

Renal colic during pregnancy: Diagnostic and therapeutic aspects. Literature review

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Citation: Tortolero Blanco L, Rodríguez Socarras M, Fabuena Montero R, et al. Renal colic during pregnancy: Diagnostic and therapeutic aspects. Literature review. Cent European J Urol. 2017; 70: 93-100.

Article history

Submitted: Dec. 13, 2015

Accepted: Nov. 21, 2016

Published online: Oct. 28, 2016

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Introduction Renal colic during pregnancy is a rare urgency but is one of the most common non-obstetric reasons for hospital admission. The management often means a challenge for the urologist and gynecologist due to the complexity involved in preserving the maternal and fetal well-being.

Material and methods We performed a literature search within the PubMed database. We found 65 related articles in English. We selected 36 for this review prioritizing publications in the last two decades.

Results The anatomical and functional changes of the genitourinary system during pregnancy are well documented; also during pregnancy, there are several metabolic pro-lithogenic factors. The most common clinical presentation is flank pain accompanied by micro or macro hematuria. US provides data identifying renal obstruction shown by an increased renal resistance index. MRI allows differentiating the physiological dilatation from the pathological caused by an obstructive stone showing peripheral renal edema and renal enlargement. Low dose CT has been determined to be a safe and highly accurate imaging technique. Once the diagnosis is confirmed, the initial management of patients should be conservative. When conservative management fails the interventional treatment is mandatory, a urinary diversion of the obstructed renal unit either by a JJ stent or through a PCN catheter has to be done. The definitive management of the stone can be done in the postpartum or deferred ureteroscopy can be considered during pregnancy.

Conclusions Renal colic during pregnancy is an uncommon urgency, so it is important for the urologist to know the management of this condition.

Key Words: renal colic ↔ pregnancy ↔ ureteroscopy ↔ JJ stent ↔ percutaneous nephrostomy ↔ lithotripsy

INTRODUCTION

Renal colic during pregnancy is relatively rare (1 in 1,500 pregnancies), but it is one of the most common non-obstetric reasons for hospital admission. The management often means a challenge for the urologist and gynecologist due to the complexity involved in preserving the maternal and fetal well-being combined with the pharmacological constraints inherent to the condition of the pregnant patient [1, 2]. Pregnancy certainly complicates the management

of renal colic, such as the adverse side effects on the fetus of ionizing radiation and drugs used in anesthesia and analgesia. These effects are often increased during the period of embryogenesis (the first 12 weeks of gestation). Fortunately, 80 to 90% of stones during pregnancy appear in the 2nd and 3rd trimester; however, it is not ruled out that these harmful agents could cause some sort of disturbance in the fetal development at any time during the pregnancy [3]. The gynecologists' main objective is to preserve the maternal and fetal health and to maintain

the proper course of pregnancy and this at times might antagonize the urologists' main objective, which is to minimize the damage to the renal unit due to the uropathy secondary to the obstruction of the urinary tract. The diversity of therapies available and the inherent need for a multidisciplinary management among urologists and obstetricians have led us to review the recent and relevant publications on this subject.

Renal colic during pregnancy, in conjunction with low urinary tract symptoms (LUTS), acute urinary retention and urinary incontinence, are some urological pathologies that are considered associates and/or aggravated by pregnancy [3].

Acquisition of evidence

We performed a literature search within the PubMed database using the search words: "renal colic during pregnancy". We found 65 related articles in English. We selected 36 for this review by prioritizing publications published in the last two decades. All the articles related to the topic were reviewed in order to provide data on diagnostic methods, medical and surgical treatment.

Epidemiology

Renal colic during pregnancy is a rare motive of consultation. The data reporting incidence is very variable: between 1/244 to 1/2400 pregnancies and for complicated renal colic near to 1/3300 pregnancies, this wide variability in the prevalence of this pathology may be due to the known geographical differences in the incidence of urolithiasis and the different diagnostic criteria used in the series reported;

a number close to 1 in 1500 pregnancies could correspond to a more realistic view, not being increased than the incidence in the childbearing non-pregnant population [1, 2] (Table 1). There is a higher incidence of renal colic during the 2nd and 3rd trimester of pregnancy and in multiparous women in a ratio of 3:1 *vs.* first time pregnant women, both kidneys are equally affected [3, 4, 5]. Despite the low prevalence of this condition, renal colic pain in pregnant women is one of the most common non-obstetric reasons for hospital admissions [1, 2, 3].

