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Urolithiasis – a challenge during pregnancy

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ABSTRACT

Urolithiasis during pregnancy is a rare condition despite the prolithogenic state determined by the physiological changes in the urinary system. The incidence is similar among pregnant women and the general female population, pregnancy not being a risk factor for the appearance of kidney stones. Urolithiasis is a challenge for the obstetrician because diagnosis and treatment require a particular approach in order not to harm the fetus. Ultrasonography is the first choice for diagnosing kidney stones even though it has a reduced sensibility. The first line of treatment in renal colic is expectant management. If this is ineffective, then urological interventions are being taken into consideration. Left untreated, urolithiasis exposes the pregnancy and the baby to higher risks of complications.

Keywords: pregnancy, urolithiasis, kidney stones, renal colic, imaging, ureteral stent, ureteroscopy, nephrostomy

INTRODUCTION

Urolithiasis is characterized by mineral deposits in the urinary tract from the renal calyces to the ureterovesical junction. Incidence rates of kidney stones seem to be rising, especially among women, with the historical male to female disparity diminishing [1]. Urolithiasis can become symptomatic during pregnancy. Pregnancy is a physiological state determining numerous changes in all organ system including the urinary tract. Even though urolithiasis is a rare event during pregnancy, renal colic is the most common non-obstetric cause of hospitalization. In these cases, it is important for the obstetrician to establish the urinary origin of the pain, to differentiate the physiological hydronephrosis from the one caused by a kidney stone and to decide the best management for mother and fetus [2].

METHODS

We reviewed the recent literature regarding urolithiasis appearance and management in pregnant patients. For this purpose, we searched PubMed, Embase and Medscape databases using keywords such as: "pregnancy" along with "urolithiasis", "kidney stone", "renal colic", "physiological changes", "imaging", "ureteral stent", "ureteroscopy" or "nephrostomy". Full-length articles were reviewed with priority for those published in the last 5 years and based on large institutional studies.

PATHOPHYSIOLOGY

Physiological systemic, renal, and mechanical changes occur during pregnancy. Some of these changes increase the risk of kidney stones development. The kidneys, pyelocaliceal system and ureters enlarge during pregnancy [2,3]. Moreover, the growing uterus determines external compression of the urinary tract, hydroureteronephrosis and therefore stasis of the urine. Urinary stasis represents a reservoir for bacterial multiplication, so there is a risk of infection associated with the urinary stasis. Bacterial infection causes a rise in the pH of the urine and alkaline urine is known to pro-

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mote the development of calcium phosphate calculi [4-6].

Elevated levels of hormones associated with pregnancy, such as progesterone, causes smooth muscle relaxation of the ureters resulting in hydroureter [4]. Relaxin is another hormone that has an influence on the structure and hemodynamics of the urinary tract. Secretion of relaxin leads to increased levels of nitric oxide, renal vasodilatation, decreased renal vascular resistance and as a result the renal plasma flow and glomerular filtration rate increase [7]. Increased renal plasma flow determines accelerated excretion of filtered loads of calcium, oxalate, and uric acid, these being the principal components of kidney stones. Hypercalciuria is additionally caused by intestinal absorption and bone mobilization of calcium due to the synthesis of 1.25-dihydroxycholecalciferol in the placenta [3-6,8].

Despite the rise in lithogenic factors in the urine, there is a compensatory increase in the inhibitors of the lithogenesis excreted in the urine, in response to increased renal plasma flow [2,4]. Examples of stone inhibitors are citrate, magnesium, glycosaminoglycans, uromodulin, nephrocalcin. Altogether, metabolic changes of factors that promote and those that inhibit lithogenesis have neutralizing effects [5].

EPIDEMIOLOGY

Despite the pathophysiological changes that a woman undergoes during pregnancy that are believed to lead to kidney stones formation, studies did not show a higher risk of urolithiasis among pregnant patients than in general population of reproductive age women [9].

The incidence of kidney stones during pregnancy is variable. Based on two recent and large cohort studies reviewed, urolithiasis occurs in 0,2% up to 0,8% of the pregnancies [10,11]. Only 0,5% of them need interventional treatment and the number of invasive procedures is decreasing [11].

Regardless of the incidence's variability among pregnant women, kidney stones are more prevalent in multiparous and are more likely to appear in the second and third trimester [9]. The majority of pregnant women with kidney stones have a history of urolithiasis [12].

