy should include participation of a perinatologist and urologist.
- The majority of pregnant women with a symptomatic upper tract stone pass their stone without intervention.
- Indications for intervention include intractable pain, pre-eclampsia, threatened pre-term labor, sepsis or renal failure.
- Medical expulsive therapy with α-blockers are contraindicated in pregnancy.
- For distal ureteral stones requiring intervention, ureteroscopy and laser lithotripsy has evolved as a definitive treatment option.
- When temporary urinary drainage of an obstructed upper tract is required percutaneous drainage under ultrasound guidance is preferred during the first trimester, while in the second orthird trimesters retrograde ureteral stent placement may also be considered.

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The diagnosis of urinary calculi in pregnancy may be challenging, requiring a high index of clinical suspicion and judicious imaging selection. Investigations and intervention must be tailored not only to the pregnant patient's symptoms, but also the stage of pregnancy. A multidisciplinary team approach consisting of the perinatology team, urologist, interventional radiologist and anesthesiologist is required. Management should proceed from conservative to more invasive approaches. In the majority of cases, expectant management as first-line therapy will be successful. Temporizing measures or definitive intervention will be required in select circumstances.

Keywords: calculi • pregnancy • ureteroscopy • urinary tract imaging

Introduction

The incidence and prevalence of kidney stones is increasing globally [1,2]. According to the National Health and Nutrition Examination Survey (NHANES) data, the self-reported prevalence of kidney stones has increased from 5.2 to 8.8% from 1994 to 2010 [3,4]. The prevalence has increased in both men (6.3–10.6%) and women (4.1–7.1%), with recent evidence suggesting a more marked increase among women [5]. The age of presentation may also be different between the sexes. Among men the incidence of nephrolithiasis increases after the age of

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20 years, peaks between 40 and 60 years of age and then decreases [6]. Among women, the incidence peaks by the late 20s and declines until 50 years of age and remains stable thereafter [6,7]. The reported incidence of kidney stones during pregnancy ranges widely from one in 250, to one in 3300 [8–11]. Riley *et al.* reported there was no evidence to indicate an increase in incidence among pregnant women over the past two decades [12]. Overall pregnant women do not seem to be at higher risk for stone formation compared with nonpregnant women of similar age [13–15].

The urinary tract undergoes a number of physiological and anatomical changes during normal pregnancy. The impact of these changes and their relevance to urinary stone formation, the evaluation of the pregnant patient with suspected renal colic and treatment decisions will next be reviewed.

Anatomic & physiologic changes affecting the urinary tract during pregnancy
There are several unique physiological and anatomic changes that occur during pregnancy that can potentially impact stone formation.

Dilation of the urinary tract: increases in renal plasma flow & glomerular filtration rate
Anatomic changes in the upper urinary tract are driven by the interplay of physical and hormonal changes that occur during pregnancy. Gestational hydronephrosis occurs in up to 90% of women by the end of the third trimester [16–18]. This dilation is the result of several factors. During the first trimester of pregnancy renal vascular resistance decreases while blood volume and cardiac output quickly increase. This increase in circulating volume and renal plasma flow by up to 80% [19] consequently elevates GFR by 40–65% up to 180 ml/min at the end of the first trimester [20]. Additionally progesterone influences smooth muscle relaxation and contributes to the dilation of renal pelves, calyces and ureters [21,22]. An increase in renal length and volume by approximately 1 cm and 30% respectively has been described [23]. Historically, some authors have suggested cutoffs of dilatation indicative of pathologic obstruction (posteroanterior diameter of the pelvis >18 mm on the right side and >15 mm on the left side during the first trimester and >27 mm on the right side and >18 mm on the left side during the second and third trimesters, or a caliceal diameter >10 mm); however, these are not commonly used clinically [24].

As pregnancy progresses ureters may be compressed by the uterus or ovarian vein plexus at the level of the pelvic brim [24]. Generally, right sided hydronephrosis is greater than on the left due to the compression of the right ureter over the distal common iliac vessels and dextrorotation of the uterus. The left ureter is less prone to compression as it crosses at a less acute angle and may be shielded by the sigmoid colon [25]. Urinary stasis increases contact time between lithogenic factors and can result in increased propensity toward crystallization and stone formation. Secondary, mild obstruction and urinary stasis may also increase the likelihood of infection. In situations of hypotension, renal units do not autoregulate as effectively as in nonpregnant patients, which can lead to poor renal perfusion and increased risk of acute tubular necrosis [26]. Therefore, additional vigilance is required for pregnant patients who may present with urinary stones and infection.

