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## **Review Article**

# An overview on urinary tract infection in pregnancy

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#### **ABSTRACT**

Urinary tract infections (UTI) include a wide range of symptoms, such as urethritis, cystitis, prostatitis, and pyelonephritis. The most frequent bacterial infections are UTIs. Lower and upper UTI's are used to categories UTI's. While pyelonephritis is an upper tract infection, cystitis is a lower tract infection. Significant physiologic changes to the entire urinary system occur during pregnancy and drastically influence the prevalence of UTI's and pyelonephritis. Both symptomatic and asymptomatic forms are possible. Gram-negative bacteria are the most frequent causes of both symptomatic and acute UTI, including *E. coli*, *K. pneumonia*, *P. areuginosa*, *Enterobacter*, and *Serratia*. The gold standard for the diagnosis of a urinary tract infection is quantitative culture methods. Untreated UTIs have been linked to severe morbidity and mortality in pregnant women and their babies. According to Edward Kass's groundbreaking research, 6% of pregnant women reported asymptomatic bacteriuria (ASB), which was linked to higher preterm and perinatal death than those with sterile urine. According to the urine culture and sensitivity results, correct treatment is therefore of utmost importance. An agent with a seven-day dosage schedule that is safe for both the mother and the fetus should be used as the therapy. To prevent a recurrence of UTI, confirmation of the pathogenic organism's full eradication is required. Precautions and good cleanliness can also aid in preventing recurrence.

Keywords: Asymptomatic bacteriuria, Pyelonephritis, Acute cystitis, Pyuria

#### INTRODUCTION

In all age groups, UTI continue to be a major cause of morbidity and medical expenses. UTI is defined as the urothelium's inflammatory reaction to bacterial invasion, which is typically accompanied by bacteriuria and pyuria. Anywhere along the urinary tract can develop a UTI. It comprises abscess, pyelonephritis, cystitis, and urethritis. Due to anatomical problems including the proximity of the urethra to the anus, it is one of the most prevalent infectious diseases seen in sexually active women, during pregnancy, and after menopause. 1 According to reports, 20% of pregnant women are diagnosed with UTI due to physiological changes such an increase in plasma volume that may induce a reduction in urine concentration and enable bacterial growth that may or may not create symptoms. Additionally, 90% of pregnant women have structural changes such as urethral dilatation and decreased bladder tone that cause urine stasis (due to

pregnancy-related increases in progesterone and oestrogen levels).<sup>2</sup> The risk of a UTI may start in the sixth week and peak between 22 and 24 weeks later. Untreated UTIs or ASB during pregnancy can have devastating effects on the mother and the fetus, increasing the risk of kidney failure, pyelonephritis, sepsis, and other complications such intrauterine growth restriction, preeclampsia, premature delivery. In order to minimize UTI-related complaints, it is crucial to screen for this illness, raise suspicion, and recognize it. This will allow you to swiftly start the right therapy.3 All pregnant women should undergo urine culture screening, the gold standard for detecting ASB, at least once during early pregnancy (12-16 weeks), according to the Infectious Disease Society of America (IDSA) and the US Preventive Services Task Force.<sup>4</sup> Romero et al conducted a meta-analysis of 8 clinical studies and found that antibiotic treatment for ASB reduced the incidence of low birthweight with a relative risk of 0.56% (95% confidence interval 0.43-0.73).

Obstetricians are concerned about it because of its link to high rates of maternal and neonatal illness and mortality.<sup>5</sup>

#### UTI CLASSIFICATION IN PREGNANCY

Pregnancy UTIs are divided as symptomatic and asymptomatic true bacteriuria (>100,000/ml). Cystitis and pyelonephritis are the two types of upper and lower tract infections that cause symptomatic bacteriuria.<sup>6</sup>

#### ASB

It is a type of UTI caused by bacteria and is identified by the presence of more than 10<sup>5</sup> colony-forming units per ml of urine in a clinically asymptomatic individual. Approximately 10% of pregnancies have ASB.7 Untreated ASB during pregnancy can result in symptomatic UTI in 20-40% of women, putting both the mother and the unborn child at risk.8 It frequently happens in the first trimester of pregnancy and may be related to prior UTIs, diabetes mellitus, multiparity, low socioeconomic level, and illiteracy.9 Low birth weight babies and intrauterine growth retardation are both more likely as a result. Preeclampsia, anemia, chorioamnionitis, and postpartum endometritis are also at higher risk. Fetal hazards include perinatal mortality, mental impairment, stillbirth, fetal growth restriction, and developmental delay. So, it is advised to perform urinalysis and keep an eye on quantity, colour, etc., of urine during the course of pregnancy. 10,11

