
Diagnosis and Treatment of Pyelonephritis During Pregnancy

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ABSTRACT

Urinary tract infections are the most common infections in pregnant women. The most common are asymptomatic bacteriuria, cystitis and pyelonephritis, the latter presenting as a complication in 1 to 2% of women. Urolithiasis is also very common, complicating approximately 1 in every 2,000 pregnancies. These entities usually occur due to physiological changes that occur during pregnancy, such as enlargement of both kidneys, increased glomerular filtration rate, as well as dilatation of the renal pelvis and ureters.

It is important to perform imaging studies to establish the diagnosis, being renal ultrasound the first line option in the pregnant patient with renal colic because it is harmless to the patient and fetus. Treatment can be conservative with hydration and pain management with analgesics.

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INTRODUCTION

Among the most common bacterial infections in pregnant women are urinary tract infections, including asymptomatic bacteriuria and pyelonephritis. With pregnancy, there are anatomical and physiological changes in the urinary tract due to compression by the pregnant uterus and hormonal changes that make them more susceptible to infections.^{1,2,3}

Renal length increases by almost 1 cm during normal pregnancy as a result of increased vascular and interstitial volume. Glomerular filtration rate increases by 30% to 50% and most likely occurs secondary to increased cardiac output. Typically, there is significant ureteral dilatation with resultant urinary stasis during the second and third trimester of pregnancy. This hydroureter is attributed to the smooth muscle relaxation effects of progesterone and mechanical compression of the ureters by the uterus at the level of the pelvic brim. The bladder is also affected, both physically and functionally. The enlarged uterus displaces the bladder cephalad and forward.^{4,5,6,7}

Because of these changes in the urinary tract during normal pregnancy, urinary tract infections are the most common

bacterial infections during pregnancy. Although asymptomatic bacteriuria is the most prevalent form of infection, acute pyelonephritis is the most serious complication, occurring in 1% to 2% of all pregnancies and is the leading cause of septic shock during pregnancy.^{8,9,10,11}

The prevalence of asymptomatic bacteriuria is estimated to be 5% to 10% and occurs most often between 9 and 17 weeks' gestation, with risk factors including increasing age and parity, diabetes mellitus, sickle cell disease and structural abnormalities. Only 1% to 2% of pregnant women will develop pyelonephritis. Almost 60% to 70% of pyelonephritis episodes occur during the second and third trimester, when urinary stasis is most intense. In 10% to 20% of cases, recurrent episodes of pyelonephritis develop before delivery. When untreated, pyelonephritis during pregnancy is associated with a high rate of infant prematurity and associated perinatal mortality. It is unclear whether pyelonephritis treated during pregnancy has any effect on the developing fetus.^{12,13,14,15,16,17}

Consequently, it is recommended that women be screened for asymptomatic bacteriuria during pregnancy to prevent the

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development of pyelonephritis. A urine sample is obtained at the first prenatal visit and during the third trimester. For asymptomatic patients, significant bacteriuria is defined as two urine cultures with $>10^5$ CFU/ml of a single organism. For symptomatic pregnant women, $>10^3$ CFU/ml is considered significant.^{18,19,20,21,22}

The diagnosis of pyelonephritis is established clinically based on symptoms of fever, flank pain and tenderness in the costovertebral angle, accompanied by pyuria or bacteriuria. Two of the most serious complications of pyelonephritis in pregnancy are sepsis and pulmonary insufficiency or ARDS, occurring in 1.9% to 17% and 0.5% to 7% of cases, respectively. Early recognition of these complications is critical to ensure a favorable outcome, therefore, it would be helpful to easily identify which patients with pyelonephritis are at higher risk for these potentially devastating complications. Fever is the most common presenting sign or symptom of sepsis in pregnancy; however, additional vital sign abnormalities may be present, indicating a more advanced case of sepsis.²³

Pregnant women with bacteriuria should be treated with penicillins, oral cephalosporins, or fosfomycin trometamol. Nitrofurantoin can be used in the first and second trimesters of pregnancy, but should be avoided in the third trimester because of the risk of hemolysis. Repeat urine culture is necessary to document eradication of bacteriuria in all patients.²⁴

Given the potential for severe morbidity, if the diagnosis of pyelonephritis is suspected, hospitalization of patients is recommended for treatment with intravenous antibiotics until symptomatic improvement and without fever for more than 24 hours, followed by an additional 10-14 days of oral antibiotics (penicillins with β -lactamase inhibitors or monobactams). Periodic surveillance with urine culture is recommended because many of these women will have recurrent episodes of pyelonephritis.²⁵

KIDNEY CHANGES ASSOCIATED WITH PREGNANCY

During pregnancy there are physiological changes in the urinary tract. The size of both kidneys increases by about 1 to 1.5 cm, which means that the renal size increases by 30% due to increased renal blood flow and interstitial volume. There are usually no changes in the number and histology of nephrons. The glomerular filtration rate (GFR) usually increases. Dilatation of the renal pelvis and ureters occurs as a result of the effect of systemic arterial distensibility; hemodynamically, peripheral vascular resistance decreases. Increased blood flow combined with decreased blood pressure results in systemic vasodilatation. These changes increase glomerular filtration rate and renal perfusion. Renal plasma flow increases by 80% in the twelfth week of pregnancy, however, it decreases in the third trimester³. The increase in GFR is observed from the first month of

pregnancy. It increases by 40-50% in the early stages of the second trimester and decreases slightly in the third trimester. The physiological increase in GFR during pregnancy decreases serum creatinine levels by an average of 0.4 mg/dL, which causes it to remain between 0.4 to 0.8 mg/dL. Blood urea nitrogen decreases to levels of 8 to 10 mg/dl. In the third trimester, urinary protein excretion increases from 100 to 200 mg/day. Protein excretion above 300 mg/day is considered abnormal and needs further evaluation, however, excretion is usually higher in uncomplicated twin pregnancies.²⁶

