

## A Review on Urinary Tract Infection in Pregnancy

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### ABSTRACT

Urinary tract infection is one among the most common infectious disease which occurs during pregnancy. Several physiological and hormonal changes during pregnancy may increase the incidence of infection among pregnant women. It can be symptomatic or asymptomatic. Asymptomatic bacteriuria can lead to the development of cystitis or pyelonephritis. Gram negative bacteria like *Escherichia coli*, *Klebsiella pneumoniae*, *roteus*, *Providencia* species, *Pseudomonas aeruginosa*, *Enterobacter* and *Serratia* are the most common etiological agent in both symptomatic and asymptomatic Urinary tract infection. Quantitative culture technique considered as the gold standard for the diagnosis of Urinary tract infection. Untreated urinary tract infections can lead to significant maternal and perinatal morbidity and mortality. Hence the proper treatment is of at most importance based on the urine culture and sensitivity reports. It is also important to conform the safety of drugs used during of pregnancy. Antibiotics like Nitrofurantoin, Trimethoprim or Cephalexin are appropriate drug of choices for the treatment. Resistance of microorganism towards the commonly prescribing antibiotics is the most challenging factor for the treatment. So before stopping the antibiotic therapy, Confirmation of the complete eradication of pathogenic organism is necessary to prevent reoccurrence of urinary tract infection. Proper hygiene and various precautions may also help in preventing its reoccurrence.

**Keywords:** Urinary tract infection, symptomatic bacteriuria, asymptomatic bacteriuria, cystitis, pyelonephritis

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### INTRODUCTION

Urinary tract infection (UTI) is broadly defined as the inflammatory response of urothelium to bacterial invasion, which is usually associated with bacteriuria and pyuria. Bacteriuria is the presence of bacteria in urine. A Urinary tract infection can occur anywhere along the Urinary tract. It includes urethritis, cystitis, pyelonephritis, epididymitis, prostatitis, perinephritis, and abscess.

Urinary tract infection considered one among the most common infectious diseases is widely seen among all age groups of individuals. However some groups of people are more prone to UTI than others. For example there is a higher risk to develop UTI

in diabetic patients [1]. Females have fourteen times more chance to develop UTI than men [2]. The differences are attributed to involvement of several factors. Such as they has a shorter urethra compare to men which open nearer to the anus so that the lower third of urethra is continually contaminated with pathogens from vagina and rectum. Women tend not to empty their bladder as completely as men.

Urinary tract infection is more commonly observed in sexually active women, during pregnancy and after menopause [3-4]. UTI is one of the widely studied health problem during pregnancy, it has been reported among 20% of the pregnant women and it is

the most common cause of admission in obstetrical wards [5]. The risk of UTI may begin in 6<sup>th</sup> week and will be at peak during 22-24<sup>th</sup> week [6].

Various factors tend to increase the risk of UTI during pregnancy. As the uterus resides directly on top of the bladder, during pregnancy uterus grows and its increased weight can block the drainage of urine from the bladder and thus cause infection. Higher levels of progesterone decrease the muscle tone of the uterus, causing them to dilate in turn reducing the flow of urine. As the uterus enlarges it may compress the ureters, making it much more difficult for urine to flow through them.

The end result of these changes is that it takes longer for urine to pass through Urinary tract giving bacteria more time to multiply. It becomes easier for the bacteria to travel up to the kidneys. During pregnancy urine become less acidic and more likely to contain glucose, both of which boost the potential for bacterial growth.

In recent years UTI in pregnancy has got more attention among obstetricians all over the world because of its maternal and perinatal effects. Untreated UTI may lead to several serious complications like intrauterine growth restriction, pre-eclampsia and preterm deliveries and caesarean deliveries [7]. And it is noted that the asymptomatic bacteriuria can lead to cystitis and pyelonephritis were it can lead to acute respiratory distress, transient renal failure, sepsis and shock during pregnancy [8-9]. Hence it is very important to know the details about complication and management of UTI during pregnancy, in order to minimize these complications associated with it.

#### **CLASSIFICATION OF UTI**

Urinary tract infections in pregnancy are classified as symptomatic and asymptomatic bacteriuria. Asymptomatic bacteriuria is defined as true bacteriuria (>100,000/ml) in the absence of specific symptoms of acute Urinary tract infections. Symptomatic bacteriuria are divided in to lower tract (cystitis) and upper tract (pyelonephritis) infections.