Alterations in renal homeostasis
During pregnancy many factors contribute to increases of lithogenic urinary constituents. Hypercalciuria of pregnancy is primarily driven by increases in GFR. Additionally, placental production of 1,25- dihydroxycholecalciferol (1,25-vit D) triggers a cascade of events that augment urinary calcium levels. 1,25-vit D increases gastrointestinal absorption and bone resorption of calcium, which suppress parathyroid hormone levels. This results in further increases in the filtered load of calcium, decreasing the renal resorption of calcium, and thus augmenting hypercalciuria. Similarly, elevated GFR results in increased natriuresis during pregnancy, although the overall effect of pregnancy is an increase in total body sodium and fluid retention as a result of a lower threshold for thirst and antidiuretic hormone release. The balance of these factors results in slightly lower plasma sodium and osmolarity during pregnancy [27]. Serum uric acid levels decrease by 25–35%, which corresponds to increased glomerular filtration and reduced proximal tubular reabsorption during pregnancy [28].

The increase in urinary excretion of lithogenic factors is balanced by similar increases in excretion of inhibitors of stone formation. Citrate, magnesium, glycosaminoglycans and thiosulfate can inhibit crystal growth and aggregation [29–31]. Increases in citrate concentrations can directly inhibit stone formation, but also result in an increase in urinary pH, which can alter the composition of stones that do form. Alkaline urine prevents uric acid stone formation but increases the likelihood of calcium phosphate (brushite) stones. In a large series (n = 5956) Meria *et al.* have demonstrated a markedly increased incidence of calcium phosphate stones among pregnant women compared with nonpregnant women of the same age (65.6 vs 31.4%; p < 0.0001) [32]. Similar findings have been corroborated by other investigators [33,34]. Additionally, a precursor to calcium phosphate stones, octacalcium phosphate pentahydrate, was found five times more commonly in the urine of pregnant

women compared with nonpregnant women [32]. Likewise, higher supersaturation of calcium phosphate and calcium oxalate have been demonstrated among pregnant women [29,30] and could account for the more rapid encrustation observed among pregnant women with urinary stents [35,36].

Despite the changes described, the net effect of the alterations in both lithogenic and inhibitory factors results in similar risk for stone formation for pregnant and nonpregnant women. The relatively short duration of pregnancy may also not be long enough for the physiological and anatomical alterations to induce *de novo* stone formation.

Presentation & evaluation

Renal colic is the most common nonobstetrical source of abdominal pain in pregnant patients requiring hospital admission [37]. Flank or abdominal pain is present in >85% of pregnant women presenting with stone disease [18]. Due to the prevalence of nonspecific abdominal or back pain, nausea and vomiting, and lower urinary tract symptomatology in pregnancy the diagnosis of urolithiasis may be delayed, missed, or mistaken for pregnancy itself in up to 30% of cases [34,38]. A high index of suspicion is required to ensure prompt diagnosis. Urolithiasis manifests most commonly in the second (39%) and third (46%) trimesters [32,39].

Gross hematuria may be present in as many as 20% of patients [38,40], although microscopic hematuria is more common (>95%). Lower urinary tract voiding symptoms are very common in pregnant women and may be exacerbated by a distal ureteral stone. Uncommonly patients may present with complications of urolithiasis such as urosepsis, premature labor or pre-eclampsia [41].

Patients who present with symptoms suggestive of urolithiasis should undergo a thorough history and physical exam. Up to 30% of patients have had a previous stone and 3.7% have had a stone during a previous pregnancy [32].

Initial laboratory investigations should include complete blood count, electrolytes, urea, creatinine, uric acid, calcium, as well as a urinalysis and culture. On urinalysis, microscopic hematuria and pyuria will be identified in greater than 95 and 42% of patients with urolithiasis, respectively [38]. Up to 50% of pregnant women with calculi have a positive urine culture [42]. If a complete metabolic evaluation including 24-h urine studies is deemed indicated, these tests should be delayed until the completion of pregnancy or weaning as associated hormonal changes may alter urine chemistries [42].

