

URINARY TRACT INFECTIONS IN PREGNANCY

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ABSTRACT

Urinary tract infections frequently affect pregnant mothers. This problem causes significant morbidity and healthcare expenditure. Three common clinical manifestations of UTIs in pregnancy are: asymptomatic bacteriuria, acute cystitis and acute pyelonephritis. *Escherichia coli* remains the most frequent organism isolated in UTIs. All pregnant mothers should be screened for UTIs in pregnancy and antibiotics should be commenced without delay. Urine culture and sensitivity is the gold standard in diagnosing UTIs. Without treatment, asymptomatic bacteriuria in pregnancy is associated with preterm delivery, intrauterine growth retardation, low birth weight, maternal hypertension, pre-eclampsia and anaemia. Acute pyelonephritis can lead to maternal sepsis. Recurrent UTIs in pregnancy require prophylactic antibiotic treatment.

Keywords: Urinary tract infections, pregnancy, antibiotics

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INTRODUCTION

Urinary tract infections (UTI) remain a leading cause of morbidity and healthcare expenditure in all age groups.^{1,2} UTI account for about 10% of primary care consultations by pregnant women and it was reported that up to 15% of women will have one episode of UTI at some time during their life.¹ The incidence of UTI reported among pregnant mothers is about 8%.^{1,2} Anatomically UTI can be classified into lower urinary tract infection involving the bladder and urethra and upper urinary tract infection involving the kidney and pelvis ureter. The majority of the UTI occur due to ascending infection.^{1,2}

PHYSIOLOGICAL CHANGES OF PREGNANCY AND ITS ASSOCIATION WITH URINARY TRACT INFECTIONS

Pregnancy increases the risk of UTIs. At around 6th week of pregnancy, due to the physiological changes of pregnancy the ureters begin to dilate. This is also known as "hydronephrosis of pregnancy", which peaks at 22-26 weeks and continues to persist until delivery.¹ Both progesterone and estrogens levels increase during pregnancy and these will lead to decreased ureteral and bladder tone. Increased plasma volume during pregnancy leads to decrease urine concentration and increased bladder volume.¹ The combination of all these factors lead to urinary stasis and uretero-vesical reflux. Glycosuria in pregnancy is also another well-known factor which predisposes mothers to UTI.

TYPES OF URINARY TRACT INFECTIONS IN PREGNANCY

There are three major types of UTI in pregnancy. They are asymptomatic bacteriuria, acute cystitis and acute pyelonephritis. The clinical presentations of these conditions vary.

Asymptomatic bacteriuria is defined as a finding of more than 10⁵ colony-forming units per mL of urine in a clinically asymptomatic person.^{1,2} This condition may be present even before the mother gets pregnant. There are reports that 1.2 to 5 % of young girls will demonstrate asymptomatic bacteriuria at some time before puberty.^{3,5} The prevalence of asymptomatic bacteriuria in pregnancy is about 10%. Lower serum interleukin-6 levels and serum antibody responses to *E. coli* antigens which occurs in pregnancy has been associated with increased incidence of asymptomatic bacteriuria in pregnancy.⁵ Neonatal complications which are associated with asymptomatic bacteriuria include intrauterine growth restriction, low birth weight and pre-term premature rupture of membrane.^{3,5,7} Maternal complications which are associated with asymptomatic bacteriuria are hypertension, pre-eclampsia and maternal anemia.¹³ Without treatment, this condition leads to symptomatic cystitis in about 30% of pregnant mothers of whom about 50% will eventually develop acute pyelonephritis.^{3,5,7} (Table 1)

Table 1. Maternal and foetal complications of asymptomatic bacteriuria in pregnancy.^{9,10}

Maternal complications	Foetal complications
Hypertension	Intrauterine growth retardation
Pre-eclampsia	Intrauterine death
Anaemia	Low birth weight
Chorioamnionitis	Prematurity
Symptomatic acute cystitis	
Acute pyelonephritis	

Acute cystitis relates to infection of the urinary bladder. Very often the urethra is also infected. The major distinguishing feature of acute cystitis from asymptomatic bacteriuria is the presence of dysuria, urgency and frequency. Usually the patient remains afebrile. Severe systemic symptoms such as nausea, vomiting, high grade fever and distress are usually absent. Most mothers may not be aware that they are having the infection because urgency and frequency are common symptoms in a normal pregnancy.