**Asymptomatic Bacteruria-** Asymptomatic bacteriuria (ASB) is bacterial urinary tract infection that occurs without any symptoms.

Were 20-30% of pregnant women with untreated asymptomatic bacteriuria may develop symptomatic UTI, such as cystitis or pyelonephritis, these UTIs represent a significant risk to both mother and baby [10-11]. There are many evidence that suggests UTIs role in the onset of preterm labor. Hence it is advisable to do a urinalysis test at each prenatal diagnosis as well as monitor urine amounts, color, etc. throughout the pregnancy

**Urethritis** is the Infection of urethra with bacteria, protozoa, viruses, or fungi. This occurs when organisms gain an access to it periurethral glands in the bulbous and pendulous portions of the male urethra and in the entire female urethra. Many sexually transmitted pathogens like *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis*, and *herpes simplex virus* are common causes in both sexes.

**Cystitis** is the infection of bladder. It is more common in women, in whom cases of uncomplicated cystitis are usually preceded by sexual intercourse. It is also defined as significant bacteriuria with associated bladder mucosal invasion, and is distinguished from asymptomatic bacteriuria by the presence of symptoms such as dysuria, urgency, frequency, nocturia, haematuria and suprapubic discomfort in afebrile women with no evidence of systemic illness [12-13].

**Pyelonephritis** is a condition suggested when at least 100,000 bacteria /mL of a single uropathogen in a midstream MSSU culture is identified with associated inflammation of the renal parenchyma, calices and pelvis in the presence of systemic illness. It can progress to maternal sepsis, preterm labor and premature delivery. Symptoms include flank or renal angle pain, pyrexia, rigor, chills, nausea, vomiting and hip pain. Symptoms of lower tract infection, such as frequency and lack of urination, may or may not be present [12-13].

#### **PATHOPHYSIOLOGY OF UTI DURING PREGNANCY**

Urine is normally considered as sterile. It is usually free of bacteria, viruses, and fungi but does contain fluids, salts, and waste products. The major defense against UTI is entire emptying of the bladder during urination. Supplementary mechanisms which

keep the tract's sterility include urine acidity, vesicoureteral valve, and various immunologic and mucosal barriers. An infection occurs when minute organisms, frequently bacteria from the vaginal, perineal and fecal flora cling to the opening of the urethra and start to multiply.

Pregnancy causes many changes in the female's body. Factors like structural and hormonal changes raise the risk of UTI in pregnancy. The anatomical factors like hydro-ureter, hydronephrosis and vesicoureteric reflux may raise the occurrence of UTI in pregnancy. Hydroureter of pregnancy has been characterized by an increase in the diameter of the ureteral lumen, hypotonicity and hypomotility of the ureteral muscle. Anatomical tortuosity has been noted in the second and third trimesters, the right ureter being more often dilated than the left [14]. Increased weight of enlarging uterus can cause urinary retention and progesterone induced urethral smooth muscle relaxation may lead to urinary stasis. Blood-volume expansion is accompanied by increases in the glomerular filtration rate and urinary output. Increase in urinary output volume along with the loss of ureteral tone may result in urinary stasis, which can lead to dilatation of the ureters, renal pelvis, and calyces. This urinary stasis and the presence of vesicoureteral reflux are responsible for UTI and acute pyelonephritis in most cases.

The increased excretion of nutrients like glucose, B-complex, vitamins etc form a good culture medium for bacterial growth indirectly [15]. In pregnancy, urine pH gets raised to a range suitable for the growth of *E.coli*. Glycosuria gets developed due to impaired resorption by the collecting tubule and loop of Henle. About 5% of the filtered glucose escapes proximal convoluted tubular resorption.

In general, pregnant patients are considered immunocompromised UTI hosts because of the physiologic changes associated with pregnancy. Also, during pregnancy, there is a great increase in the moistness which tend to increase the growth of bacteria [16].

These changes, along with short urethra (approximately 3-4 cm in females) and difficulty with hygiene due to a distended pregnant belly, increase the frequency of

urinary tract infections (UTIs) in pregnant women. Indeed, UTIs are among the most common bacterial infections during pregnancy.