Pathophysiology

The anatomical and functional changes of the genitourinary system during pregnancy are well documented, some of which are: increased glomerular filtration, increased diuresis, hydronephrosis (90% right kidney, 67% in the left kidney) generated by the progesterone in the early stages of pregnancy which acts on the smooth muscle of the ureter reducing its diameter, accompanied by an increased urinary volume. The combination of these two latter phenomenon generates the dilatation of the upper urinary tract. The uterus in anteversion position during the third trimester can cause extrinsic compression and favor the dilatation of the ureter in the latter stages of the pregnancy [6, 7]. Endoscopically, into the bladder of a pregnant woman during the third trimester, an indentation of the bladder dome is observed due to the enlarged uterus and the ureteral meatus is located in a higher position than usual; these changes not only might influence as predisposing factors for nephrolithiasis, but can also hinder the diagnosis of obstructive uropathy in pregnant patients [1, 8].

Table 1. Prevalence of renal colic in pregnancy

Author	Year	Studied Population	Nephrolithiasis cases	Prevalence	Age (range)	Gestational Age
Ho-Ying Ngai	2013	NA	Total: 30 12-> calculus 18-> pain (colic)	NA	27.2 (18-38)	1 ^o ->5 (17%) 2 ^o ->15 (50%) 3 ^o ->10 (33%)
Lata H (18)	2011	520	2	0.4%	26 (16-40)	3 ^o ->2 (100%)
Yung-Shun J	2007	5,042	18	0.35%	30.11 (23-39)	1 ^o ->2 (11.1%) 2 ^o ->6 (33.3%) 3 ^o ->10 (55.5%)
Swartz MA	2007	1,297,625	2,239	0.17% 1.7/1000/year	26.6 (21-32)	1 ^o ->101 (4.5%) 2 ^o -> 594 (26.5%) 3 ^o ->1512 (67.5%)
Lewis DF	2003	21,010	86	0.4%	NA	NA
Drago JR	1982	1,696	9	0.5%	NA	NA

