Urinary tract infection in pregnant women

Abstract

Urinary tract infections (asymptomatic bacterial urine, cystitis and acute pyelonephritis) are the most common complications of pregnancy. They are caused by the anatomical and physiological changes of pregnant women. Early diagnosis and management are essential to avoid possible maternal and infant sequelae. Diagnosis is done by identifying pathogens through urine culture. The most common microorganism is *Escherichia coli.* Treatment is carried out under antibiotic coverage, and management can be outpatient or inpatient treatment, as appropriate.

Key words: Pregnancy Urine analysis; Bacterial urine; Cystitis; Pyelonephritis.

Introduction

Urinary tract infection (UTI) is defined as the presence of bacteria that can cause changes in the function and morphology of the bladder, collecting system or kidney (1). Due to the anatomy of urogenital tract, urination habits, pregnancy and other physiological conditions, it is mainly related to women. Among pregnant women, it is considered to be very important because it is one of the most common obstetric complications, second only to anemia and cervical vaginitis (2).

During pregnancy, the anatomical and physiological changes of urinary system lead to hydronephrosis, vesicoureteral reflux and physical and chemical changes of urine. In addition, hormone disorders, such as the increase of progesterone, lead to the decrease of urethral and bladder muscle tension and the decrease of ureteral peristalsis, resulting in urinary stasis; Thus, an environment is created that promotes bacterial overgrowth and may develop into septic lesions (2, 3, 4).

Three entities are considered UTI: asymptomatic bacteriuria, acute cystitis and acute pyelonephritis. Asymptomatic bacterial urine refers to the presence of at least 1X105 colony forming units / ml in urine culture without any suggestive symptoms or signs. In symptomatic infections, lower urinary tract involvement can be found, called acute cystitis, where invasion of the bladder mucosa is limited; Or upper urinary tract, that is, acute pyelonephritis, involving renal parenchyma, calyces and pelvis (5).

In the United States, ITU produces more than 7 million visits a year, accounting for 15% of all non hospitalized antibiotics. In addition, the annual cost of public health is $1.6 billion (6).

At present, it is estimated that about 10% of pregnant women will appear at least one picture at some time during pregnancy. Therefore, the latest knowledge of early detection and treatment is very important because it can have serious consequences for mothers and fetuses (3,4). This is why all UTI is considered complex if it occurs during pregnancy (4).

The purpose of this review is to collect and provide the latest evidence on the diagnosis, clinical **manifestations** and management of ITU, so as to prevent potential maternal and infant complications, reduce its morbidity and mortality, and promote optimal prenatal care.

Method

Search pubmed, Cochrane Library plus, Google Scholar and update for phrases such as "UTI during pregnancy", "urinary tract infection" and "UTI and pregnancy". Including original articles or research and subject revision. The inclusion criteria were publications published in English and Spanish between 2015 and 2019. 15 articles meeting the above criteria were reviewed and the information required for the review was provided according to the achievement of the objectives.

Epidemiology

ITU is the most common bacterial infection during pregnancy (3). 5-10% of pregnant women have at least one UTI attack during pregnancy (2,7). The prevalence of asymptomatic bacteriuria is between 2-10%, similar to non pregnant patients, but the recurrence rate is high (8). The prevalence of acute cystitis is 1-4%, the prevalence of pyelonephritis is 0.5-2%, and the risk of pregnancy or postpartum recurrence is as high as 25% (9).

In 30-40% of cases, untreated asymptomatic bacterial urine may evolve into cystitis and even acute pyelonephritis (10). However, if eradicated in time (3,8), this risk will be reduced by 80%. Asymptomatic bacteriuria is more common in early pregnancy, while cystitis and pyelonephritis are more common in the middle and late stages of pregnancy (8). These institutions together account for 5-10% (3, 7) of pregnant women's hospitalization income.

Microbiology

It is common to isolate the same UTI pathogen from the general population. For example: *Escherichia coli* (up to 80%), *Klebsiella pneumoniae, Proteus mirabilis, saprophytic Staphylococcus* and *Enterobacter* (1, 5, 8, 11). Other staphylococcal *strains* may represent sample contamination rather than infection (11,12). However, it should not be ignored that up to 10% of ITU can be caused by group B Streptococcus strains, especially *Streptococcus* agalactiae (SGB). This finding implies a large colonization of pathogens in the urogenital tract and leads to the importance of screening all pregnant women from weeks 35 to 37 (3, 11).

