

Urinary Tract Infections in Pregnancy

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INTRODUCTION

Obstetricians commonly encounter women with Urinary Tract Infection (**UTI**) in pregnancy. They account for a number of hospital admissions and antenatal consultations. It is associated with adverse feto-maternal outcome. If left untreated it can lead to development of pyelonephritis in the mother. Fetus is at risk of preterm delivery. Many at times the asymptomatic bacteruria goes undetected and therefore creates problems in late pregnancy. The condition is most of the time undetected, under diagnosed and partially treated. Although the diagnosis and treatment is simple and easy however it requires vigilance and follow-up. Therefore, the purpose of this chapter is to examine the prevalence of UTI among pregnant women and to evaluate the clinical presentations and evidence based treatment options.

Keywords: Urinary Tract Infection; Pregnancy; Leukocytes; Pyelonephritis; Cystitis

Abbreviations: Urinary Tract Infection (**UTI**), Asymptomatic Bacteruria (**ASB**), Body Mass Index (**BMI**), Antenatal Clinics (**ANC**), General Practitioners (**GP**), Genitourinary Medicine Clinics (**GUM**), Venereal Disease Clinics (**VD**), Adult Respiratory Distress Syndrome (**ARDS**)

DEFINITIONS

Urinary Tract Infection (**UTI**) is the infection anywhere in the urinary tract involving the urethra, bladder, ureters and kidneys. Disease may recur during pregnancy and if one experiences two or more episodes over a period of six months or three or more episode in one year then it's termed as recurrent UTI. It can either be because of relapse by the same organism which was treated first or a reinfection by new organism. Relapse is when the treated organism still persists after two weeks of therapy [1].

Bacteruria

"It is defined as the presence of 10,000 CFU/ml of urine sample" [2].

Significant Bacteruria

"It is defined as 100,000 CFU/ml in Mid-Stream Urine (**MSU**) or 100CFU/ml from a catheterized specimen" [2]. The Infectious Diseases Society of America (**IDSA**) recommends that, significant bacteruria in asymptomatic women is defined as "bacterial monoculture in the quantity of $\geq 10^5$ Colony-Forming Units (**CFU**) per ml in two consecutive mid-stream clean-catch urine specimens or $\geq 10^2$ CFU/ml in urine collected from single urinary bladder catheterization" [3].

Asymptomatic Bacteruria

It's a condition which goes unrecognized because of lack of symptoms. It is defined as "persistently and actively multiplying bacteria in significant numbers that is 10^5 bacteria per milliliter (**ml**) within the urinary tract without any obvious symptoms" [4]

CLASSIFICATION

Anatomically UTI is classified based on the basis of organs involved

1. Involvement of urethra (Urethritis)
2. Bladder (Cystitis)
3. Kidneys (Pyelonephritis)
4. Blood (Urosepsis)

The UTI could be either lower urinary tract infection, which could be either asymptomatic bacteruria or symptomatic acute cystitis or less common but more serious involving the upper urinary tract leading to acute pyelonephritis [1].

EPIDEMIOLOGY

Prevalence

UTI is a problem frequently encountered among antenatal consultations. Its prevalence varies between 7-10% of pregnancies [5]. It limits social and functional activities and is a source of concern for obstetricians as well as the pregnant females.

The prevalence of symptomatic UTI during pregnancy is estimated to be 18.9% and asymptomatic bacteria as 8.5% [6-8].

Other studies have reported the prevalence of asymptomatic UTI to be 2 % to 13 % in pregnant women [9,10].