NA – not available

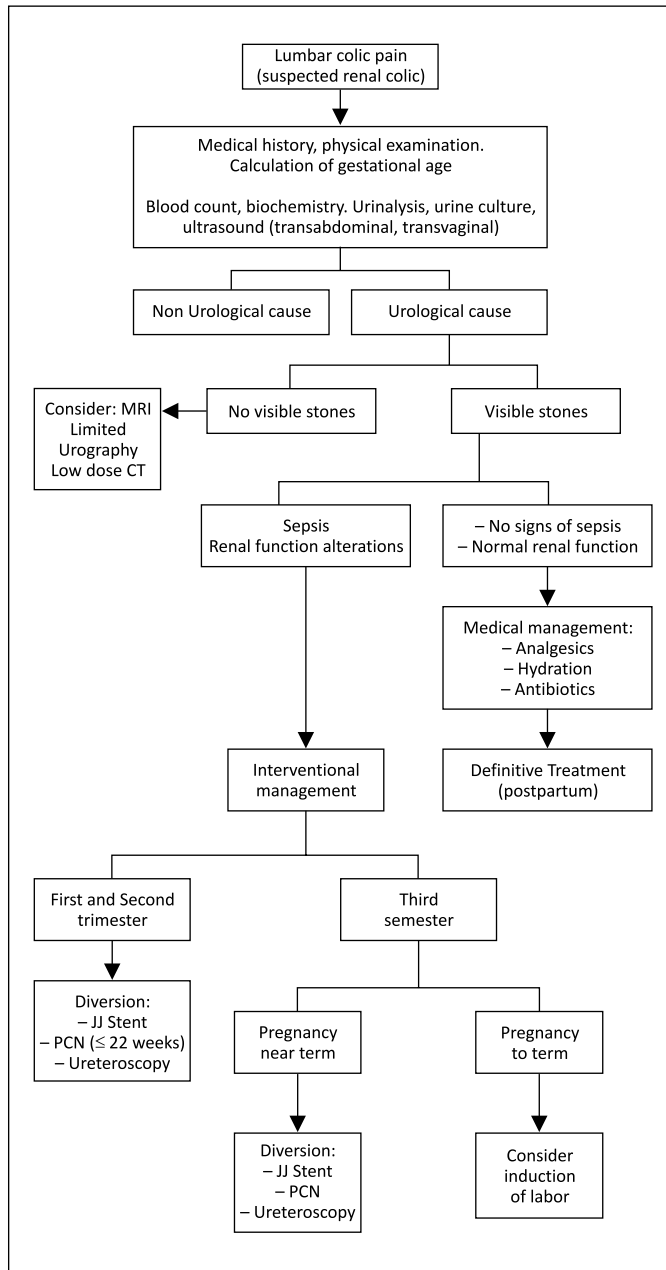


Figure 1. Summary illustrating the management of renal colic during pregnancy.

During pregnancy, there are several metabolic pro-lithogenic factors, such as increased urinary excretion of calcium and uric acid; however, in pregnant women factors that can act as inhibitors of calculus formation are observed such as: increase of magnesium citrate excretion that acts by inhibiting the formation of calcium stones, the excretion of glycosaminoglycans and acid glycoproteins is also increased which inhibits the formation of oxalate, and the relative alkalinity of the urine that can occur as a result of the respi-

ratory alkalosis during pregnancy, which decreases the uric acid formation. The underlying balance of all the factors previously described makes the incidence of urolithiasis and renal colic during pregnancy not greater than the incidence in the childbearing non-pregnant population [3, 8, 9].

The most common obstetric complication related to renal colic during pregnancy is preterm labor [8]. Women admitted with nephrolithiasis have nearly doubled the risk of preterm labor than women without stones; however, performing a surgical procedure (endourological, nephrostomy or others) and the trimester of pregnancy appears to increase the risk of preterm labor. It has been suggested that dehydration from vomiting induced by colic can trigger preterm labor due to the release of antidiuretic hormone and oxytocin [10].

Diagnosis

The most common clinical presentation of renal colic is flank pain accompanied by micro or macro hematuria (Figure 1). Nevertheless, the condition of *acute abdomen* during the second or third trimester of pregnancy is difficult to assess because the pregnant uterus changes the position of the colon, ovaries, appendix and bladder, which can modify the location of the pain. Differential non-obstetrics diagnoses are appendicitis, cholecystitis, pyelonephritis and with regard to obstetric causes of *acute abdomen*: abruption and preeclampsia with hepatic involvement [11]. The patient should be questioned about the history of nephrolithiasis and the presence of abnormalities in the urinary tract and/or metabolic diseases.

Blood cell counts, biochemistry and urine sediment are laboratory tests that have proven to be useful in the diagnosis of renal colic [12].

As we have to avoid fetal exposure to radiation, the usage of ultrasound (US) imaging has emerged to be the first-line image test with a positive predictive value of 77%, in addition to its affordability and safety. US imaging allows for the evaluation of other abdominal organs, it can be used with transabdominal and/or transvaginal probes and it also provides data identifying renal obstruction shown by an increased renal resistance index. Some clinical studies have shown that the renal resistance index >0.7 suggests ureteral obstruction with a 95% specificity. The use of doppler to identify ureteral asymmetrical *Jet* provides valuable information on total ureteral obstructions; however, if a partial obstruction exists it may decrease its effectiveness. The physiological hydronephrosis of a pregnant patient may hinder the diagnosis and decrease the US sensitivity to 74%

and the specificity to 67%, which is insufficient for an accurate diagnosis. It has been identified that there are up to 40% of failures using the US imaging as the proper diagnostic tool as in general the US imaging is not only needed to the demonstration of the existence of obstruction, but the US imaging must in addition show stone location and size [11, 13].

Some authors have proposed to perform dilatation curves of the upper urinary tract during pregnancy, showing an upper urinary tract diameter increase of 0.5 mm/per week until 24 to 36 week, or 0.3 mm/per week until the 32nd week, then remaining stable until the end of pregnancy, this would distinguish between physiological and pathologic hydronephrosis [8, 11, 14].

