



Review Article

Managing Urinary Tract Infections In Pregnant Women: Pathogens, Risks, And Antibiotic Therapies

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ABSTRACT

Urinary tract infections (UTIs) during pregnancy present significant challenges and risks to both maternal and fetal health. This study examines the etiology, epidemiology, risk factors, classification, signs, symptoms, preventive methods, and antibiotic treatment patterns of UTIs in pregnant women. UTIs, primarily caused by Symptomatic and Asymptomatic bacteria such as Escherichia coli and other gram-negative organisms, affect up to 10% of pregnancies, with symptomatic and asymptomatic bacteriuria being common classifications. Risk factors such as age, gravidity, gestational age, and genetic predispositions contribute to UTI susceptibility. Symptoms range from urinary discomfort to systemic illness, necessitating prompt treatment to avoid complications like preterm delivery and pyelonephritis. Hygiene practices, hydration, and antibiotic therapy, guided by culture and sensitivity reports, are vital for management. Notably, newer antibiotic agents targeting multidrug-resistant organisms show promise in treating UTIs, including aztreonam/avibactam, cefiderocol, and ceftazidime/avibactam. This comprehensive analysis underscores the importance of vigilance, timely intervention, and judicious antibiotic use in mitigating the impact of UTIs on maternal and fetal outcomes during pregnancy.

INTRODUCTION

Urinary tract infection (UTI) is the broad term encompassing infection, affecting any part of the urinary tract (bladder, urethra, kidney). Women are more susceptible to UTIs compared to men, primarily due to lower urinary tract anatomy and its closeness to the reproductive organs [2]. UTIs

are prevalent among women, aged 18-40 making it one of the most common infections in this demographic. UTIs are often affiliated with multifarious vaginal infections and is commonly caused by pathogens arising from the alimentary canal. Generally, UTIs are categorized, based on

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the site of infection either in the lower or upper urinary tract. *Escherichia coli*, *Enterococcus faecalis* and *Streptococcus* species are the primary causative agents of UTIs [3]. Extensive research has demonstrated that there is a strong correlation between *Escherichia coli* type 1 fimbria and cystitis, while other strains that possess pathogenic fimbria are extensively linked to pyelonephritis [4,5]. UTIs can occur extensively in pregnant women. During pregnancy, women face a heightened susceptibility to UTIs. This vulnerability is particularly prominent from week 6 and reaches its peak between weeks 22-24 [6,7,8]. 90% of pregnant women experience ureteral dilation. Notable signs and symptoms include abdominal pain, dysuria or cloudy urine, fever, chills, spasms, vaginal discharge, urinary frequency and urinary urgency (supra pubic pain) [9]. The Food and Drug Administration (FDA) has established guidelines for conducting clinical trials to assess antimicrobials in treating urinary tract infections. Where FDA plays a crucial role in health care by assuring safety and effectiveness.

The FDA classifies drugs A, B, C, D and X:

- Category A indicates safety for pregnant individuals.
- Category B involves no demonstrated fetal risk in animal studies with insufficient human data.
- Category C includes adverse fetal effects in animal studies or lacks both animal and human data.
- Category D suggests increased fetal risk in animal studies, yet potential benefits could outweigh risks.
- Category X indicates clear fetal risk in animal studies with no discernible benefits.

Etiology

UTIs in women are caused from bacteria colonizing the urogenital tract, typically sourced from the rectal and perineal areas. Common bacterial species include *Escherichia coli*,

Enterococcus, *Klebsiella*, *Pseudomonas*, and other *Enterococcus* or *Staphylococcus* strains. *Escherichia coli* is the most predominant, followed by *Klebsiella* (10). Gram-negative organisms are responsible for the majority of UTI cases, with *Escherichia coli* being a primary causative agent in 85% of community-acquired infections (11). Specifically, among women aged under 50 years.