Imaging of renal stones in pregnancy

When selecting the optimal imaging modality the clinician must balance the need for accurate and timely diagnosis with the potential risks of radiation exposure to the mother and fetus. In the following section we consider each of the available investigations and highlight preferred modalities and second-line options.

Ultrasound is considered an appropriate first-line modality to assess renal stones in pregnancy because it is ordinarily easy to obtain and has no known ill effects for either the mother or fetus (Figure 1). An abdominal ultrasound may identify a stone directly or indirectly (hydroureteronephrosis, absence of urinary jet) and may identify alternative pathology (appendicitis, bowel obstruction, infections or inflammatory bowel disease or placental abruption) [40]. The sensitivity of ultrasound varies widely for detecting urinary calculi in pregnancy (34–86%) [38,43]. Additionally, in pregnant patients calculi are more commonly found in the ureter and therefore more difficult to identify with ultrasound alone [33,44–45]. As well, the position of the fetus may affect imaging quality and the ability to diagnose ureteral stones. With the use of ultrasound alone, and findings suspicious for stone presence, one study found ureteroscopy was unable to diagnose a stone in 12% of cases [42].

To improve ultrasound imaging characteristics, a number of radiologic signs and adjunct measurements have been described. The detection of hydroureter distal to the iliac vessels is highly suggestive of obstruction as opposed to physiological hydronephrosis of pregnancy [46]. The left collecting system usually only has mild to moderate dilation and the presence of severe left hydroureteronephrosis suggests pathological obstruction [47]. The visualization of urinary jets suggests the absence of an obstructing urinary calculus [48]. Visualization of urine jets are optimized by aggressively hydrating the patient prior to image collection [47]. However, absence of a jet can be a normal observation in 13% of pregnant patients and is more commonly noted on the right side [49]. Additionally, up to 65% of patients with urolithiasis will have asymmetry of urinary jets [43,50] but this can be a subtle finding and difficult to interpret. Endovaginal ultrasound can also assist detection of distal ureteral calculi (Figure 2) [48]. Doppler ultrasound with measurement of resistive index (RI) has been described to help distinguish physiologic dilation of pregnancy from obstruction [51]. At best a RI of 0.70 is associated with 87% accuracy in the detection of obstruction, however other studies have shown less promising outcomes for this metric [52–54].

Historically, plain film investigations and limited intravenous urography (IVU) had been considered appropriate second line investigations for pregnant women with suspected stones. These modalities have been largely replaced by more informative options such
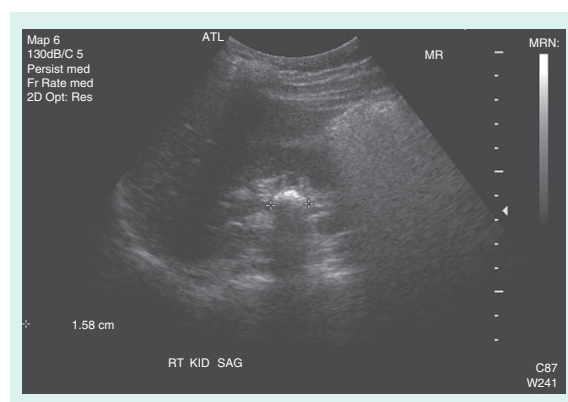
Figure 1. Right renal pelvic stone detected by transabdominal ultrasound in a pregnant women.

as MRI and low-dose CT. Conventional high-dose CT is contraindicated due to high radiation exposure.