The most typical organism found in urine samples from women with ASB is *E. coli*. There are frequent correlations between enterobacterial species such *Streptococcus, Klebsiella sp.* <sup>12</sup>

#### Acute cystitis

Acute cystitis is an infection of the bladder that frequently spreads to the urethra. About 1% of all pregnant mothers are affected. The presence of symptoms like dysuria, urgency, frequency, nocturia, haematuria, and suprapubic discomfort in afebrile women with no signs of systemic illness distinguishes it from ASB, which is defined as significant bacteriuria without associated bladder mucosal invasion. <sup>13,14</sup> When a pregnant woman with symptoms has bacterial growth on a urine culture, the diagnosis is established by the presence of pyuria (>7 white blood cells/ml) and a quantitative count of 10<sup>5</sup> colony forming units (cfu)/ml or 10<sup>3</sup> cfu/ml. <sup>15</sup> In 15–50% of patients, pyelonephritis, an upper urinary tract infection, complicates acute cystitis. <sup>16</sup>

## Pyelonephritis

Pyelonephritis is an infection of the kidneys and upper urinary system. It is a serious pregnancy complication that can cause serious morbidity for both the mother and the fetus. <sup>17</sup> It is a disease that is suspected when a midstream MSSU culture identifies at least 100,000 bacteria/ml of a single uropathogen with concomitant inflammation of the

renal parenchyma, calices, and pelvis in the presence of systemic illness. <sup>18</sup> Pyelonephritis is most common in the second and third trimesters. <sup>19</sup> Pyuria is typically prevalent in pyelonephritis-affected women, and its absence may indicate a different diagnosis or total obstruction. Immunosuppression, already existing diabetes, a history of sickle cell anaemia, a neurogenic bladder, frequent or chronic UTIs before pregnancy, tobacco use, age <20 years, and being late for prenatal care are additional risk factors for complex UTI in pregnancy. <sup>20</sup>

#### **EPIDEMIOLOGY**

In comparison to most data gathered in the 1980s and the end of the 1990s in diverse populations throughout the world, the incidences of ASB and the related problems documented by Kass in 1962 are higher. 17,21 Up to 15% of women will experience one episode of UTI at some point in their lives, and UTI accounts for roughly 10% of the primary care consultations made by pregnant women. Pregnant women report getting UTIs about 8% of the time. 13,22 Women are 14 times as likely than men to have a UTI. Pyelonephritis is the most common cause of shock in pregnant women and affects 2% to 4% of pregnancies. It is more frequently right-sided but can be bilateral in up to 25% of cases, and it has a 23% recurrence rate right after birth. Pyelonephritis is most common in the second trimester of pregnancy. ASB, with a rate of up to 2% to 7%, is the main risk factor for UTI in pregnant women. Contrarily, 1.3% of pregnancies are complicated with cystitis. ASB is more common in women with low socioeconomic status and sickle cell trait carriers. A postpartum UTI is likely to occur in about 25% of cases of ASB that are not treated during pregnancy. Between 2 to 13% of studies from the United States, Europe, and Australia found ASB. It has been asserted in the past that bacteriuria increases the risk of anemia and high blood pressure during pregnancy. It is advised that all pregnant women get an ASB screening at their first prenatal appointment due to the high prevalence and probable severity of pyelonephritis. Treatment for ASB reduces clinical infection rates to 3%-4%.<sup>23</sup>

#### **ETIOLOGY**

Numerous bacterial species, majority of which are part of normal perineal flora, are responsible for causing urinary infections in females. About 70-80% of pregnancies are caused by *E. coli*, making it the most frequent cause of UTI. Other pathogens that cause UTI include *proteus sp.* (2%) and *K. pneumonia* (5%) as well as *Enterobacter sp.* (3%) and *S. saprophyticus* (3%) and group B betahemolytic *Streptococcus* (GBS; 2-5%).<sup>2,14,24,25</sup>

## Infection with group B streptococci

A penicillin-versus-placebo treatment for GBS bacteriuria was compared in a randomized, controlled trial. Results showed that women who took antibiotics experienced significantly lower rates of premature membrane rupture and preterm delivery. Although it is unknown whether GBS bacteriuria is the same as GBS vaginal colonization, pregnant women who have the condition ought to be treated as GBS carriers and given a preventative antibiotic during childbirth. <sup>17,26</sup>