Epidemiology

UTI is a common issue often encountered during prenatal check-ups. The prevalence of UTI in pregnancies ranges from 7-10%, impacting social and functional activities and causing concern for both obstetricians and expectant mothers [12]. Symptomatic UTI prevalence during pregnancy is estimated at 18.9%, while asymptomatic bacteriuria is around 8.5% [13,14]. Additionally, other studies have indicated asymptomatic UTI rates of 13% in pregnant women [15,16].

CLASSIFICATION OF UTI

In pregnancy, urinary tract infections are categorized into symptomatic and asymptomatic bacteriuria. Asymptomatic bacteriuria refers to true bacteriuria without specific symptoms of acute urinary tract infections. Symptomatic bacteriuria is further divided into lower tract (cystitis) and upper tract (pyelonephritis) infections [17,18].

SYMPTOMATIC BACTERIURIA

Symptomatic bacteriuria is divided into lower urinary tract infections (cystitis) and upper urinary tract infections (pyelonephritis). Cystitis, primarily affecting women and often linked to sexual activity, involves notable bacteriuria with bladder mucosa invasion. It differs from asymptomatic bacteriuria due to symptoms like dysuria, urgency, frequency, nocturia, hematuria, and suprapubic discomfort in afebrile women without systemic illness.

Urethritis

It is an infection affecting the urethra, involving bacteria, protozoa, viruses, or fungi. It occurs



when microorganisms enter the periurethral glands in the bulbous and pendulous regions of the male urethra and the entire female urethra. Pathogens transmitted through sexual activity, such as *Chlamydia trachomatis*, *Neisseria gonorrhoea*, *Trichomonas vaginalis* [19].

Cystitis

- an infection of the bladder, is more prevalent in women, often following sexual intercourse in cases of uncomplicated cystitis. It is characterized by significant bacteriuria involving bladder mucosal invasion. This condition differs from asymptomatic bacteriuria due to the presence of symptoms like dysuria, urgency, frequency, nocturia, hematuria, and suprapubic discomfort in afebrile women without systemic illness [20].

ASYMPTOMATIC BACTERIURIA

A UTI can affect any part of the urinary tract, including urethritis, cystitis, pyelonephritis, epididymitis, prostatitis, and abscess. UTIs are extensively studied during pregnancy, as untreated cases can lead to serious complications such as intrauterine growth restriction, preeclampsia, preterm deliveries, and cesarean deliveries. Timely and appropriate treatment, guided by urine culture and sensitivity reports, is crucial. Confirming the complete eradication of the pathogenic organism is essential to prevent UTI recurrence. Antibiotics like Nitrofurantoin, Trimethoprim, or cephalexin are suitable choices. Asymptomatic bacteriuria can progress to cystitis and pyelonephritis, potentially causing acute respiratory distress, transient renal failure, and septic shock during pregnancy [21,22] Asymptomatic bacteriuria is prevalent among the elderly, particularly in long-term care residents. Studies indicate that its incidence rises with age, with a higher prevalence in women than in men. Among older women, the occurrence of asymptomatic bacteriuria surpasses 15%, reaching up to 50% for those in long-term care facilities. Pregnant women are advised to undergo screening

for asymptomatic bacteriuria during the first trimester and receive treatment if the results are positive [23]

RISK FACTORS OF UTI

Age

Urinary tract infections (UTIs) are prevalent during pregnancy, especially among women aged 26-35. This age bracket experiences a heightened risk due to early pregnancies, notably in remote areas. Research indicates that advanced age is considered a UTI risk factor during pregnancy, attributed to declining glycogen levels, reduced *Lactobacillus*, and increased vulnerability to bacterial adherence. Among pregnant women, UTI prevalence is highest in the 26-30 age group, followed by 21-25 and 31-35. The age range observed in studies spans from 18 to 45 years, highlighting the significance of age-related factors in UTI susceptibility during pregnancy [24].