Fetal radiation exposure

Much of our knowledge of the effect of radiation on humans comes from epidemiologic studies of post-World War II Japan and the Chernobyl nuclear disaster [55]. Initial reports suggested that fetal doses of <5 rads (50 mGy) were associated with low risk for inducing abortion, congenital anomalies or perinatal mortality. More recent evidence suggests that the imaging related risk to the fetus increases when the radiation exposure is above 150 mGy [56,57]. Below 50 mGy the risk of radiation induced abnormalities do not appear to be increased from baseline [56,58]. Teratogenicity of radiation exposure is dependent on gestational age at the time of exposure. The approximate threshold to induce birth defects or miscarriage in the first trimester is considerably lower (20 mGy) when compared with the second and third trimesters (50 mGy) [58]. In contrast with teratogenesis, which requires a threshold radiation dose to increase risk, radiation is considered to have a stochastic effect on carcinogenesis in which there is no 'safe threshold'.
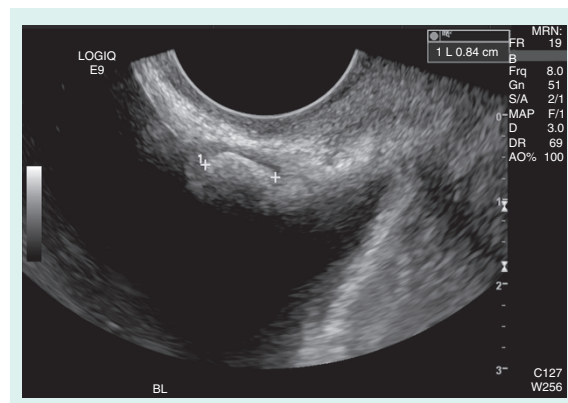

Figure 2. Transvaginal ultrasound showing right ureterovesicle junction stone.

Overall, the risk of childhood cancer secondary to *in utero* exposure to 10 mGy of radiation is estimated to be one in 10,000 [58]. The approximate fetal doses associated with common imaging modalities are listed in Table 1 [42,59].

Low-dose CT

Low-dose and ultra-low-dose CT protocols have been developed in order to minimize radiation exposure while maximizing sensitivity and specificity to detect urolithiasis. Low dose CT (defined as <4 mGy) has been found to be a safe and accurate imaging modality when compared with standard dose CT (10 mGy) [60]. Optimal patients for low dose CT have a BMI <30 in which sensitivity and specificity are maintained above 90% [60].

The initial clinical experience with low dose CT in a series of 20 pregnant patients with a mean gestational age of 26.5 weeks demonstrated modest diagnostic accuracy (13/20), and confirmed very low radiation exposure (7.1 mGy) [59]. Optimization of low dose CT protocols and reconstructive methods have since allowed improved diagnostic accuracy and further reductions in radiation dose to 1.8 ± 0.7 mGy [61]. Newer software currently under investigation may additionally reduce radiation dose [62]. There are no reports to date, however, of the use of these modifications in the pregnant population. The use of low-dose CT in pregnancy has been endorsed by the American Urological Association as an appropriate imaging modality for women in the second or third trimester when ultrasound is nondiagnostic [60].

Magnetic resonance urography

One approach that completely eliminates radiation exposure for pregnant women with suspected calculi is magnetic resonance urography (MRU) (Figure 3). There are no known harmful fetal effects from 1.5 Tesla MR imaging. MR urography compared favorably to Doppler US and isotope renography in a study of pregnant women [63]. Gadolinium enhanced T2-weighted pulse sequence MRU has demonstrated up to 93–100% accuracy in identifying pathologic ureteral obstruction from hydronephrosis of pregnancy [63,64]. Characteristic findings of urolithiasis on MRU include, direct visualization of a stone at a point of ureteral constriction (ureteropelvic junction, ureterovesical junction), renal edema or peri-renal extravasation, and a 'double kink' sign in which there is constriction at the UVJ and pelvic brim with a column of urine seen proximally [63]. Limitations of MR imaging include lack of a specific stone signal, availability, and duration of the scan. Several protocols have been developed to attempt to optimize MR urography for stones [64–67]. Of these

the half Fourier single-shot turbo spin echo (HASTE) protocol has demonstrated a sensitivity of 84%, specificity of 100% [67] and diagnostic accuracy of up to 100% in a small series [65].

A small heterogeneous retrospective cohort study comparing MRU, low-dose CT and renal ultrasound in 51 pregnant patients suggested that ultrasound with low-dose CT retained the highest positive predictive value for stone detection [68]. However, methodological limitations prevent generalization of this observation. The American Urological Association report on imaging of ureteral calculi in pregnancy made several recommendations on the use of MRI in pregnancy. Noncontrast MRI should be considered as the preferred secondary investigation for pregnant women in the first trimester as this is the period in which the fetus is most susceptible to potential radiation induced injury. The use of gadolinium is not recommended during the first trimester of pregnancy as it is known to cross the placenta [69] and the effects on the fetus are unknown [60,70]. MRI usually defines the level of obstruction and can provide an estimate of stone size [60].