Risk factors

The main risk factor of ITU is pregnancy (7); During pregnancy, the history of ITU in the first few weeks of pregnancy or early pregnancy is the most relevant susceptibility factor (3). Other risk factors include genitourinary malformations, sexually transmitted infections, diabetes, sickle cell anemia, immunosuppression and low socio-economic levels (5, 8, 13).

Risk factors for recurrence of ITU in women of childbearing age include under 15 years old at the first attack of ITU, the mother's family history of ITU, frequency of sexual intercourse, use of spermicide, new sexual partner and multiple births (9).

Pathophysiology

Infection contaminates the sterile urinary tract by invading fecal residues or pathogens in the normal flora from the vaginal and perianal areas upward (14).

During pregnancy, the body will undergo a variety of changes to adapt to the state of pregnancy, and the urinary system is no exception. The kidney increases to 1 cm and the glomerular filtration rate increases by 30-50% (14). In addition, at about 7 weeks of pregnancy, slight hydroureter can be observed due to the increase of progesterone. This leads to ureteral dilatation, decreased smooth muscle tension, reduced ureteral peristalsis and relaxation of bladder sphincter. In addition, around week 22-26, the continuous growth of the uterus causes mechanical obstruction through bladder displacement, resulting in urinary stasis. (4, 5, 8,14). Due to the increase of glucose and amino acids in urine, the ph value of urine changes, so the environment is more conducive to bacterial growth (4, 5, 13, 14).

Asymptomatic bacteriuria

- **Clinical table**

By definition, asymptomatic bacteriuria has no symptoms or signs, so there is no clinical table for this entity, so the importance of screening at different stages of pregnancy (4, 5, 8, 13) is affirmed.

- **Diagnosis**

The diagnosis of asymptomatic bacterial urine is to extract samples from quantitative urine culture medium before sterility test. Positive colony formation (CFU) > 80% after identification; Increased to 95% after ⩾ 2 consecutive trials (7, 11).

Quantitative urine culture screening is recommended for all pregnant women during or 16 weeks before the first prenatal examination (1.7 weeks). In addition, it is recommended to continue reactive band screening at each subsequent prenatal examination (2). In addition, for patients with multiple risk factors, urine culture is recommended quarterly (7).

In the presence of SGB in urine culture, high genital tract colonization should be suspected and increase the risk of pyelonephritis, chorioamnionitis and early neonatal sepsis. The presence of SGB > 100000 CFU in urine justifies antibiotic treatment and postpartum prevention of asymptomatic bacteriuria without the need for rectovaginal culture at 35 to 37 weeks. However, in the presence of SGB < 100000 CFU, antibiotics are not recommended for the treatment of bacterial urine, because in most cases, it will be re cloned quickly after treatment, so the risk of these complications will not be reduced. However, in this case, prenatal prevention of GBS without rectovaginal culture is recommended (6,7).

- **Management and treatment**

If you have a record of antibiotics, treatment usually starts with a minimum of antibiotics. However, if not, the standard duration of empirical treatment is 4-7 days, as shown in **Table** *1*.

After treatment compliance, urine culture should be performed 7-15 days after treatment, and the expected cure rate is 80-90%. In the case of the persistence of the table, the antibiotic map should evaluate better antibiotic sensitivity, otherwise it is recommended to repeat urine culture every month. In addition, prophylactic antibiotic treatment of asymptomatic recurrent bacteriuria should be given after two completely ineffective treatments (1, 11).

Table 1. Empirical treatment of asymptomatic bacteriuria during pregnancy

Antibiotic	Dose
Furantoin	100 mg VOC / 12 hours
Amoxicillin	500 mg VOC / 8 hours
Ampicillin	500 mg VOC / 6 hours
Cephalexin	500 mg VOC / 6 hours

Source: L ó PEZ m, Cobo T, Palacio m, gonc é A. Urinary tract infection and pregnancy. Barcelona, Spain: Barcelona Clinical Hospital; 2017

Acute cystitis

- **Clinical table**

When you have a localized bladder infection, the expected symptoms are dysuria, bladder spasm, and multichirality. No systemic symptoms (6, 8, 13).