Obstetric factors

Gravidity plays a crucial role in the prevalence of urinary tract infections during pregnancy. Research indicates a higher occurrence among women experiencing their first pregnancies (53.85%) compared to those with multiple pregnancies (46.15%). This study highlights the heightened susceptibility of nulliparous women to UTIs in comparison to multiparous women. Furthermore, parity and gestational age have been consistently identified as significant factors influencing the prevalence of urinary tract infections, as reported in numerous studies. Understanding these obstetric factors is crucial for effective management and prevention strategies during pregnancy [25]

Gestational age

Gestational age emerges as a pivotal factor in the susceptibility of pregnant women to urinary tract infections (UTIs). Particularly, those in their third trimester and those with multiple pregnancies face elevated risks. Anatomical and hormonal variations during pregnancy, leading to urethral



dilation and urinary inertia, contribute to the increased likelihood of UTIs. Studies consistently reveal that the majority of pregnant women with UTIs are in their third trimester, followed by the second and first trimesters. Bacteriuria peaks at five to ten weeks of gestation, followed by ten to fifteen weeks and fifteen to twenty weeks. Understanding these patterns is vital for targeted preventive measures [26]

Genetic factors

Genetic factors contribute significantly to urinary tract infection (UTI) susceptibility. The presence of P-antigens on the ABO blood group in uro-epithelial cells acts as receptors for *E. coli* adhesion. Individuals with secretor status secrete ABO blood group antigens in body fluids, covering *E. coli* adhesion receptors, reducing UTI risk. Conversely, those without secretor status have exposed receptors, leading to recurrent UTIs. Approximately 4-7% of pregnant mother's experience UTIs, with 25-30% developing acute pyelonephritis, attributed to pelvic dilatation, ureter obstruction, and hormonal changes [27]. Abnormalities like fistulae and urinary tract trauma increase UTI risks in pregnant women, especially when lacking regular checkups. Metabolic factors, such as diabetes mellitus, elevate UTI prevalence, exacerbated by glucose in urine [28]. Understanding these genetic and metabolic influences is crucial for comprehensive UTI management.

SIGNS AND SYMPTOMS [29]

- Experiencing pain or discomfort during urination
- Increased frequency of urination beyond the usual
- Urgency sensation while urinating
- Presence of blood or mucus in the urine
- Cramps or lower abdominal pain
- Pain during sexual intercourse
- Symptoms like chills, fever, sweats, and incontinence

- Waking up during sleep to urinate
- Changes in urine volume, either more or less
- Cloudy, foul – smelling, or unusually strong urine
- Pain, pressure, or tenderness in the bladder area.
- Kidney-related symptoms; back pain, chills, fever, nausea, and vomiting, when bacteria spreads to the kidneys.

METHODS TO PREVENT UTI DURING PREGNANCY

These can conveniently be categorized into hygiene, Diet, Activities and Medications.

- drink plenty of water to help flush bacteria out of the urinary system
- prevent holding urine for extended periods.
- Wear all cotton undergarments
- ensure genital and surroundings hygiene and urinate both before and after sexual intercourse.
- use mild, unscented soaps, powder, sprays that may irritate the urethra.
- use barrier methods of contraception to prevent sexually transmitted infections, which can increase the risk of UTIs.
- report any symptoms of a UTI, such as pain or burning during urination.

ANTIBIOTIC TREATMENT

UTI can affect any part of the urinary tract, including urethritis, cystitis, pyelonephritis, epididymitis, prostatitis, and abscess [30]. UTIs are extensively studied during pregnancy. Antibiotic use is crucial for treating UTIs especially given high prevalence, particularly in women. Antimicrobial treatment selection is influenced by factors like infection site, severity and bacterial considerations. Most published studies on antibiotics prophylaxis centers minimized the occurrence of UTIs. [31] An untreated case can lead to serious complications such as intrauterine growth restriction,