The second line imaging tool used is magnetic resonance (MRI) with a positive predictive value of 80%. The MRI allows for the differentiating of the physiological dilatation from the pathological caused by an obstructive stone showing peripheral renal edema and renal enlargement. MRI combined with urography (MRU) has been extensively studied as an alternative imaging technique when compared to the standard CT. It offers highly accurate anatomical detail of the entire urinary tract, but does not expose the patient to ionizing radiation, an obvious benefit in pregnant patients. However, MRU offers poorer spatial resolution, requires prolonged imaging times, is associated with increased costs and also has inferior sensitivity for detecting calcifications and calculi when compared to the standard and low dose CT. In addition, while MRI is generally considered safe during pregnancy, there is a scarcity of knowledge regarding the safety of magnetic resonance during the first trimester, especially as it pertains to radio frequency exposure [14, 15].

Historically 3-shot or limited *intravenous urography* (IVP) has been considered as an imaging modality of choice in pregnant patients suspected of having renal colic. Limited IVP is consistent of a preliminary radiography before and after 30 minutes after contrast injection with each simple abdominal x-ray exposing the fetus to a radiation of 0.1 to 0.2 rad, below the threshold of 1.2 rad from which the risk of damage begins to increase. The disadvantages of this method are fetal radiation exposure, the need to use intravenous contrast and the difficulty of its interpretation with the fetal skeleton in the images and perhaps most importantly, our generalized dependence on the cross-sectional imaging has largely rendered IVP obsolete and, in some facilities, unavailable. The radiation exposure should be avoided particularly during the first trimester of embryogenesis. It has demonstrated that the use of leaded thyroid shields on the uterus decreases the fetal radiation exposure [16].

Computerized tomography (CT) is an image test that uses a large dose of radiation exceeding the recommended as safe, therefore its use is not recommended. CT is associated with an increase of 2.4 times the risk of cancer in children and an increased incidence of fetal malformations [17]. CT should only be used when the benefits outweigh the risks. If there is a life-threatening situation of the mother and/or fetus, ureteroscopy may be considered as a diagnostic option, especially in the period when the fetus is at or near the term condition [8–11, 18, 19].

Low dose CT has been determined to be a safe and highly accurate imaging technique. When CT is required, the use of a low dose protocol CT is preferable in the pediatric population and among patients with recurrent stone disease due to concerns regarding the initial and cumulative radiation exposure, respectively. For many reasons significant concern remains prevalent among radiologists and urologists regarding the indications of low dose CT in the setting of pregnancy. These fears persist despite the longitudinal data that support the relative safety of imaging using this technique during pregnancy in the obstetrics and teratology literature. Of note, the American College of Obstetricians and Gynecologists currently recognizes and endorses the prudent use of CT during pregnancy to aid in the diagnosis and management of significant medical problems, including the evaluation of urinary stone disease [14, 15].

Treatment

Once the diagnosis is of ureteral stone is confirmed, the initial management of the patient should be conservative, with a success rate of 70–80% with spontaneous passage of the stone. The medical treatment involves the administration of analgesics, hydration and antibiotics if any indication of urinary infection or sepsis exists [20].

Subcutaneous injection of sterile water has been compared with paracetamol use in a randomized study supporting its effectiveness. Continuous epidural blockade (T11-L2) has been recommended as an option and seems to benefit the spontaneous expulsion of the stone [21]. When conservative management fails or one of these conditions applies: sepsis, renal failure, solitary kidney and bilateral obstructive uropathy; the interventional treatment is mandatory, a urinary diversion of the obstructed renal unit either by a JJ stent or through a percutaneous nephrostomy (PCN) catheter has to be done. Both procedures have been performed in pregnant patients successfully, with assumable risks and complications.

Table 2. Analgesic used for the management of renal colic in pregnant women

Medication	Category	Fetal adverse effects	Indications
Morphine	C	It can produce dependence in the fetus. Withdrawal symptoms (convulsions, tremors, overactive reflexes, diarrhea, vomiting)	Safe dose and limited time (The risk-benefit relation should be assessed)
Dexketoprofen	D	1 ^o -> Trimester. Cardiac malformations, gastroschisis. 3 ^o -> Trimester. Closure of ductus arteriosus. Pulmonary hypertension	Contraindicated
Metamizole	D	Closure of the ductus arteriosus cannot be excluded. Complications: Impaired platelet aggregation in newborn and mother	Contraindicated. It is not expected to be used during the third semester. The risk-benefit relation should be assessed
Tramadol	C	No evidence of embryotoxicity in humans	Contraindicated
Codeine	C	It crosses the placental barrier. Prolonged delivery. It can cause respiratory depression in the fetus.	Contraindicated (Third Trimester)
Ibuprofen	B/D (3 ^o t)	Cardiopulmonary toxicity. Kidney failure with oligohydramniosis. Prolonged labor.	Contraindicated (Third Trimester)
Paracetamol	B	No adverse effects at therapeutic doses.	Analgesic Antipyretic
Pethidine	B/D (3 ^o t)	no data on teratogenic effects. Suction problems. RN respiratory depression.	Analgesic