Acute pyelonephritis is infection of the kidney and the pelvic ureter. It is a serious systemic illness affecting 1-2% of all pregnancies and the most common non-obstetric cause of hospital admission during pregnancy.³ This complication is characterised by high-grade fever, chills and rigors, headache, nausea, vomiting, lumbar pain and in serious cases, reduced urine output. Without treatment it can cause preterm labour and maternal septicaemia. Recurrent pyelonephritis has been implicated as a cause of intra uterine growth restriction and foetal death. The overall incidence of recurrence is about 2-3% and it can recur during the same pregnancy.³

AETIOLOGICAL AGENTS

Escherichia coli (*E. coli*) is the major aetiological agent in causing UTI, which accounts for up to 90% of cases.¹ *Proteus mirabilis* and *Klebsiella pneumoniae* are less frequent offenders. Less commonly, enterococci including *Gardnerella vaginalis* and *Ureaplasma ureolyticum* are known agents in UTIs. Gram-positive organisms are even less common in which Group B streptococcus, *Staphylococcus saprophyticus* and *Staphylococcus haemolyticus* are recognised organisms.^{1,5}

SCREENING

Due to the high prevalence of asymptomatic bacteriuria in pregnancy and its serious consequences, it is justifiable to screen for this condition in pregnancy. Various methods

are used to screen for asymptomatic bacteriuria; among these are urinalysis to look for protein, white blood cells, red blood cells, urine dipstick for nitrites and leukocyte esterase. Although these tests are easily available and rapid, they have relatively poor predictive values and false negatives results are common.^{1,8} The gold standard for detecting bacteriuria in pregnancy is urine culture. The limiting factor is the relative high cost and delay in results (it takes 24 to 48 hours to culture the organism). Therefore it is recommended that physicians will have to balance between the cost and effectiveness of the screening test before deciding on it.

TREATMENT

Asymptomatic bacteriuria should be treated with antimicrobials even though the mother has no clinical symptoms. Various studies have proven that early treatment of asymptomatic bacteriuria in pregnancy reduces the incidence of acute pyelonephritis and decreases the incidence of pre-term delivery and low birth weight infants.^{1,2,8} Early recognition and treatment of asymptomatic bacteriuria can reduce up to 70% of acute symptomatic UTIs.³

The antibiotic of choice should be safe for both mother and baby (Table 2). Amoxicillin is a safe choice but in recent years *E. coli* has become increasingly resistant to amoxicillin. Alternative drugs are now used as first line treatment. Cephalosporins and nitrofurantoin are safe for pregnant mothers; as both have high urinary concentration and are effective against *E. coli*. There is insufficient data to recommend any specific type of treatment regime in symptomatic UTI in pregnancy. Common antibiotics such as nitrofurantoin and cefuroxime are effective and complications are rare.⁴ Nitrofurantoin has the advantage of sparing the disruption of normal vaginal flora but should be avoided at third trimester because a potential risk of haemolysis if the foetus is G6PD-deficient.⁵ Sulphonamides can be used in first and second trimester but it is best avoided in third trimester because it competes for bilirubin-binding sites on albumin in the foetus and causes severe jaundice and kernicterus especially in pre-term babies.^{1,3} Quinolones and tetracyclines have possible toxic effects on the foetus and these medications are contraindicated in pregnancy.^{1,5,6} A 7 to 10-day course of oral antibiotic treatment is usually adequate in a majority of the cases of asymptomatic bacteriuria and acute cystitis.^{1,3} Patients should be advised to come for a repeat urine culture 1-2 weeks after completing antibiotics. Mothers who are treated for shorter period of time are more likely to have higher recurrence rate and this may lead to serious consequences.