preeclampsia, preterm deliveries, and cesarean deliveries. Timely and appropriate treatment, guided by urine culture and sensitivity reports, is crucial. Confirming the complete eradication of the pathogenic organism is essential to prevent UTI recurrence. [32] Asymptomatic bacteriuria can progress to cystitis and pyelonephritis, potentially causing acute respiratory distress, transient renal failure, and septic shock during pregnancy. The majority of antimicrobial agents utilized for UTIs attain elevated concentrations in the urinary tract, surpassing the levels absorbed in the bloodstream. Antibiotics endorsed by global guidelines are category B classification according to the US Food and Drug Administration. [33].

PYELONEPHRITIS

Ensuring sufficient intravenous hydration is crucial for maintaining optimal urinary output. With the right antibiotic therapy and hydration, the majority of patients typically show improvement within 24-72 hours. Admitting pregnant women with pyelonephritis for intravenous antibiotic treatment and providing supportive care is advised. [34] If the patient shows no response to antibiotic treatment, it is advisable to obtain blood culture and sensitivity. The primary focus of most clinical trials has been on parenteral antibiotics,

specifically cefazolin, ceftriaxone, and combinations such as ampicillin or cefazolin with gentamicin. These antibiotics play a central role in managing uterine conditions during pregnancy. [35]

ACUTE CYSTITIS

The chosen antibiotics should encompass common pathogens and can be modified as necessary until the identification of the organism along with its sensitivity profile.

Doses taken according to the drugs could be:

Cephalexin:

500mg twice daily

Nitrofurantoin:

50mg four times a day (avoid at 36 + weeks) Fosfomycin a derivative of phosphonic acid, is effective in treating uncomplicated UTIs caused by susceptible strains of E. coli and Enterococcus species. [36]

NEWER ANTIBIOTIC AGENTS FOR MULTI DRUG RESISTANT INFECTION

The development of multiple drug-resistant organisms has prompted the investigation of older antimicrobials (primarily aminoglycosides and tetracycline) as well as the development of new antibiotics and combinations, such as:

NEWER ANTIBIOTIC	Class	Resistant	MOA	Therapeutic benefits	reference
Aztreonam /avibactam	Beta-lactam inhibitor (monobactam)	Pseudomonas aeruginosa	Inhibits cell wall synthesis	Urological infection (pyelonephritis)	37
Cefiderocol	Beta-lactam inhibitor (cephalosporin)	P aeruginosa	Preventing cell wall synthesis	Nosocomial pneumonia, acynetobacter infection	38
Ceftazidime /avibactam	Beta-lactam inhibitor(monobactam)	Enterobacter cloacae	Penicillin binding proteins	(MDR)Blood stream infection	39
Eravacycline	tetracyclines	Acynetobacter baumannii	Inhibits bacterial protein synthesis	Nosocomial infections-	40

Glycylcyclines	tetracycline	Klebsiella pneumonia	Impair protein synthesis	Multi drug resistant Acinetobacter baumannii infection -- ventilator associated pneumonia	41
Meropenem	carbepenam	Pseudomonas spp	Peptidoglycan (cross-linking)	Enterobacteriaceae infection	42
Fosfomycin	Amino glycoside	Escherichia coli	Inhibits peptidoglycan formation	MDR (pyelonephritis)	43

CONCLUSION

This analysis highlights the importance of effectively managing urinary tract infections (UTIs) during pregnancy. With Escherichia coli and gram-negative bacteria as the main pathogens, UTIs impact up to 10% of pregnancies. Recognizing the associated risk factors, ensuring timely diagnosis, and applying appropriate antibiotic therapies are essential to prevent complications such as preterm birth and pyelonephritis. Emphasizing hygiene, proper hydration, and the use of new antibiotic treatments for multidrug-resistant infections are critical steps. By adopting these preventive strategies, healthcare providers can reduce UTI-related complications and promote better maternal and fetal health outcomes during pregnancy.

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