#### **ETIOLOGY OF UTI DURING PREGNANCY**

Urinary infections in women are caused by a number of bacterial species, the majority of which are from normal perineal flora. Most of the cases Gram-negative organisms are the causative agents for UTI. *Escherichia coli* is one of the major causative organism in 85% of community-acquired infections [17]. Organisms like *Klebsiella pneumoniae*, *Proteus* and *Providencia* species, *Pseudomonas aeruginosa*, *Enterobacter* and *Serratia* species may also cause UTI. In rare conditions some organisms like *Salmonella* species, *Mycobacterium tuberculosis*, *Chlamydia trachomatis*, *Candida* species are also seen as infective agents for UTI [18]. Gram-positive organisms like *Staphylococcus saprophyticus*, *Enterococcus faecalis* may also be a causative organism in 5% to 15% of UTI cases [19]. Sometimes multiple microbial organisms may be found causing infections in patients with renal calculi, chronic renal abscesses, indwelling urinary catheters, or a fistula between the bladder and either the bowel or the vagina.

Apart from these pathogens, pregnancy-induced physiological changes in the urinary system may also act as the promoting factor for UTI. Dilation of the ureters and renal calyces is evident as early as 12 weeks and is studied to be caused by progesterone-induced relaxation of their muscular layers. More importantly, as the uterus enlarges, it begins to compress the ureters at the pelvic brim, particularly on the right [20-21]. Vesicoureteral reflux may first appear or worsen during gestation in some women, particularly multiparas. Anatomical changes in bladder position in late pregnancy also may render it more susceptible for the infection. Finally, bladder and urethral trauma, periurethral tears, large vulvar lacerations, and epidural analgesia for labor and delivery predispose to urinary retention and the need for catheterization arises.

#### **EPIDEMIOLOGY**

UTIs are studied to be 14 times more frequent in women than in men. Bacteriuria occurs in 2 to 7 percent of pregnancies, particularly in multiparous women, a similar

prevalence as seen in non pregnant women. The prevalence of UTI during pregnancy increases with maternal age. As the organisms responsible for infection (in terms of species and virulence factors) are observed to be same in pregnant and non pregnant women, the basic mechanism of entry of bacteria into the urinary tract is likely to be the same for both groups [22].

A retrospective analysis of 24,000 births found the prevalence of UTI during pregnancy to be 28.7% in whites and Asians, 30.1% in blacks, and 41.1% in Hispanics. When socioeconomic status is controlled, no significant interracial differences seem to exist. Several patient-level factors are associated with an increased frequency of bacteriuria during pregnancy. Compared with non-indigent patients, indigent patients have a 5-fold increased incidence of bacteriuria. The risk is doubled in women with sickle cell trait. Other risk factors for bacteriuria include diabetes mellitus, neurogenic bladder retention, history of vesico-ureteral reflux, previous renal transplantation, and a history of previous UTIs [23-25]. Maintenance of proper hygienic condition in practices and clothing, changes in coital patterns (eg. position, frequency, postcoital antibiotics) can offset recurrence in individuals with high risk of getting the disease.

Bacteriuria often develops in the first month of pregnancy and is frequently associated with a reduction in concentrating ability, suggesting involvement of the kidney. The smooth muscle relaxation and subsequent ureteral dilatation that accompany pregnancy are thought to facilitate the ascent of bacteria from the bladder to the kidney. As a result, bacteriuria during pregnancy has a greater propensity to progress to pyelonephritis (up to 40 percent) than in non pregnant women [26-27].

#### **SIGN AND SYMPTOMS OF UTI DURING PREGNANCY**

In **urethritis**, the main symptoms are dysuria and urethral discharge. Discharge can be purulent, whitish, or mucoid. Characteristics of the discharge, such as the amount of purulence, do not reliably differentiate gonococcal from non-gonococcal urethritis.

**Cystitis** onset is usually sudden, typically with frequency, urgency, and burning or painful voiding of small volumes of urine. Nocturia, with suprapubic pain and often low back pain, is common. The urine is often turbid, and microscopic hematuria can occur. A low-grade fever may develop. Pneumaturia can occur when infection results from a vesicoenteric or vesicovaginal fistula or from emphysematous cystitis. Since the frequent urge to urinate is common during pregnancy, it may be hard to tell the presence of cystitis, especially if symptoms are mild. A doubt of an infection should be clarified, because untreated cystitis puts the patient at high risk for getting a kidney infection, especially while pregnancy.

In **acute pyelonephritis**, symptoms may be the same as those of cystitis. One third of patients have frequency and dysuria. However, with pyelonephritis, symptoms typically include chills, fever, flank pain, colicky abdominal pain, nausea, and vomiting. If abdominal rigidity is absent or slight, a tender, enlarged kidney is sometimes palpable. Costovertebral angle percussion tenderness is generally present on the infected side.