Recently the American Urological Association developed a report on imaging of ureteral calculi [60] and dedicated a section to imaging in pregnant women. In an evaluation of 12 relevant articles of imaging in pregnant women it was concluded that the strength of evidence in this population was low reflecting observational studies yielding inconsistent findings or that had other significant limitations. In this context, the authors continue to recommend ultrasound as the first-line investigation for pregnant women suspected of colic for all stages of pregnancy. If ultrasound is nondiagnostic then noncontrast MRI could be considered in the first trimester or a low-dose CT protocol in the second and third trimesters [60].

Management

Due to the complexities of treating a pregnant patient with symptomatic stone disease, a multidisciplinary approach is recommended. Involvement of a perinatologist, urologist and radiologist are essential in opti-

mizing care for the mother and fetus. In some cases consultation with specialized anesthesia may be necessary (prior to surgery or for optimization of pain control) or interventional radiology (in the event that percutaneous nephrostomy tube placement is required). Key aspects of the clinical presentation determine the preferred option for a given scenario (Figure 4).

Expectant therapy

Approximately 70–80% of pregnant patients with symptomatic upper tract calculi will pass their stone spontaneously with conservative management [18,71]. One report documented higher spontaneous passage among pregnant women as compared with nonpregnant women (81 vs 47%; p < 0.0001) [32]. This phenomenon has been attributed to the physiologic effect of progesterone on smooth muscle relaxation and ureteral dilation resulting from intermittent compression by the gravid uterus [39].

Patients should be fluid resuscitated aggressively and medical management initiated to control symptoms of nausea and emesis. Effective yet safe pain management is an important consideration in this patient population. Codeine has been associated with a possible teratogenic effect when used in the first trimester [72–74]. Nonsteroidal anti-inflammatory drugs are contraindicated due to the association with fetal pulmonary hypertension and the risk of premature closure of the patent ductus arteriosus [75,76]. Opiates are generally considered safe, however prolonged use during the pregnancy and near to delivery may still have deleterious effects. Medical expulsive therapy is commonly used in a nonpregnant population but has not been properly evaluated in pregnant patients. In the absence of adequate studies on the use of α-blockers, calcium channel blockers, or corticosteroids the use of these medications is not recommended [42]. In patients found to have asymptomatic nonobstructing stones the preferred treatment option in the absence of an acute indication to intervene is observation with serial ultrasounds. Once the patient has delivered routine management of the stone is undertaken.

| Table 1. Estimated fetal doses associated with maternal radiologic procedures.		
Investigation	mGy	Rads
KUB	1.4–4.2	0.14–0.42
Limited IVU (3 film)	1.7–10	0.17–1.0
CT (Conventional	8–49	0.8–4.9
CT (Low Dose)	≤7	≤0.7
MAG3 or DTPA	0.2–4	0.02–0.4
CT: Computed tomography; DTPA: Diethylene triamine pentacetic acid; IVU: Intravenous urography; KUB: Kidney, ureter, bladder; MAG3: Mercaptoacetyltriglycine 3.		
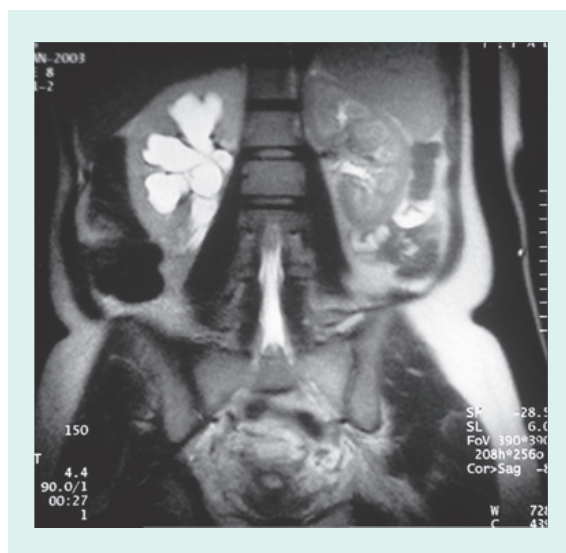
Figure 3. MRI showing right sided physiologic hydronephrosis of pregnancy.