CLINICAL FEATURES

Patients with *acute pyelonephritis* present with chills, fever ($>38^\circ\text{C}$), pain on palpation in the costovertebral angle (positive Giordano's sign), weakness, nausea, vomiting and possible abdominal or pelvic pain. In addition, lower urinary tract symptoms such as dysuria, pollakiuria and urinary urgency are common. Sepsis may occur, with 20% to 30% of cases resulting from urinary tract infection; during pregnancy, sepsis may occur in 1.9% to 17% of cases. Patients with *emphysematous pyelonephritis*, a necrotizing infection characterized by the presence of gas in the renal parenchyma or perirenal tissue, usually present with fever, flank pain, and vomiting that do not respond to initial treatment with parenteral antibiotics, and pneumaturia may be present. *Chronic pyelonephritis* is usually a repeated renal infection, leading to scarring, renal atrophy and subsequent renal failure. Many patients usually have no symptoms, but may have a history of recurrent urinary tract infections. *Xanthogranulomatous pyelonephritis* is usually also a form of chronic kidney infection and the kidney is almost always hydronephrotic and obstructed.^{27,28,29}

The diagnosis of pyelonephritis is made by establishing the presence of bacteriuria together with clinical data of infection. The diagnostic approach can be initiated by a general urine examination (collected with sterile technique), which should demonstrate evidence of urinary tract infection, such as the presence of pyuria, leukocyte casts, more than 20 bacteria per field, or a urine culture with $\geq 100,000$ colony-forming units in a urine sample. In addition, at least one clinical finding of the following signs and symptoms must be present: fever ($>38^\circ\text{C}$), pain in the lumbar region, or pain on palpation in the costovertebral angle (positive Giordano's sign).^{30,31}

Pyuria is present in most women with pyelonephritis and its absence should prompt consideration of a differential diagnosis or complete obstruction. Imaging studies are not routinely used to diagnose pyelonephritis. However, in patients who are critically ill or who also have symptoms of urolithiasis or a history of stones, diabetes, history of urologic surgery, immunosuppression, repeated episodes of pyelonephritis or urosepsis, imaging of the renal pathway may be useful in assessing complications. In pregnant women, renal ultrasound is the imaging modality of choice to

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avoid contrast or radiation exposure. This technique can be performed at any time during pregnancy without complication. The disadvantages of this technique may be free fluid and gas in the abdominal cavity due to the pregnancy itself.^{31,32}

TREATMENT IN THE PREGNANT WOMAN

Antibiotic therapy and supportive care are the mainstays of pyelonephritis treatment. The choice of empirical antibiotic regimen should be based on the risk of infection by resistant microorganisms (i.e. complicated or uncomplicated pyelonephritis) and antibiotics should be adapted as soon as culture results are available. The most commonly administered drugs are amoxicillin with clavulanic acid and cephalosporins. These drugs may be given empirically and may be modified later based on urine culture results. Treatment for acute pyelonephritis requires hospitalization and intravenous antibiotics for at least 48 hours after fever or other acute symptoms have been controlled. After that, treatment may be continued by mouth for 10 to 14 days. This is in addition to antipyretic and anti-inflammatory drugs, not forgetting adequate hydration for the patient.³³

Most patients respond to treatment within 48 hours. The most commonly used first-line drugs are b-lactam antibiotics (ampicillin or 2nd or 3rd generation cephalosporins) combined with gentamicin or carbapenemics in case of complications. Clinical and therapeutic decisions are influenced by numerous factors. In addition to knowledge about the most common local pathogens causing urinary tract infections, pregnancy-related adaptive changes affecting drug metabolism, stage of pregnancy, transplacental distribution of drugs and possible influences on the fetus must also be known. To date, there is still no consensus on the choice of particular drugs and duration of treatment for bacteriuria in pregnant women.^{32,33}

Recommendations on which drugs to use for urinary tract infections vary from country to country, with first-line treatment in Canada including trimethoprim and nitrofurantoin in addition to penicillins, and in the UK, cephalosporins. Interestingly, some studies in Turkey revealed some differences in drug susceptibility of uropathogens according to trimesters of pregnancy. The most frequently detected pathogens (*E. coli* and *Klebsiella* spp.) showed the highest drug susceptibility to I.V. imipenem administration, representing 100% regardless of pregnancy progress.^{33,34}

CONCLUSION

Urinary tract infections are the most common in pregnant women. The most common are asymptomatic bacteriuria, cystitis and pyelonephritis, the latter being a complication that occurs in up to 1 to 2% of pregnant women. In several studies it has been determined that pyelonephritis is a

common cause of sepsis, which occurs in up to 1.9% to 17% of pregnant women.

In addition, urolithiasis is a common entity, ranking as the most common cause of abdominal pain during pregnancy. The average age of presentation is 24 years of age in patients and approximately 80% to 90% of patients are usually affected in the second or third trimester of pregnancy. It has been shown that multiparous patients with a history of urolithiasis may have up to 25% of recurrences. It is important to perform a complete diagnostic approach, which consists of performing a general urine examination and, if symptoms persist after medical treatment, to perform a blood culture.

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