The definitive management of the stone can be done in the postpartum or deferred ureteroscopy can be considered during pregnancy. There are reports of extracorporeal lithotripsy being performed in pregnant patients without the knowledge of being pregnant and no congenital and/or chromosomal abnormalities have been reported, however, it is contraindicated during pregnancy. Percutaneous lithotripsy has been successfully performed during pregnancy although is not a procedure to be done routinely due to the need of anesthesia, radiological control and prone position [22–26].

The choice of analgesic to be used should be performed carefully, with the avoidance of using NSAIDs due to their association with pulmonary hyperten-

sion and premature closure of the ductus arteriosus when used during the third trimester. Furthermore, another choice of analgesic, codeine, should be avoided during the first trimester as it has been linked to birth defects when used during this period. An analgesic that can be used safely during pregnancy is morphine with apparently no reported side effects when used in small doses and over a limited time [27, 28] (Table 2).

Ureteral catheterization

The ureteral catheterization is a technique managed by almost all urologists; it can be performed under local anesthesia or sedation thus avoiding the risks associated with general anesthesia in these patients [29, 30].

Several authors propose performing this procedure by guided ultrasound in order to avoid ionizing radiation involved by fluoroscopy, although this could be used in a restricted way if the ultrasound is not available.

As an efficient and low-invasive method, a JJ catheter can be inserted under ultrasonography guidance, thereby avoiding the hazard of radiation, in most situations.

However, the insertion of a JJ stent has several drawbacks, including the potential of bladder irritability, stent encrustation and infection. Encrustation is a particular concern during pregnancy because hyperuricosuria and hypercalciuria are often present during the pregnancy and frequent stent replacements might be required for affected patients. Pregnancy related asymptomatic bacteriuria might also be a factor contributing to encrustation. It has been suggested that the stent should be changed every 4–6 weeks to prevent encrustation. Hydration and antibiotics should be added to the treatment when necessary. It should be noted that the stents can shift to the bladder because of ureter dilation during pregnancy and some patients who undergo JJ stent insertion might experience lumbar pain and lower urinary tract symptoms because of ureteral vesical reflux, in addition, some patients might undergo preterm labor. In these situations, PCN tube placement and ureteroscopy are recommended as alternative options [23, 29, 30].

Renal colic during pregnancy is not necessarily caused by kidney or ureteral calculi. Some hydronephrosis cases may be caused by enlarged uterus oppression. Furthermore, for renal colic patients without ureteral calculi, a diagnostic ureteroscopy and/or ureteral DJ stents can help relieve obstruction. These methods are also effective in reducing pain and promoting drainage in hydronephrosis [31].

Percutaneous nephrostomy

With its high success rate, the introduction of a PCN tube for treating urolithiasis is a technique that can be performed safely during pregnancy. PCN can be performed under local anesthesia guided by ultrasound. Septic and/or pyonephrosis are its main indications allowing immediate possibility of obtaining drainage samples for urine culture. Nephrostomy advantages are the possibility of introducing different sizes of drainage tube, providing the future access for potential percutaneous treatment of stones after birth and also preventing the manipulation of the ureter using endoscopy and avoiding the risks of perforation and infection spread, when it exists. It seems more cost effective when compared to ureteral catheterization. However, PCN treatment has several disadvantages such as the potential for tube

obstruction by debris, tube dislodgement, infection, bleeding, need to carry an external collecting bag, need for periodic changes and the technical complexity in the third trimester. It has been proposed as a technique of choice for pregnancies of ≤ 22 weeks [11, 12, 20, 23].

Ureteroscopy

This procedure has gained popularity in recent decades with an increase in the number of publications that support its use in pregnancy, probably due to the improvements in flexible and rigid ureteroscopes with smaller calibers and the progress in technology for lithotripsy that allows treatments for larger and different compositions of stones. Therefore, there is a growing trend on treating symptomatic patients during pregnancy [31–36].