Indications for intervention

Indications for intervention are similar to the non-pregnant patient and include: urinary tract infection, sepsis, unremitting symptoms (pain, nausea and vomiting), renal impairment or obstruction of a solitary kidney, with the added consideration of complications of the pregnancy such as pre-term labor and pre-eclampsia. In general it is optimal to avoid surgical intervention during the first trimester where the risk of miscarriage is greatest and the third trimester where pre-term labor may be induced. Several authors have indicated that the second trimester is the safest period for pregnant women to undergo nonobstetrical surgery in terms of maternal and fetal perinatal complications [77–83]. When considering surgical intervention during pregnancy it is important to include a high-risk obstetrical team and perinatologist in treatment decisions.

Options for intervention

Temporizing therapies when required include placement of either an external nephrostomy tube or an internal ureteral stent. Generally, the selection of either is based on the need to provide temporary renal drainage when definitive management of the stone is best rendered either later in the pregnancy or after delivery.

The decision to perform ureteral stenting versus placing a nephrostomy tube is made based on the stage of pregnancy and with patient preference and tolerability in mind. Should renal drainage be required in the first trimester, nephrostomy tube placement is favored as it can be accomplished using ultrasound and local anesthesia. Nephrostomy tubes

may however become dislodged, cause discomfort, pre-dispose to infection, encrust or block. There have been numerous reports of accelerated encrustation of ureteral stents and other foreign bodies in the urinary tract during pregnancy [18,25,34,36,84–85]. Additional reported complications include premature delivery, sepsis and hematuria [86].

Ureteral stents avoid the necessity of an external urinary collection device. In the second and third trimesters they may be placed under limited fluoroscopic guidance to reduce radiation exposure. There are reports of using ultrasound guidance to aid insertion as well [87,88]. In the cooperative patient it may be possible to a place ureteral stent under local anesthesia or with intravenous sedation. Due to higher stone metabolite turnover the potential for rapid stent encrustation exists and stents should be changed every 4–6 weeks [18,34–36,84–85]. Patients should be counseled that they may experience urgency, frequency, dysuria, and incontinence secondary to stent irritation of the bladder. These symptoms may be more bothersome in pregnant patients and difficult to ameliorate as the use of α-blockers and anticholinergics are contraindicated in pregnancy.

Ureteroscopy in pregnancy

Historically, definitive therapy for urolithiasis in pregnancy was delayed until the postpartum period. With improved technology including finer caliber semi-rigid and flexible ureteroscopes, holmium: yttrium-aluminum-garnet (Ho:YAG) lasers and adjunctive devices ureteroscopy has become more widely utilized option for some patients during pregnancy. Indications include failure of conservative management, or based on patient preference/request. Contraindications to ureteroscopy include infection/sepsis, large volume or multiple stones, abnormal anatomy or obstetrical complications [39].