During childbirth, urinary catheterization is a common procedure that might introduce bacteria and cause UTI. Changes in bladder reactivity and bladder excessive expansion during postpartum period may predispose to UTI.<sup>27</sup>

The risk of UTI is significantly increased in women who engage in sexual activity. The distal urethra's urothelium can become traumatized during sexual contact, which increases bacterial invasion. Inoculation can be facilitated by the vagina acting as a repository for stomach germs. Gram negative bacteria from the bowel flourish in urine, in contrast to majority of vulval and perineal commensal microorganisms. As a result, aerobic gram-negative bacilli from the gastrointestinal system are the main source of urine infections. The issue might be made worse by a swollen, gravid abdomen that makes it difficult to maintain personal hygiene. Same bacteria that cause UTIs in non-pregnant patients also cause UTIs in pregnant women.<sup>28</sup>

#### **PATHOPHYSIOLOGY**

The same uropathogens that frequently cause UTI in nonpregnant patients also cause UTI in pregnant women. Ureteral dilatation occurs in 90% of pregnant women and lasts till birth (hydronephrosis of pregnancy). Increased urine stasis and ureterovesical reflux are caused by increased bladder volume, decreased bladder tone, and decreased ureteral tone. This decreased the kidneys' defenses against bacterial reflux. Bacterial reservoirs may exist in urinary stasis. The glomerular filtration rate and urine output both rise in response to blood volume expansion. Urine stasis, which can arise from an increase in urine output volume and the lack of ureteral tone, can cause the ureters, renal pelvis, and calyces to enlarge. This dilatation seems to start at 10 weeks gestation, increase throughout pregnancy, and resolve between 6 and 12 weeks after delivery. Progesterone also causes urinary stasis by relaxing the ureteral smooth muscle.<sup>29</sup>

Because of urine pH, vesicoureteral valve, and other immunological and mucosal barriers, urine is devoid of germs, viruses, and fungus. The major defense against UTI is complete bladder emptying during urination. The pathophysiology of urinary tract infection may be influenced by a variety of bacteria that have the ability to infiltrate the urinary tract. When bacteria from the vaginal, perineal, and fecal flora spread to the entrance of the urethra and begin to grow, infection develops.<sup>30</sup>

Significant physiologic changes to the entire urinary system occur during pregnancy and significantly alter the occurrence of UTIs and pyelonephritis. The presence of glucose in the urine and an increase in urinary amino acid levels during pregnancy are other causes of UTI. Glycosuria results from proximal collecting tubule and loop of Henle dysfunction in glucose reabsorption. Although it has been hypothesized that its presence will interfere with *E. coli* ability to adhere to the urothelium.<sup>31</sup>

Due to the physiologic changes brought on by pregnancy, pregnant individuals are typically regarded as an immunocompromised potential UTI host. Additionally, there is a significant increase in wetness during pregnancy, which tends to boost the growth of bacteria.<sup>32</sup>

#### CLINICAL SIGNS AND SYMPTOMS

ASB is characterized by a lack of symptoms. These patients can have a record of recurrent UTI or ASB from a previous pregnancy.

Cystitis usually begins suddenly, often with urgency, burning, or painful emptying of little amounts of urine. Nocturia with suprapubic discomfort. Hematuria can happen and urine is murky. A low-grade fever could appear. When an infection occurs from a vesicoenteric or vesicovaginal perforation or from emphysematous cystitis, pneumaturia may happen.

#### **Pyelonephritis**

Dysuria, fever, shivering, flank pain, constant abdomen unease, nausea, vomiting, and lethargy are symptoms of acute pyelonephritis.<sup>33</sup>

#### **COMPLICATIONS**

#### Motherhood

Acute Respiratory Distress Syndrome (ARDS) or pulmonary edema may be present as a result of endotoxin-mediated alveolar injury. Monitoring of urine production and oxygen levels is recommended. Anemia is caused by the release of endotoxins. Endotoxin secretion may also trigger uterine contractions in preterm labor. Preeclampsia, septic shock, an ongoing infection, acute pyelonephritis, chorioamnionitis, acute cystitis with symptoms and hypertension.<sup>34</sup>

#### Fetus

Low birth weight, premature birth, embryonic death and growth retardation within the womb.<sup>35</sup>

#### **DIFFERENTIAL DIAGNOSIS**

Important differential diagnosis includes nephrolithiasis, placental abruption, intraamniotic infection, and bacterial infection in pregnant women who report with fever and flank or lower back pain. Significant flank or back discomfort and abnormal urine results are symptoms of nephrolithiasis.