Statistically, there seems to be an increased risk for an adverse birth outcome such as preterm birth, low birth weight, preeclampsia and cesarian section, in pregnancy complicated by urolithiasis comparing to the pregnant patients without kidney stones [10]. Premature uterine contractions might be caused by the release of oxytocin and antidiuretic hormone as a response to the dehydration suffered by the mother from the vomiting associated in renal colic [13].

DIAGNOSIS

The clinical and paraclinical diagnosis of the nephrolithiasis in the pregnant patients is a challenge because of physiological hydronephrosis which is typically asymptomatic but if it is associated with unilateral renal colic, urolithiasis should be considered [4]. Clinical manifestations include nonspecific symptoms. In order of frequency appear flank pain, macroscopic and microscopic hematuria, nausea and vomiting, fever, dysuria, urgency of urination, pyuria [4-6].

Calculi migrate through the dilated urinary tract and symptoms vary depending on the localization of the stone. Stones situated in the upper urinary tract (lumbar ureter) cause unilateral flank pain, while calculi migrated in the lower urinary tract determine dysuria or urgency of urination [14]. Presence of fever and pyuria are signs of urinary tract infection and increased risk of urosepsis or renal abscesses. Microscopic hematuria on urinalysis (70%) is more frequent than gross hematuria (15%) and is caused by migration of the stone in the urinary tract [15].

The first step in the paraclinical diagnosis is performing a basic laboratory testing that include complete blood count, creatinine blood test, blood urea nitrogen (BUN), inflammatory markers, urinalysis and urine culture, stone analysis if possible [4]. Complete blood count and inflammatory markers detect the presence of systemic inflammation. Serum creatinine and BUN are useful methods to investigate renal function. Urinalysis is considered positive for microscopic hematuria if there are present more than 3 red blood cells/high power field. Only the presence of hematuria has a low specificity and cannot diagnose urolithiasis [16]. Urine culture has an important role in identifying an associated urinary tract infection which would furthermore affect the prognosis [17].

These laboratory findings are corroborated with imaging examination to obtain a certain diagnosis.

Ultrasonography is the gold standard for diagnosis of kidney stones in pregnancy because it is non-irradiant for the fetus, inexpensive and reproducible. This imaging exam detects the obstructing calculi and dilated ureters. Its limitations consist of the difficulty to visualize the ureters, difficulty to localize the stone and inability to differentiate accurately between physiological and pathological hydronephrosis from obstruction. To distinguish between these two, the patient could be examined during ultrasonography in a lateral position, with the symptomatic side facing up [2,5].

Ultrasound with Doppler studies has the advantage of recording the renal blood flow and renal intraarterial resistance. Resistive index (RI) is an index of renal intraarterial resistance defined as the difference between the peak systolic velocity and the peak diastolic velocity, divided by the peak systolic velocity; a value of RI greater than 0.70 is considered pathological and specific for the ureteral obstruction. Moreover, color Doppler ultrasound gives information about the urinary jet flowing through the ureters. Normally, there is a symmetry between right and left ureteral jets but in case of stone obstruction, ureteral jet is absent on the side of the urolithiasis [2,4,18,19].

Ultrasonography (US) findings suggestive for the diagnosis of urolithiasis are: hydronephrosis greater than physiological hydronephrosis of pregnancy; value of RI on Doppler ultrasound above 0.70 in the kidney with renal colic; presence of calculi in the urinary tract; unilateral absence of ureteral jets [2,4,19,20].

Transvaginal ultrasound is another diagnostic imaging for nephrolithiasis during pregnancy. The advantage of this investigation is a higher sensitivity to visualize the distal ureter and ureterovesical junction in comparison to transabdominal ultrasound [5,8,20].

Plain abdominal radiography, intravenous urography, CT, MRI, are other diagnostic tests for kidney stones in general population, but these are associated with risks for fetus [6]. The use of ionizing radiation and contrast substance during the first and second trimester increases the risk of abortion, congenital malformation, carcinogenesis, and intrauterine growth restriction [21]. Clinicians should weigh the risks and benefits of pregnant patients.

In case US is equivocal and clinical suspicion of urolithiasis is high, MRI is the second line investigation of choice [5,6]. Although MRI is not an investigation that uses ionization radiation, it is of little use to explore the urinary tract. The use of gadolinium is not recommended in pregnancy because of its potentially toxic effects to the fetus [2,5]. Half-fourier acquisition single-shot turbo-spin echo (HASTE) magnetic resonance urography (MRU) without contrast is a fast-acquiring investigation which takes only 15 minutes to explore the area of interest (in contrast to a duration > 45 minutes of traditional MRI). MRU permits a better visualization of the urinary tract and can exclude other differential diagnoses. Although HASTE MRU appears to be superior to traditional MRI, its use is limited because of the costs and availability [4-6]. Signs of urolithiasis on MRU images are intraluminal filling defects created by stones, perirenal fluid, renal edema and "double kink" sign characteristic to obstruction of the ureterovesical junction [22,23].