Table 2. Common antibiotic choices for UTI in pregnancy¹

Antibiotic	Recommended dosage	Pregnancy Risk category
Nitrofurantoin	50 to 100mg 6 hourly	B
Cephalexin	250mg 6 hourly	B
Ampicillin	250mg 6 hourly	B
Amoxicillin-clavulanic acid	250mg 6 hourly	B
Amoxicillin	500mg 8 hourly	C
Trimethoprim-sulfamethoxazole	160mg 12 hourly	C

Category B: Animal studies do not demonstrate foetal risk but no controlled study in humans. Category C: No controlled study in humans available, animals' study revealed adverse foetal effects.

For acute pyelonephritis in pregnancy, hospitalisation is often indicated even though it is not mandatory. It is easier to monitor for complications if the mother is treated as an in-patient. Indications for admissions include severe distress, dehydration, poor oral food tolerance, maternal and foetal complications and where intravenous antibiotic is necessary. Urine culture and sensitivity is mandatory in the management of acute pyelonephritis, and this should be obtained before starting antibiotics. Empirical treatment with parenteral antibiotics should begin as soon as possible. The clinical condition must be closely monitored for any complications. Antibiotic of choice is based on common aetiology and resistance pattern in the community. When results of the culture and sensitivity are available, the treatment regime can be altered accordingly. *E. coli* is the major causative agent in acute pyelonephritis. With good hydration and antibiotic treatment, most patients respond within 24-48 hours. If patient's symptoms persist despite appropriate antibiotics, further investigations are needed to evaluate the possibility of underlying predisposing factors such as renal calculi and renal tract abnormalities or a perinephric abscess formation. The latter needs surgical drainage. Septicaemia is present in about 15% of patient with acute pyelonephritis. Blood culture and sensitivity should be obtained if the patient does not respond to antibiotic treatment.³ Intravenous antibiotic therapy should be continued for a further 24-48 hours after initial response, evidenced by subsiding fever, disappearance of lumbar pain and improvement in patient's general physical appearance. Oral antibiotics are preferably continued for further 1-2 weeks.³

Group B streptococcal (GBS) vaginal colonisation is proven to be associated with pre-term premature rupture of membranes, neonatal sepsis and congenital pneumonia. This organism also contributes to 5% of UTI. Studies have shown that pregnant mothers who received penicillin treatment for GBS bacteriuria have significantly lower

incidence of pre-term delivery and premature rupture of membranes. It therefore make sense that mothers with GBS bacteriuria should be treated with antibiotics.

UTI recur in 4-5% of pregnancies especially when the initial infection is inadequately treated. Pregnant mothers with urinary tract calculi, diabetes mellitus and a past history of UTI are more prone to recurrence. Prophylactic antibiotics with cephalexin and nitrofurantoin are effective treatment. Further evaluation of urinary tract abnormalities with radiological imaging is recommended at 3 months postpartum after anatomical and physiological changes of pregnancy have resolved.³

CONCLUSION

UTI in pregnancy is associated with significant morbidity for both mother and baby. All pregnant mothers should be screened for UTI. Untreated UTI will lead to pre-term premature rupture of membrane, maternal chorioamnionitis, intrauterine growth retardation and low birth weight baby. Early treatment with antibiotics has significantly reduced the above complications. Urine culture and sensitivity remain the gold standard in diagnosing UTI. If patients' condition are not improving despite adequate and appropriate use of antimicrobials, further investigations for underlying predisposing factors are necessary. Prophylactic antibiotic is indicated for recurrent UTI.