RISK FACTORS FOR DEVELOPING UTI IN PREGNANCY

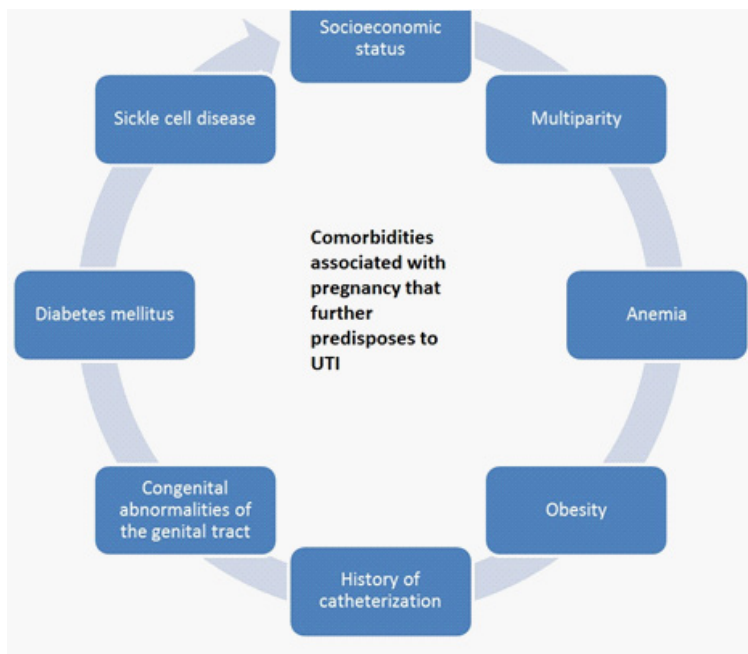
Physiological Changes in Pregnancy

During pregnancy there is urinary stasis under the effect of progesterone which together with physiological and anatomical changes predispose to asymptomatic bacteruria which may progress to either acute cystitis and or acute pyelonephritis. When compared with non-pregnant, pregnant women are double at risk to be affected with symptomatic urinary tract infection [11]. This is due to the urinary stasis during pregnancy caused by anatomical and physiological changes in the urinary tract such as pressure effect by the gravid uterus on the ureters and the relaxant effect of progesterone on the urinary tract muscles [12].

Associated Comorbidities

A number of conditions are associated with urinary infection. Rising age, parity, sexual activity, diabetes mellitus, sickle cell disease and anomalies of urinary tract are all risk factors for urinary tract infection [13].

Obesity has also been linked to increase chances of urinary infection. Subak et al., reported that all women who had normal BMI had no urinary infection but most women with BMIs higher than 26 had urinary infection that was a risk factor for urinary continence [14].



Other Associated Risk Factors

- Excessive friction and trauma at sexual intercourse
- An allergic reaction to chemical washes, vaginal douches and soaps
- Normal anatomy of female urethra
- Decreased fluid intake due to nausea and vomiting

PATHOGENESIS

The disease can be caused by bacteria, virus, fungi or helminthes. Mostly the same pathogens which cause UTI outside pregnancy are responsible during pregnancy as well. Most infections are caused by *Enterobacteriaceae*, with *Escherichia coli* (63–85%) of cases, and among the remaining: *Klebsiella pneumoniae* (~8%), coagulase-negative *Staphylococcus* (up to 15%), *S. aureus* (up to 8%) and Group B Streptococci (**GBS**) (2–7%) [15,16]. Presence of Group B Streptococcus (**GBS**) in maternal vagina and associated bacteruria is a well-established risk factor for premature rupture of membrane, preterm labour and neonatal infection [17].



SYMPTOMS AND SIGNS

Urinary infection usually presents itself in a variety of ways. Patient can be completely asymptomatic being diagnosed on urine analysis alone or may present with acute cystitis and ascending pyelonephritis. Commonest presentations are

- Pain or burning sensation when passing urine
- A white/cloudy coloured urine
- Feeling that you need to pass urine frequently
- There may be no symptoms but this cannot mean that you cannot pass the infection to your partner

DIAGNOSIS

1-Urine microscopy and dipstick for nitrates and leukocytes examination and the result is available immediately

2-Urine culture and sensitivity and result is available in a weeks' time

In the majority of women no further investigation is required to confirm the diagnosis.

All pregnant women should be screened for bacteruria at first prenatal visit or at 12-16 weeks of gestation [18].

Repeat testing in women whose first samples are negative should not be done for all women but for women with high risk factors (like diabetes, sickle cell disease) it should be repeated in pregnancy [19].

TREATMENT

General Measures

Increased fluid intake, hygiene, Double voiding, post coital voiding and using loose undergarments and avoiding deodorants can reduce the susceptibility towards UTI.

Treatment of Asymptomatic Bacteruria and Cystitis

The focus of practice continues to be curative rather than preventative. Most expecting mothers only consider attending a medical facility when feeling unwell.

Health education and pre-natal care is a relatively new concept although birth in health facilities is considered to be the normal practice.

It is usually easy that all pregnant women had mid-stream specimen of urine sent for culture at their first antenatal visit and proper antibiotic treatment was given to those with significant bacteruria whether they are symptomatic or not.

Table 1: Treatment regimen for asymptomatic bacteruria and cystitis in pregnancy.

20-Grabe M, Bartoletti R, Bjerklund-Johansen TE, Çek HM, Pickard RS, Tenke P, Wagenlehner F, Wullt B. Guidelines on urological infections. European Association of Urology; 2014.

Antibiotic	Duration of therapy	Comments
Nitofurantion	100mg q12hrs, 3-5days	Avoid in G6PD deficiency
Amoxicillin	500mg q8hrs, 3-5days	Increasing resistance
Co-moxicillin/clavulanate	500mg q12hours, 3-5days	
Cefalexine	500mg q8hours, 3-5days	Increasing resistance
Fosfomycine	3grams single dose	
Trimethoprim	Q12hours, 3-5days	Avoid in first trimester, term

The beneficial effect of treatment of ASB is evident from review of 14 RCTs from Cochrane library which include 2302 pregnant women with ASB were treated with antibiotics as compared to placebo or untreated women. Five of these trials which included 820 pregnancies revealed that antibiotics effectively cleared ASB (RR = 0.25, 95% CI: 0.14–0.48). Analysis of 11 trials including 1955 pregnancies demonstrated that antibiotic treatment of ASB may reduce the incidence of pyelonephritis by 52–86% (RR = 0.25, 95% CI: 0.14–0.48) [20].

