

Dear editor:

Re: Resubmission of manuscript reference no: 65932

We have revised our paper (Does Delaying Ureteral Stent Placement Lead to Higher Rates of Preoperative acute pyelonephritis during pregnancy?)according to the reviewers' suggestion and marked what we have revised in the revised manuscript. The reviews's comments were highly insightful and enabled us to greatly improve the quality of our manuscript. We have given a point-to-point answer to the reviewer's questions and showed them in following below. Revisions in the text are shown using **red highlight** for additions. Moreover, we employed an English-language editing service, **Charlesworth** to polish our words and grammars.

Thank you very much!

Best Regards,

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Response to reviewer

1.The main reasons of renal colic in pregnancy are urinary stones and hydronephrosis". Please explain on the pathophysiology the development of urinary stones and hydronephrosis in pregnancy

Response: We agree with this suggestion, so we explain on the pathophysiology the development of urinary stones and hydronephrosis in pregnancy in the **Introduction sections**(page 3, line 9-15). The content is as follows:

Antenatal hydronephrosis and hydroureter both result from compression of the ureter at the pelvic brim by the growing uterus and smooth muscle relaxation induced by elevated progesterone levels[5-6]. Moreover, the secretion of placental 1,25-dihydroxycholecalciferol and parathyroid hormone are reduced, resulting in transient hypercalciuria during pregnancy. These substances in the urine combine with each other and the obstruction of the urinary tract leads to the deposition of crystals in the urine in the poorly drained part, thereby forming stones[7].

We also added and modified references.

5. Biyani CS, Joyce AD. Urolithiasis in pregnancy. II: management. BJU Int. 2002 ;89:819-23. [PMID: 11972503 doi: 10.1046/j.1464-410x.2002.02773.x.]
6. Smith PD. Effects of pregnancy and progestational agents on the urinary tract. Am J Obstet Gynecol.1972;15;114:281-2.[PMID:4673812.doi: 10.1016/0002-9378(72)90080-4.]
- 7.Srirangam SJ, Hickerton B, Van Cleynenbreugel B. Management of urinary calculi in pregnancy: a review. J Endourol. 2008;22:867-75. [PMID: 18377238. doi: 10.1089/end.2008.0086.]

2. "Clinical features associated with acute pyelonephritis during pregnancy include asymptomatic bacteriuria[5], age younger than 20, childbirth, smoking, late diagnosis and treatment, sickle cell traits and prior (non-gestational) diabetes, asymptomatic bacteriuria[6-8]." These are the risk factors not clinical features. Please provide the clinical features.

Response: We agree with this suggestion, So we modified "Clinical features associated with acute pyelonephritis" in the **Introduction sections**.(page 3, line 20-25). At the same time, we revised the references.

The clinical features of acute pyelonephritis during pregnancy include fever (>38°C), chills, low back pain, nausea, vomiting, or costal and spinal angle pain, with or without typical symptoms of cystitis. Pregnant women need special attention when they develop acute pyelonephritis. Acute pyelonephritis not only adversely affects pregnant women, but also causes anemia, renal insufficiency or respiratory insufficiency; it also affects the fetus^[8].

References:

8. Johnson JR, Russo TA. Acute Pyelonephritis in Adults. N Engl J Med. 2018;4;378:48-59. [PMID: 29298155. doi: 10.1056/nejmcp1702758.]

3. Conservative treatment is effective for 70-80% of renal colic during pregnancy. Please explain on the conservative treatment.

Response: We agree with the comment. We explain on the conservative treatment in the **Introduction sections**. (page 3, line 27-31):

Pregnant women who develop a stone may need three types of medication: painkillers, antibiotics and anesthesia drugs. Patients with simple renal colic without other complications should be given antispasmodic, analgesic and anti-infective treatment, and if necessary, uterine contraction suppression treatments should be given^[10].

4. Authors mentioned a few diagnostic criteria for renal colic and acute pyelonephritis. Does all the patients met all the criteria to be included or there were certain criteria need to be met in order to be included in the studies i.e. symptoms, labs or imaging.

Response: We agree with your comment.

Diagnostic criteria for renal colic: left or right low back pain, with or without

fever, frequent urination, urgency, hematuria, obvious percussive pain in the kidney area, and B-ultrasound confirmed stones or hydronephrosis on the affected side. The patients could be diagnosed as renal colic who met the following points: percussion pain in the renal area, and B-ultrasound prompts hydronephrosis or hydronephrosis. We added this content in section of **Materials and methods**(page 4, line 18-20).

The diagnostic criteria for acute pyelonephritis: the presence of flank pain, fever ($>38^{\circ}\text{C}$ or 100.4°F), and/or costovertebral angle tenderness, with or without the typical symptoms of cystitis, or is confirmed by the finding of bacteriuria in the setting of these symptoms. The diagnosis can be confirmed if the patient meet the following three points: renal colic, fever, and positive urine culture. We supplemented this contents on(**page 5, line13-15**) in **Materials and methods sections**.

5. Please elaborate on the preoperative fetal complications i.e. what are those complications?

Response: Thank you very much for your questions.

Preoperative fetal complications include premature delivery, threatened premature delivery, premature rupture of membranes, or fetal loss which mentioned on **page 5, line 17-19**.

6. It will be helpful to include a graph for Table 4 and 5 to compare the outcome side by side.

Response: Thank you very much for your advices. We have combined Table 4 and Table 5 into new table 4 and marked them red in the revision manuscript.

Renal colic symptoms were eliminated after surgery in all patients. Laboratory data showed improvement as well (Table 4 in **page 11**). As the patient's creatinine was normal before and after surgery, creatinine levels were not compared.

Table 4 Comparison of outcomes in TOS patients before and after surgery

Variable	Before TOS(n =100)	After TOS(n =100)	p
WBCs(*10 ⁹ /L), ($\bar{x} \pm s$)	13.48±3.48	9.96±1.95	<0.01
CRP(mg/dL),median (Q1, Q3)	2.64(1.04,4.35)	1.35(0.54,2.36)	<0.01
Hydronephrosis (mm),median (Q1, Q3)	26.50(15.00,75.00)	10.50(0,18)	<0.01

7. [Please review the article for grammatical errors.](#)

Response: we employed an English-language editing service, **Charlesworth** to polish our words and grammars. And we reviewed the article for grammatical errors one more time.