Table 3. Surgical procedures in pregnant women

Author	Year	Number of cases	Age (range)	Gestational Age in weeks (range)	Procedure	Incidence of complications	Type of Complications	Size of lithiasis in millimeters (range)
Son Yang	2013	54	27.1	26.5	1. Ureteroscopy lithotripsy 2. Nephrostomy 3. Placing JJ stent catheter	1 → 3 (14.3%) 2 → 5 (31.2%) 3 → 9 (52.9%)	Embedding catheter Irritative symptoms Preterm labor	13.14 (7–22)
Deters	2013	7	28 (20–35)	24 (13–33)	Ureteroscopy US laser lithotripsy	1 → 14%	Preterm labor (Caesarea) 33 weeks.	10.8 (5–22)
Bozkurt	2012	32	27.8 (20–39)	24 (15–34)	Ureteroscopy a) Lithotripsy	9	Urinary infection Sepsis Urinary fistulae Pain/dysuria	8 (5–19)
Lain, KA	2012	116	28 (16–41)	Second, Third semester	Ureteroscopy: a) Laser lithotripsy b) Ultrasonic lithotripsy c) Extraction bag	9 (7.75%)	Clavien II: Preterm labor Clavien III: Drilling ureter. ITU.	3–16 mm
Polat	2011	16	25 (19–34)	30 (23–35)	Rigid ureteroscopy a) Intracorporeal lithotripsy pneumatic	0	NO	9.45
Travassos	2009	9		19 (13–28)	Ureteroscopy a) Gallstone extraction bag JJ stent (7 days)	0	NO	8 (6–10)
Majid Rana	2009	19	22 (18–27)	20 (14–34)	Rigid ureteroscopy a) Intracorporeal lithotripsy pneumatic	0	NO	11 (8–18)
Asagari	1999	6	32 (19–34)	(1–4)	ESWL (mean 22kV, range 18–26)	0	No fetal malformations No chromosomal abnormalities Birthweight: 2.85 (2.22–3.45) kg	12 (5–18)
Kavoussi	1992	6	(18–30)	(12–33)	Ultrasound guided PCN	1 (16.6%)	Recurring PCN tube occlusion	18.8 (2–20)

Some studies have revealed the use of ureteroscopy in the pregnant patient with various sources of lithotripsy and extraction of stones (laser, pneumatic, ultrasound, nitinol basket) in a wide range of gestational ages and with different stone sizes with successful results and with a low percentage of urological and obstetric complications. However, this technique should be performed by experienced endourologists (Table 3) [11, 23, 24]. It seems that the ultrasound guided ureteroscopy is an option in complex cases, with the safety and success rate, without residual stones, near 70%. A recent meta-analysis has shown that ureteroscopy is safe and does not increase the risk of endoscopic complications in pregnant patients [7].

The disadvantages for the technique are the need for general anesthesia, in some cases, and the long operative time associated with the size of the stone. The holmium laser seems to have an excellent safety profile in pregnant women, while other energy sources such as hydro or ultrasonic have been associated with audition loss by the fetus and may induce uterine contractions [7, 23].

Routine JJ stent placement after ureteroscopy is not recommended by some studies because of the stent related complications. However, the insertion of a ureteral stent to facilitate the passage of residue pieces is recommended [23].

Open surgery

It is a viable alternative in some selected cases. General anesthesia and surgery has been linked to birth defects when used during the first trimester and in later stages of pregnancy with delayed intrauterine growth, prematurity and fetal death [9]. Shnider reported the preterm birth rate of 6.5%, 8.6%, 11.9% in the first, second and third trimesters, respectively [12]. The indication of open surgery is limited to septic patients with symptoms where endourological techniques have failed or are unavailable.

CONCLUSIONS

Renal colic during pregnancy is an uncommon medical issue, so it is important for the urologist to be aware of the management of this condition when it occurs. In addition to the urological risks such as sepsis, acute renal failure and rupture of the urinary tract; obstetric complications such as preterm labor and premature rupture of membrane are major risks associated with this issue. In conclusion, these underlying risks are the reason why preserving the maternal-fetal well-being should be the main target when dealing with these patients.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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