It is important to complete the course of antibiotics. If treatment is haphazard or incomplete it may be necessary to start the therapy again.

Follow Up

As there is risk of recurrence in 1/3rd of these women follow up cultures should be done 1-2 weeks after treatment and then repeated monthly [4,21].

The diagnosis of cystitis is based on patient presenting with symptoms of cloudy urine, dysuria, frequency, urgency, abdominal or suprapubic pain. Urine analysis reveals the presence of small bacterial colony counts ($\geq 10^2$ – 10^3 CFU/ml) [22]. Treatment is similar but long courses for 5-7 days therapy may be required

Pyelonephritis

Undiagnosed, untreated or unrecognized lower urinary tract infection can ascend to cause pyelonephritis. It is seen more frequently in the second and third trimester (80-90%). Out of one third of cases of untreated ASB can progress to pyelonephritis [23].

The overall incidence of pyelonephritis in pregnancy is 2% as compared to less than 1% in the general population [24].

Patients with pyelonephritis present with high grade fever, rigors, nausea and vomiting lumbar pain and cost vertebral tenderness. Septicemia is a late but serious sequel of pyelonephritis [25].

Presence of risk factors like, sickle cell anemia, diabetes, nephrolithiasis, illicit drug use,

history of previous pyelonephritis, asymptomatic bacteruria and maternal urinary tract defects all predisposes to development of pyelonephritis [26,27].

Patients with pyelonephritis needs intravenous antibiotics till they become afebrile for 48 hours when they can be shifted to oral therapy [27].

Table 2: Treatment regimen for pyelonephritis in pregnancy.

Grabe M, Bartoletti R, Bjerklund-Johansen TE, Çek HM, Pickard RS, Tenke P, Wagenlehner F, Wullt B. Guidelines on urological infections. European Association of Urology. 2014.

Antibiotics	Dosage
Ceftriaxone	1-2g I/V or I/M q24hours
Aztreonam	1g I/V q8-12hours
Piperacillin-tazobactam	3.375-4.5g I/V q6hours
Cefipime	1g I/V q12hours
Imipenem-Cilastatin	500mg I/V q 6hours
Ampicillin +	2g I/V q 6hours
Gentamicin	3-5mg/kg/day I/V in 3 divided doses

There is risk of recurrences of pyelonephritis in 6–8% of pregnant women prophylactic treatment is recommended (e.g at bed time give nitrofurantoin 50–100 mg or cephalexin 250–500 mg), with urine culture at the beginning of the third trimester. If bacteruria is confirmed on investigations then prophylaxis is replaced by regular treatment [22]. In case of urosepsis hemodynamic, metabolic and respiratory support may be required [28].

Follow Up

Repeat urine cultures after 1-2 weeks of treatment and later on monthly should be performed. Daily small doses of drugs like nitofurantion 50-100mg, cephalexin 250-500mg is recommended for recurrent cystitis or Its import to return for follow up after completion of treatment or in the case of an evident relationship of the disease with sexual activity, only after intercourse [31].

FETOMATERNAL RISKS

ASB can progress to symptomatic UTI including acute pyelonephritis 30–40% of untreated vs. 3–4% in treated patients [20,30].

UTI in pregnancy has been linked with higher chances of women to develop Pre-eclampsia (31.1% vs. 7.8%, $p < 0.001$) compared to those without reported UTI [31].

Preterm labour, acute renal failure, Adult Respiratory Distress Syndrome (**ARDS**), septicemia is other reported complications of UTI's in pregnancy [32].

Bacteriuria in pregnancy accounts for a significantly higher number of newborns with a low birth weight, low gestational age and higher neonatal mortality rate [33].

RECOMMENDATIONS

As UTI may recur or ascend to pyelonephritis and is associated with poor fetomaternal outcome. Every hospital should have a policy and guide the patients with information regarding where to seek help like

- 1- Obstetrician at Antenatal Clinics **(ANC)**
- 2- General Practitioners **(GP)**
- 3- Genitourinary Medicine Clinics **(GUM)**
- 4- Or Venereal Disease clinics **(VD)**

KEY POINTS

- Microscopy and culture of urine must be undertaken
- Absence of RBCs and WBCs and microorganisms should exclude intravesical pathology and cystoscopy is thus rarely indicated
- Assessment of medical conditions
- Whichever form of treatment is given there is a significant risk of recurrence

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