In general population, CT is the most used imagistic method to diagnose kidney stones, but during pregnancy it should be avoided, if possible, particularly in the first trimester [8]. CT represents the third-line diagnostic method and only low-dose computed tomography of less than 50 mGy is accepted during the second and the third trimester [4]. This low-dose protocol seems to be safer, but childhood neoplasm induced by radiation is still debated [23].

Intravenous urography uses both radiation and iodinated contrast. Its use has declined over the last years and has been replaced by the imaging modalities mentioned above [2].

Finally, ureteroscopy can be used for definitive diagnosis of urolithiasis when other methods fail to visualize the kidney stone [15].

TREATMENT

Conservative treatment

Guidelines on urolithiasis recommend that during pregnancy the first line treatment should be the expectative management if there are no signs of complications. During the follow-up period, if any complication appears or if the non-operative therapy is ineffective, an urologic intervention will be required [24].

Stone passage during pregnancy might occur in as much as 70-80% of the cases. Because of the physiological dilation of the ureter throughout this period, calculi might be eliminated spontaneously even easier. Most patients are eligible for conservative treatment, especially if there is only one small stone (less than 1 cm) and no sign of infection [25].

The first conservative measures that can be applied are hydration and pain medication that is compatible with pregnancy. Patient should be monitored with biological and imaging examinations, as well as clinically [26].

Medical expulsive therapy

In order to facilitate the passage of the kidney stones, some adjuvant medications can be used, but their advantage has always been debated. Alfa-blockers are known to inhibit the contraction of smooth muscles of the ureter and are recommended as medical expulsive therapy (MET). Two recent retrospective studies have evaluated the use of Tamsulosin as being safe in the second and third trimester of pregnancy. MET seems not to have any adverse outcomes at birth, regarding the gestational age at delivery, birth weight, or Apgar score. Even though in the first study by Bailey et al. there were 2 cases of sudden infant death syndrome out of 27 women who used Tamsulosin, these events might

have been coincidental [27]. Later, Theriault et al. reported the results from their study on a larger population of pregnant women treated with Tamsulosin. Out of 69 cases in the MET group, no infant death was registered during 1-year postnatal follow-up [28]. Regarding the efficacy, Tamsulosin appears to increase the rate of kidney stone passage (62,5%) comparing to the rate of spontaneous passage without MET (45.5%), but without statistical significance (p = 0.09). Moreover, fewer women needed interventional treatment in the MET group (23%) versus expectative management (27%) [28].

Urological procedures are primary indicated when the obstruction is bilateral or in case of a unique kidney. If conservative management fails and symptoms persist, fever, infection or obstetrical complications appear, then interventional treatment is required. There are temporary solutions as percutaneous nephrostomy or ureteral stents as well as permanent treatment consisting of ureteroscopic stone removal [11,12,25]. The decision is taken by the patient, obstetrician, urologist, and interventional radiologist together.

Percutaneous nephrostomy

Percutaneous nephrostomy (PCN) is an alternative drainage method when other procedures fail or in case of pyonephrosis [29,30]. Nephrostomy tube placement is safe using ultrasound guidance and it is performed under mild sedation or local anesthesia. With the patient in lateral decubitus position, initially a needle is introduced in a posterior renal calyx under US guidance. Afterward, the placement can be confirmed with a contrast injection using fluoroscopic imaging and then the guide wire is introduced into the renal pelvis under fluoroscopy. Finally, after the dilation of the tract, the drainage catheter is placed over the guide wire and fixed to the skin [29,31]. The greatest concerns regarding percutaneous nephrostomy are radiation and anesthetic exposure. Ionising radiation can be reduced by using low dose techniques or pelvic shielding, but theoretical risk of fetal exposure still exists. In order to avoid this risk, successful nephrostomy tube insertion can be performed under ultrasonography guidance exclusively [29]. Also, the fetus undergoing anesthesia is debated even though Fentanyl and Midazolam, which are used for sedation, are not associated with fetal anomalies. Another option is local anesthesia with pain control pills permitted during pregnancy [31]. A recent study that included 49 pregnant women who underwent nephrostomy showed no adverse delivery outcomes and all of them had significant relief of their pain, 56% of them having natural childbirths. The rate of preterm birth was similar to that in the general population (15%) and pregnancy complications such as preeclampsia, gestational hypertension or premature rupture of membranes appeared in 14 patients [31]. PCN is a safe and efficient method, but during pregnancy there is a higher risk of encrustation leading to a shorter period between exchanges of the catheter (2 weeks) [31].