A growing body of literature has shown that ureteroscopy in appropriately selected patients is feasible and safe in the second and third trimesters with comparable stone free rates as for nonpregnant patients. Several retrospective case series, which represent data for 235 pregnant patients, have shown stone free rates in the range of 63–93% [89–99]. The technique of ureteroscopy reported in the literature varies and includes a combination of ureteroscopic aided basket retrieval, laser and pneumatic lithotripsy. In most series, minimal complications were reported, however, these have included pre-term labor and delivery, ureteral perforation and urinary tract infections (UTIs) [96,100–102]. A meta-analysis that included data for 109 pregnant patients reported no differences in the incidence of ureteral injury or UTI as compared with a nonpreg-
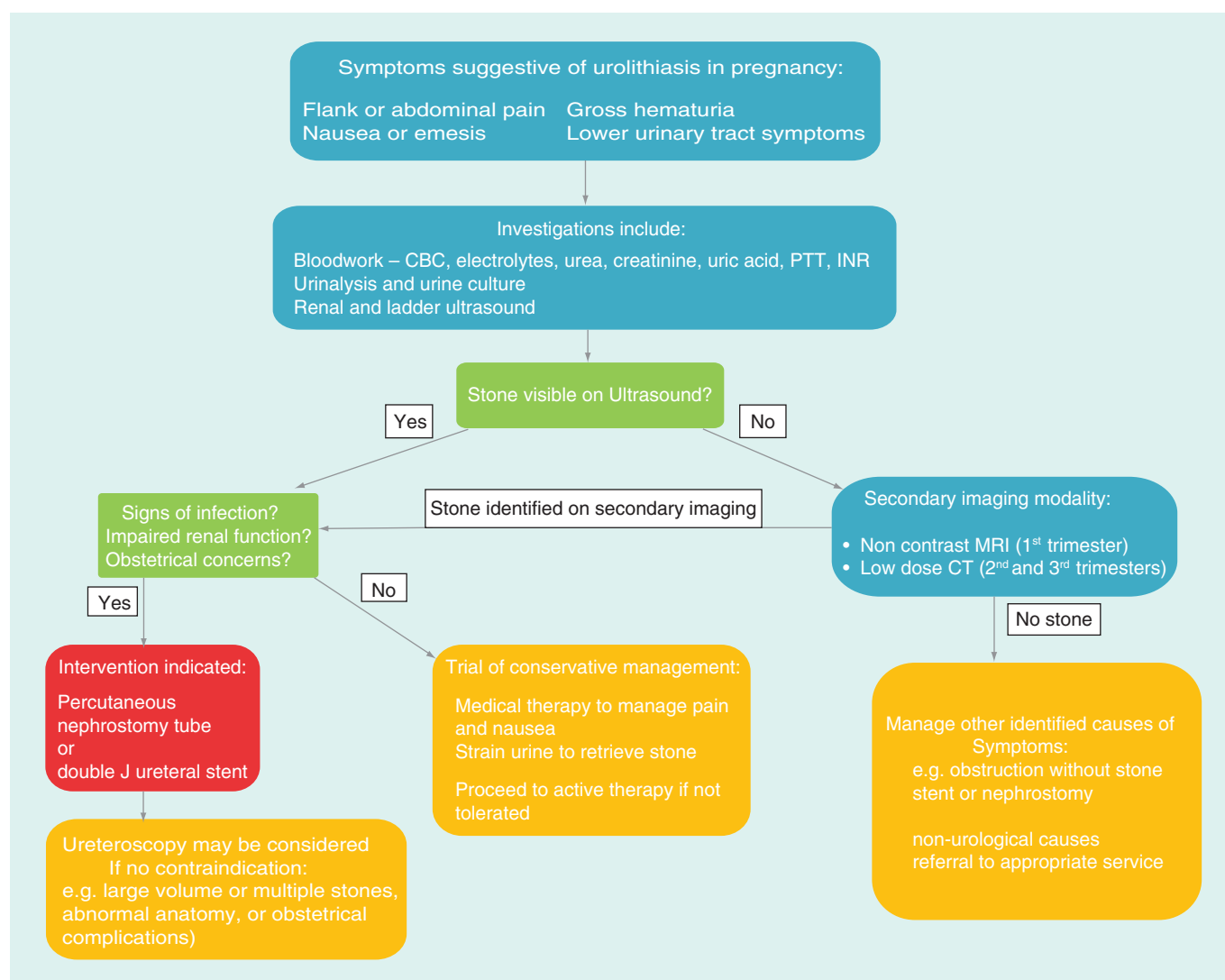
Figure 4. Algorithm for the management of stones in pregnancy
CBC: Complete blood count; CT: Computed tomography; INR: International normalized ratio; PTT: Partial thromboplastin time.

nant population [101]. UTI may be the most common complication occurring in up to 4% of cases [103]. In most cases a post-procedural double J stent is placed (50–100%) to minimize the risk of obstructive complications [94,96,103].

Although clinical evidence is lacking regarding the optimal intracorporeal lithotripter during pregnancy, there exist theoretical concerns that ultrasonic lithotripsy could impact fetal ear development or electrohydraulic lithotripsy could stimulate uterine contraction [36,92]. More focal energies as provided by pneumatic lithotripters or the Ho:YAG laser are felt to be safe in pregnancy [93,98–99,101,104–105].