#### **DIAGNOSIS**

The diagnoses for acute pyelonephritis, cystitis, and asymptomatic bacteriuria are carried out by checking the presence of bacteria in the urine, usually based on a clean midstream urine sample. There must be a minimum of  $10^5$  colony-forming units per milliliter (Cfu/mL) of single uropathogens for diagnosis of acute pyelonephritis and asymptomatic bacteriuria where as only  $10^3$  cfu/mL is needed for the diagnosis of cystitis. Up to one third of cystitis cases would be missed if the criterion for diagnosis is same as for upper tract infection [28]. Although urine cultures are expensive, require laboratory expertise and take 24–48 h for results to become available, quantitative culture remains the gold standard for diagnosis of urinary tract infection in pregnancy as the performance of rapid urine screening tests in pregnancy is poor [29-30].

Urine microscopy has a lower sensitivity (40% to 70%) but a high specificity (85% to 95%) for the diagnosis of UTI. Pyuria is present in most cases of pyelonephritis--

estimated to be about 90%. Presence of pyuria increases the sensitivity (95%) and specificity (71%) for the diagnosis of acute pyelonephritis. White cell casts always point to an upper tract infection [31]. Urine culture is positive in 90% of cases of pyelonephritis, and 20% of hospitalized cases have positive blood cultures.

Dipstick urinalysis has become the most frequently used test due to its reliable rates and fast results. Studies have shown that dipstick urinalysis in combination with clinician judgment, greatly improves diagnostic accuracy in the patient with nonspecific symptoms. Urine dipstick results appear positive when there is a presence of nitrate and/or if there is a positive reaction greater than or equal to trace leukocyte esterase [32].

The diagnosis of pyelonephritis can usually be made by history, physical examination, and laboratory tests. Imaging may be necessary when the diagnosis is in question; Computed tomography (CT) with intravenous (IV) contrast is the test of choice when evaluating the urinary tract. The most common CT finding in pyelonephritis is wedge-shaped lesions of decreased attenuation with or without swelling. Anatomic abnormalities and perinephric abscesses can also be seen on contrast-enhanced scans. Renal ultrasound is also used to evaluate the collecting system and pyelonephritis and may show ureteral dilation, suggesting obstruction. Although renal ultrasound is helpful, a CT scan is more sensitive. Magnetic resonance imaging may be used in patients who are allergic to iodinated contrast [33].

#### **OUTCOMES DURING PREGNANCY**

Untreated UTI during pregnancy may cause severe maternal and paternal complications. 30% of patients with untreated asymptomatic bacteriuria may develop symptomatic cystitis and up to 50% may develop pyelonephritis [10]. Asymptomatic bacteriuria is also associated with intrauterine growth retardation and low-birth-weight infants [11].

Studies clearly shows the presence of pregnant UTI to be associated with premature labor, hypertensive disorders of pregnancy such as pregnancy-induced

hypertension and preeclampsia, anemia and amnionitis [34]. It may also have a risk of urosepsis and chronic pyelonephritis [35]. In addition, acute pyelonephritis has been studied to be associated with anemia [36].

Neonatal outcomes that are associated with UTI include sepsis and pneumonia specifically due to group B streptococcus infection [37-38]. Untreated UTI may have a risk to get low-birth-weight infants/premature infants [34].

#### **TREATMENT OF UTI DURING PREGNANCY**

UTIs are managed more aggressively in pregnant women than in non-pregnant women. Urine samples should be sent for culture and empiric treatment given while awaiting results. Nitrofurantoin, trimethoprim or cephalexins are appropriate antibiotic choices (although restrictions apply depending on the stage of pregnancy). Quinolones, e.g. norfloxacin, should not be used during pregnancy [39-40].

Any discussion of treatment should be prefaced with a discussion of behavioral methods that may be used to ensure good hygiene and reduce bacterial contamination of the urethral meatus, thereby preventing inadequate treatment and recurrent infection. Avoid baths, Wipe front-to-back after urinating or defecating, Wash hands before using the toilet, Use washed cloths to clean the perineum, Use liquid soap to prevent colonization from bar soap, Clean the urethral meatus first when bathing. The above mentioned are the common behavioral methods suggested to avoid the disease.