Double-J stent insertion

Double-J stent insertion is an internal drainage method for pregnant women with symptomatic urolithiasis after conservative treatment fails, especially if the stone is small and it appears in the later stages of the pregnancy [15]. It is used to temporary ease the obstructive uropathy until delivery [32]. The procedure can be performed under any kind of anesthesia with the patient in gynecological position. In order to avoid urinary tract infection, urine culture sample is performed, and a dose of prophylactic antibiotic is administered before the intervention [33]. Under cystoscopy visualization, a sensor guidewire is passed through an open-ended catheter from the urethral meatus, going by the ureterovesical orifice until it reaches the renal collecting system. Then, the stent is placed in this position by sliding over the guidewire [15,34]. Ureteral stent seems to be as effective as PCN leaving out the risk of bleeding and the inconvenience of external drainage [30]. As we have mentioned above, ureter becomes dilated during pregnancy making the insertion of the stent easier. On the other hand, this also might increase the risk of stent dislocation. A study comparing these two methods has shown that patients undergoing double-J stent insertion had a greater rate of reintervention at a shorter period of time after the procedure than those who had a percutaneous nephrostomy [34]. No significant obstetrical complications were noted in the reviewed studies [15,30,34]. However, ureteral stenting might lead to complications such as: urinary tract infection (20%), bladder irritation, hematuria or stent encrustation [15,33].

Ureteroscopy lithotripsy

These methods are only temporary, kidney stones not being removed and leading to the necessity of another definitive procedure after the delivery. Besides, patient's postoperative tolerance of percutaneous nephrostomy and ureteral stent is reduced, thus making ureteroscopic stone removal the preferred choice. Moreover, ureteroscopy is more cost efficient than ureteral stent at any time during the pregnancy [32]. A slight disadvantage is represented by the need of general or spinal anesthesia. The procedure can be performed either with a semirigid ureteroscope in the first and second trimester or a flexible one in late pregnancy [35]. For

the stone destruction holmium:YAG laser is less harmful for the fetus than pneumatic lithotripter. Complete stone fragmentation is succeeded in most of the cases. Overall, ureterolithotripsy is safe in all trimesters of the pregnancy [12,35]. Complete fragmentation is defined by stone remains smaller than 4 mm. Ultrasonography can be used in order to identify any residual stone or to determine if the patient is stone-free. After the procedure, uterine contractions occurred in a few cases, but did not lead to premature birth [15]. Otherwise, fever, urinary tract infection and delaying the intervention more than 36 hours were incriminated for the appearance of premature uterine contractions more than the procedure itself [17]. Taking into consideration the technological advances in endourology, definitive treatment of urolithiasis by ureteroscopy will be elected option in the next years [15,25].

DISCUSSION

The literature that we have reviewed suggests a higher risk of pregnancy and maternal complications related to urolithiasis [10,36-38]. A large population-based study conducted in Ontario, Canada from 2004 until 2014 on 1.39 million pregnant women showed a significantly increased risk for preterm birth, low weight at birth and preeclampsia among those diagnosed with a kidney stone [10]. Besides, another large-cohort study found higher rates of gestational diabetes in pregnancies complicated by stone-disease (6,75%) comparing to stone-free patients (5.27%) [37].

These medical conditions can also affect the fetus, thus leading to adverse neonatal outcomes as well. For example, gestational diabetes can lead to hyperglycemia and furthermore to fetal anomalies [37]. Low-birth weight was significantly associated with urolithiasis [38].

Moreover, these pregnancies are more likely to be terminated by cesarean section, possibly because of the above-mentioned complications or other circumstances [11]. Another cause might be that women in late pregnancy who need urological intervention for the obstructive uropathy would decide to deliver earlier undergoing cesarean section before the interventional treatment in order to avoid any potential harm to the baby [37].

CONCLUSIONS

Urolithiasis can appear in pregnant patients as frequent as in general population, but diagnostic and therapeutic management is more complex and requires the collaboration between obstetrician, urologist, and patient. We believe that this review will help the obstetricians to better understand this condition, counsel and offer the best management to women encountering this condition during their pregnancy.

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