The differential diagnosis includes pregnancy-related issues including preterm labor, chorioamnionitis, or placental abruption as well as acute intraabdominal disorders such appendicitis, pancreatitis, or cholecystitis.<sup>36</sup>

#### **DIAGNOSIS**

Acute pyelonephritis, cystitis, and ASB are diagnosed by examining the presence of bacteria in the urine. For the diagnosis of acute pyelonephritis and ASB, a concentration of at least 10<sup>5</sup> cfu/ml of a single uropathogen is required, but only 103 cfu/ml are required for the diagnosis of cystitis. Urine culture is the gold standard for detecting bacteriuria in pregnancy. However, urine cultures are pricy, call extensive laboratory competence, and take 24 to 48 hours to provide findings.<sup>37</sup> In 90% of cases of pyelonephritis, it is positive. Prior to beginning antibiotic therapy, cultures should be acquired as soon as feasible. For the diagnosis of UTI, urine microscopy has a poor sensitivity (between 40% and 70%) but a good specificity (between 85% and 95%). Pyuria is found in around 90% of instances of pyelonephritis. The diagnosis of acute pyelonephritis is more sensitive (95%) and specific (71%) when pyuria is present. White blood casts are a dead giveaway for an upper tract infection.<sup>38</sup>

Due to its dependable rates and quick results, the dipstick method (for nitrites and leukocyte esterase) has emerged as the most used test. With dipstick analysis and clinical judgement, accuracy in patients with vague symptoms is significantly increased. Protein, white blood cells, and red blood cells are examined during a urine test. False negative test findings are frequent, and these tests have relatively low predictive values.

A complete blood count, electrolytes, and serum creatinine test are among the laboratory tests that are typically used to diagnose pyelonephritis. Pyelonephritis can be diagnosed routinely in patients who are critically ill, have symptoms of renal colic or a history of renal stones, have diabetes mellitus, a history of prior urologic surgery, immunosuppression, repeated episodes of pyelonephritis, or have urosepsis using computed tomography (CT), renal ultrasound (to avoid contrast or radiation exposure)/MRI.

When comparing inpatient treatment for pyelonephritis to screening for bacteriuria in pregnant women, Rouse and colleagues found that screening resulted in a significant reduction in overall costs. One patient's test for bacteriuria to detect the onset of pyelonephritis cost \$1,605, but one patient's pyelonephritis treatment cost \$2,485. In a family practice obstetric population, Wadland and Plante carried out a comparable analysis and discovered that screening for ASB was cost-effective. <sup>17,29,39</sup>

#### PHARMACOLOGICAL TREATMENT

Antibiotic therapy was observed to be successful in eradicating ASB and lowering the frequency of pyelonephritis, premature delivery, and low birthweight when compared to placebo or no therapy. 40 The effect of administering antibiotics for asymptomatic UTIs on recurring bacteria in the urine during pregnancy, the possibility of premature delivery, and the occurrence of pyelonephritis after pregnancy were all assessed in a Cochrane review of 13 studies. Antibiotic sensitivity of gram-negative urinary pathogens acquired from pregnant women with asymptomatic bacterial infections or cystitis was examined in study conducted by Jamie et al.

Table 1: Pharmacological treatment of UTI in pregnancy. 17,18,22,29

Antibiotic	Indication	Dose	Pregnancy category	Lactation	Monitor
Nitrofurantoin	Asymtomatic bacteriuria, recurrent cystitis	100 mg BD for 5 to 7 days	B contraindicated term (38-42 weeks)	Enters breast milk discontinue	Renal function, liver function
Cephalexin	Asymtomatic bacteriuria, recurrent cystitis	500 mg orally every 6 hrs. for 5-7 days	Safe	Safe	Use with caution in renal, hepatic disease patients
Amoxicillin clavulanate	Asymtomatic bacteriuria	500/125 mg orally q 8 hrs. for 5-7 days	-	Present in milk	Hepatic impairment
Amoxicillin	Asymtomatic bacteriuria	500 mg orally q8 hrs for 5-7 days	Safe	Safe	Use with caution in renal and hepatic diseases
Cefuroxime	Asymtomatic bacteriuria	250 mg orally BD for 3-7 days	-	-	Hepatic injury, kidney injury
Fosfomycin	Asymtomatic bacteriuria	3 gm orally as single dose in 3-4 oz of water	Caution by manufacturer	Excreted in breast milk	Hepatic injury
Ceftriaxone	Pyelonephritis	1-2 gm IV OD	A	Use with caution	Immune mediated hemolytic

Continued.