Percutaneous nephrolithotomy in pregnancy

Percutaneous nephrolithotomy (PCNL) is contraindicated in pregnancy due to the need for prone posi-

tioning and the potential need for prolonged fluoroscopy time. With the adoption of supine PCNL and a greater reliance on ultrasound imaging during PCNL, the technique in pregnant women has been described in a few case reports [106–108]. In one report, a patient progressed to PCNL after persistent pain despite stent placement and failed ureteroscopy. In this case ultrasound guided PCNL was conducted in the supine position with stone fragmentation using a pneumatic lithotripter without complications [106]. In a second report Shah *et al.* performed PCNL for a 1.8 cm stone in a patient who refused nephrostomy tube changes as an alternative to pregnancy termination [107]. Minimal fluoroscopy was used in this case and no complications were reported. Despite these reports, PCNL is still considered a procedure best reserved for those patients in whom it is indicated after their delivery.

Extracorporeal shockwave lithotripsy in pregnancy

Similarly to PCNL, shockwave lithotripsy (SWL) is contraindicated in pregnancy due to theoretical risks to the fetus. The effects of SWL on fetal developmental were assessed in a small animal model study [109]. In this rabbit study no histopathologic differences were noted in heart or brain specimens obtained after delivery. However, in lung, liver and renal tissue there was congestion and intraparenchymal microhemorrhages in animals that had been exposed to SWL early in gestation. The authors concluded SWL is not a safe treatment during early pregnancy [109]. In a rat model, the impact of shockwave rates was evaluated and demonstrated that rats nearest the focal area had lower birth weights than controls, however no gross or microscopic damage was identified [110].

In a survey of 824 women who underwent ultrasound-guided SWL, six pregnant patients were inadvertently treated during the first month of gestation [111]. The children of these pregnancies had no identified malformations or chromosome anomalies. This small series however, does not provide sufficient evidence to justify the use of SWL during pregnancy given the theoretical and potentially devastating risks.

Metabolic workup

Once the acute episode of nephrolithiasis has resolved and the patient has recovered from delivery, pregnant women with stones may benefit from a detailed metabolic evaluation [112]. A qualified urologist or nephrologist can undertake the appropriate investigations electively.

Perinatal complications of urolithiasis in pregnancy

Symptomatic urolithiasis during pregnancy may increase the risk of perinatal complications, however, the evidence is conflicting [10,113–114]. Banhidy et al. performed a population-based case–control study in which patients with congenital abnormalities were compared with those without birth defects [113]. Of the 22,843 newborns with congenital abnormalities, 0.3% had mothers with urolithiasis during pregnancy compared with 38,151 newborns without abnormalities whose mothers had a 0.39% incidence of stones during pregnancy. This finding would suggest there is no association between fetal abnormalities and stones during pregnancy. The authors also noted that mothers with kidney stones did not have a higher incidence of preterm birth or low birth weight infants. By contrast, other population-based studies and case series have reported that pregnant women with stones may have a higher incidence of pre-term birth [114,115], low-birth weight neonates [114], Cesarian section rates [10,114] and mild pre-eclampsia [10]. Lewis et al. reported pre-term premature rupture of membranes in 7% of pregnant patients admitted with stones versus 3% of those without stones in pregnancy [8].

Conclusion

Women in general appear to be developing urolithiasis with increasing frequency. Consequently, it is expected that the incidence of pregnant women with stones may also increase. A diagnostic and therapeutic approach that takes into account the individual patient's symptoms, stage of pregnancy and stone characteristics should be the intent in each case. A multidisciplinary approach involving the high-risk perinatal obstetrical team, urologist, radiologist and anesthesiologist is essential to optimize outcomes.

Future perspective

While our knowledge of urinary stone disease during pregnancy has improved, there remain several areas of controversy that require further study. Is there a 'safe' dose of radiation below which the risk of anomalies is infinitesimally small? Are medical expulsive therapies appropriate during pregnancy? How can we study these types of questions in an ethically appropriate way? Some questions are not amenable to study with our traditional concept of a randomized controlled trial due to rarity of events or lack of clinical equipoise between potential treatments. Perhaps the evolution of epidemiological techniques that can be grouped as "Big Data" offer a possibility. In "Big Data" studies, databases that can include millions of patients are created most often through linking multiple large administrative databases with clinically relevant data. This approach can be maintained over several decades and very rare outcomes can be followed based on observation of what usually happens, which can include off label use of therapies. Perhaps with this in mind we will be able to detect a minimal risk threshold for radiation or convincingly demonstrate the safety of a category B medication in pregnancy.

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