#### **Asymptomatic bacteriuria**

Asymptomatic bacteriuria can be screened by using a urine culture at 12 to 16 weeks gestation [41]. All pregnant women with conformed asymptomatic bacteriuria should be treated with antibiotics. The choice of antibiotic can be guided by the known sensitivities; preferred drugs are following [42-43].

- Amoxicillin (if susceptible): 250 mg three times a day
- Nitrofurantoin: 50 mg four times a day (avoid at 36+ weeks)
- Trimethoprim: 300 mg once a day (avoid in the first trimester)
- Cephalexin: 500 mg twice a day (least preferred option)

All antibiotics should be given for seven days to ensure cure [44]. The eradication of bacteriuria can be confirmed by doing a urine culture after completion of the therapy. It is recommended that urine cultures are repeated regularly until delivery [42, 45].

#### **Acute cystitis**

Selected antibiotic should cover common pathogens and can be changed if required after the identification of organism with its sensitivity profile. The following are appropriate choice

- Nitrofurantoin 50 mg four times a day (avoid at 36+ weeks)
- Trimethoprim: 300 mg once a day (avoid in the first trimester)
- Cephalexin: 500 mg twice a day

Almost 20-40 % cases *E coli* are the common organism that shows resistance to Ampicillin and Amoxicillin [46]. Hence these agents are no longer considered optimal for treatment of UTIs caused by this organism. Fosfomycin, a phosphonic acid derivative, is useful in the treatment of uncomplicated UTIs caused by susceptible strains of *E coli* and *Enterococcus* species.

In order to avoid recurrent infection in pregnancy the drug must be continued to 10-14 days instead of 1, 3, and 7-day common antibiotic courses [47]. A follow up urine culture can be requested one to two weeks after the antibiotic course has been completed to ensure eradication.

The pain associated with acute cystitis can be relieved with Paracetamol [45]. Women with frequent UTIs during pregnancy may need an antibiotic prophylaxis. If the UTIs are thought to be related to sexual intercourse, a postcoital dose of Nitrofurantoin 50 mg or Cephalexin 250 mg may be used [48].

#### **Pyelonephritis**

Patients with systemic symptoms such as fever, flank pain and nausea or vomiting may have a chance of acute pyelonephritis. Symptoms of lower UTI such as frequency and dysuria may or may not be present [47,48]. Pyelonephritis in pregnancy can have serious consequences such as maternal sepsis, pre-term labour and premature delivery and requires prompt and aggressive treatment [47].

The standard course of treatment for pyelonephritis consists of hospital admission and intravenous (IV) administration of Cephalosporin's or Gentamicin continued until the patient has been afebrile for 48 hours. Oral antibiotics are then used for 10-14 days [49]. IV fluids must be administered with caution. Patients with pyelonephritis can become dehydrated because of nausea and vomiting and may need IV hydration. However, they are at high risk for the development of pulmonary edema and acute respiratory distress syndrome (ARDS).

Fever should be managed with antipyretics like Acetaminophen and nausea and vomiting with Antiemetics. Most Antiemetics can be used for adverse effects caused by antibiotics, but Doxylamine, Emetrol (pregnancy class A), Dimenhydrinate, and Metoclopramide (pregnancy class B) are preferred.

#### **METHODS TO PREVENT UTI DURING PREGNANCY**

Many general guidelines and suggestions can help women to avoid urinary tract infections in most instances. These may be expediently divided into the categories of hygiene, clothing, diet, activities, and medications. The following steps may reduce the chances of developing UTI during pregnancy.

- Drink plenty of water and cranberry juice (choose one that doesn't contain sugar).
- Check out the urine color often for abnormalities; if present try to get a medical advice.
- Don't ignore the urge to urinate, and empty the bladder completely while urinating.
- After a bowel movement, wipe yourself from front to rear to prevent bacteria in the stool from getting near the urethra. Keep the genital area clean with mild soap and water.
- Clean the genitals and the areas surrounding them and urinate before and after sexual intercourse.
- Avoid feminine hygiene products like sprays, powders and strong soaps that can irritate the urethra and genitals and make them a better breeding ground for bacteria. And don't use douches during pregnancy.
- Wear all-cotton undergarments.
- Take showers rather than baths whenever possible. Avoid bubble baths which tend to irritate urethral opening.

**CONCLUSION**

This article has reviewed the incidence of UTI in pregnancy including the pathogenesis, etiology, complications, diagnosis and treatment. The review also covers the preventive measures that can be employed by pregnant women to prevent the development and reoccurrence of UTI.

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