Antibiotic	Indication	Dose	Pregnancy category	Lactation	Monitor
					anemia
Ertapenam	Pyelonephritis	1 gm/day IV/IM	В	Present in breast milk	CNS disorders Renal impairments
Trimethoprim	ASB, cystitis	200/300 mg BD	Avoid in first trimester	Safe in short term	Renal function

The infectious agent(s) can typically be eliminated with a seven- to ten-day antibiotic course. Shorter treatment durations, including one-day therapy, have been recommended by some experts. There is still debate over when pregnant patients should receive shorter antibiotic regimens of treatment. In ampicillin-sensitive isolates, Masterton achieved an 88 percent cure rate with a single 3 gm dosage of ampicillin. According to several other trials, cure rates for bacteriuria ranged from 50 to 78 percent when a single administration of amoxicillin, cephalexin (Keflex), or nitrofurantoin was administered.

When taken as directed, a single 3 gm sachet of Fosfomycin is effective.

Analgesia is required because significant renal angle discomfort affects many women. Simple analgesics are usually sufficient, but opiates may be required in extreme circumstances or if there is concurrent renal colic. Nonsteroidal anti-inflammatory medicines (NSAIDs) should be avoided since they raise the risk of stomach mucosal ulcers and impaired renal perfusion in mothers and the fetal condition oligohydramnios and early ductus arteriosus closure.

If the lady has restricted mobility or needs to be bedridden for a while, thromboprophylaxis should be utilized. Low molecular weight heparin and progressive compression stockings are advised.

Acute pyelonephritis episodes dramatically enhance the risks of premature labor. Often, tocolysis is required. If there is evidence of suspected preterm labor, antenatal steroids for fetal lung development should be taken into consideration. Regarding tocolysis and the administration of prenatal steroids, we point readers to the RCOG recommendations.<sup>41</sup>

Because of how some antibiotics affect the developing fetus, some should not be used during pregnancy. They consist of the following-1. Tetracyclines can harm fetus's teeth and bones. 2. Avoid fluroquinolones during pregnancy and nursing as they are harmful to growing cartilage. 3. During the first and third trimesters, avoid taking trimethoprim-sulphamethoxazole. 4. If at all possible, avoid using aminoglycosides because they have been linked to ototoxicity after extended exposure during fetal development.<sup>42</sup>

#### PREVENTIVE ACTIONS

You can prevent UTI from developing and saving yourself. The trouble of subsequently treating it by taking the following precautions: Practicing good hygiene, such as cleaning the genital region and urinating after sexual activity, had a protective impact, after using the bathroom, wipe your genital area from front to back to keep it clean, the chemical in cranberry juice may help prevent bacteria from adhering to the lining of the urinary tract. This action aids in infection control and prevention, vaccination, eat foods and supplements high in vitamin C or ascorbic acid, which can raise urine acidity, the acidity prevents infection and aids in the death of germs. Urinating whenever the desire strikes: This promotes faster removal of microorganisms from the urinary system. Taking specific supplements, such as a vitamin C, cranberry, and probiotic combination, may help treat recurring UTIs in females. Drinking enough fluids, especially water, can assist the urinary tract's bacteria be flushed out. Consuming yogurt, which includes live lactobacilli. Remember not to wear tighter or wet clothing, and wear cotton underwear and avoid clear of soap or cleansing products that might harm your genitalia.<sup>43</sup>

#### **CONCLUSION**

UTIs, whether symptomatic or asymptomatic, present a major risk to expectant mothers. This article has reviewed the pathophysiology, etiology, complications, diagnosis, preventative strategies, and therapy of UTI in pregnancy. Urine cultures should be used to check for ASB in pregnant women, and the right antimicrobials should be used to treat it. On the basis of cost, safety during pregnancy, and availability, broad-spectrum antibiotics with activity against *E. coli* should be selected as the initial course of treatment for symptomatic UTI. While pyelonephritis necessitates hospitalization and intravenous antibiotics, ASB and cystitis are best treated with oral antibiotics. A 7-day course of treatment is preferable to a one-dose course.

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