References

- Delzell JE, Lefevre ML. Urinary tract infections during pregnancy. *Am Fam Physician*. 2000;61(3):713-21 [[PubMed](#)] [[Full text](#)]
- Orenstein R, Wong ES. Urinary tract infections in adults. *Am Fam Physician*. 1999;59(5):1225-37 [[PubMed](#)] [[Full text](#)]
- Gabbe. Infection of the urinary tract. Chapter 40 in Gabbe: Obstetrics-Normal and problem pregnancies. 4th ed. Churchill Livingstone. 2002:1067-70
- Vazquez JC, Villar J. Treatments for symptomatic urinary tract infections during pregnancy. *Cochrane Database Syst Rev*. 2003;(4):CD002256. [[PubMed](#)]
- Fitzgerald MA. Urinary tract infection: providing the best care. Medscape, 2002. <http://www.medscape.com/viewarticle/436592> [[Full text](#)]
- O'Donnell JA, Gelone SP, Abrutyn E. Selecting drug regimens for urinary tract infections: Current recommendations. *Infections in Medicine*. 2002;19(1):14-22 [[Abstract](#)]
- Romero R, Oyarzun E, Mazor M, et al. Meta-analysis of the relationship between asymptomatic bacteriuria and pre-term delivery/low birth weight. *Obstet Gynecol*. 1989;73(4):576-82 [[PubMed](#)]
- Bachman JW, Heise RH, Naessens JM, et al. A study of various tests to detect asymptomatic urinary tract infections in an obstetric population. *JAMA*. 1993;270(16):1971-4 [[PubMed](#)]
- McGladdery SL, Aparicio S, Verrier-Jones K, Roberts R. Outcome of pregnancy in an Oxford-Cardiff cohort of women with previous bacteriuria. *QJM*. 1992;83(303):533-9 [[PubMed](#)]
- Uncu Y, Uncu G, Esmer A, Bilgel N. Should asymptomatic bacteriuria be screened in pregnancy? *Clin Exp Obstet Gynecol*. 2002;29(4):281-5 [[PubMed](#)]

Urinary Tract Infections In Pregnancy Multiple Choice Questions (MCQ)

- The following are risk factors for urinary tract infections (UTIs) in pregnancy:
 - Glycosuria in pregnancy.
 - Hydronephrosis of pregnancy.
 - Renal calculi.
 - Renal tract abnormalities.
 - Previous episodes of urinary tract infections.
- Complications from untreated asymptomatic bacteriuria include:
 - Maternal anaemia
 - Acute cystitis
 - Preterm delivery
 - Low birth weight infant
 - Amniotic fluid embolism
- The following agents are known to cause urinary tract infections in pregnancy:
 - Proteus mirabilis*
 - Klebsiella pneumoniae*
 - Ureaplasma ureolyticum*
 - Group B streptococcus
 - Staphylococcus haemolyticus*
- The following statements are true regarding management of urinary tract infection in pregnancy:
 - Asymptomatic bacteriuria only requires reassurance.
 - Acute pyelonephritis requires parenteral antibiotics.
 - Nitrofurantoin is contraindicated in first trimester.
 - Tetracycline is contraindicated in pregnancy.
 - Group B streptococcus should be treated with penicillin.
- The following statements are true regarding urinary tract infection in pregnancy:
 - E. coli* is the commonest organism isolated from urine culture.
 - Group B streptococcal vaginal colonization is associated with preterm delivery.
 - Blood culture and sensitivity is indicated in acute pyelonephritis.
 - Recurrence of urinary tract infection does not occur in the same pregnancy.
 - The gold standard for diagnosing UTIs in pregnancy is urine culture and sensitivity.

Urinary Tract Infections In Pregnancy

Answer: T= True F=False

- T T T T T
- T T T T F
- T T T T T
- F T F T T
- T T T F T

Lifestyle intervention (diet and exercise) is at least as effective as drug therapy in preventing diabetes in people with glucose intolerance.

Gillies CL, Abrams KR, Lambert PC, *et al.* Pharmacological and lifestyle interventions to prevent or delay type 2 diabetes in people with impaired glucose tolerance: systematic review and meta-analysis. *BMJ.* 2007;334:299 [[PubMed](#)] [[Full text](#)]

Based on an analysis of 17 trials (8084 participants), this meta-analysis found that lifestyle intervention reduced diabetes by 49%. This compare favourably with anti-diabetic drugs (risk reduction 30%) but somewhat less than orlistat (risk reduction 68%)