- **Diagnosis**

After the sterility test, at least one positive urine culture greater than 100000 CFU was diagnosed through the recommended clinic (7). It is usually associated with pyuria, bacterial urine and occasional microscopic or abnormal gross hematuria (2). In addition to antibiotic sensitivity tests, confirmatory studies should also be conducted for women screened for response strips with leukocyte +, nitrite +, protein > 1 + or erythrocyte > 1 + and suggestive clinical presence (7).

- **Management and treatment**

Management is usually based on experience, as there is usually no antibiotic sensitivity at the time of diagnosis and adjusted according to the antibiotic map (7). Table 2

describes the recommended experience scheme with a standard duration of **7 days.**

In addition, it is recommended to take 200 mg fenazopyridine orally every 8 hours for urinary analgesia for at least 2 days. Patients in outpatient management are recommended to have a relative rest, consume 2-3 liters of liquid every day, improve micturition habits, such as avoiding bladder emptying delay of more than 3-4 hours, proper hygiene and post anal cleaning, and treat vaginitis.

Similarly, the resolution of the urine culture checklist should be checked within 7-15 days after the end of antibiotic treatment and repeated once a month (2.7).

It is considered important to distinguish between recurrence and reinfection.

Recurrence is the persistence of previously detected microorganisms and usually occurs within the first two weeks after treatment. Management is an empirical treatment different from the previous regulation, lasting for 7-14 days. Urinary tract examination was not reported before the second recurrence.

If there is abnormal anatomy or function of urinary tract, it should be recommended to extend the treatment for 4-6 weeks. Reinfection, on the other hand, is a new infection, usually associated with different bacteria. Antibiotic suppression therapy is also recommended after two ineffective combination treatments for recurrent cystitis (7,10).

Table 2. Empirical treatment of acute cystitis during pregnancy

Antibiotic	Dose
Furantoin	100 mg VOC / 12 hours
Amoxicillin	500 mg VOC / 8 hours
Ampicillin	500 mg VOC / 6 hours
Amoxicillin / clavulanic acid	500 mg VOC / 8 hours
Trimethoprim / sulfamethoxazole	160 / 800 mg VOC / 12 hours (excluding the second quarter)

Source: Cuyuch Hern á ndez J, l ó PEZ Rosa V, Mej í a s á nchez D. Urinary tract infections and obstetric and perinatal complications of pregnant women aged 15 to 30 in specialized family health units in the community of chalguapa, Santa Ana, from January to December 2015. San Salvador, El Salvador: University of El Salvador; 2016.

Acute pyelonephritis

- **Clinical table**

When the infection rises to the kidney, the clinical manifestations will change. Fever, general discomfort, nausea, vomiting, flank pain and costal vertebra allergy. You may have pyuria, but hematuria is rare. In this case, common complications include shock, anemia, renal failure, or renal abscess (6, 8, 13).

- **Diagnosis**

After obtaining suggestive medical history, physical examination and obstetric evaluation according to gestational age, it was confirmed by urine culture of more than 100000 CFU collected by medium jet after sterility examination. In pregnant patients, there is no need to collect samples through the bladder catheter, only in pregnant women at high risk of contamination (2,7).

In addition, hemogram, electrolyte, creatinine, CRP and blood culture are recommended because up to 20% of patients with pyelonephritis will develop bacteremia. Routine additional imaging examinations, such as renal ultrasound, should not be required. Its use is limited to recurrent attacks, severe systemic diseases, suspected abscesses or hematomas, or inability to receive treatment (7).

- **Management and treatment**

The optimal treatment of pyelonephritis is the key, because screening and treatment are the main interventions to reduce the risk of maternal and infant complications (1). This method will depend on the general situation and conditions of the patient. Pregnant women ⩾ 24 weeks, fever ⩾ 38 ° C, sepsis, dehydration, threat of preterm birth, recurrent pyelonephritis, complications, oral intolerance, treatment failure or inability to outpatient treatment after 72 hours should be hospitalized (7).

– Outpatient management

According to the antibiotic map, low spectrum antibiotics should be used. Otherwise, empirical treatment is shown in **Table 3.**

After fever symptoms disappear for at least 48-72 hours, it is recommended to repeat oral antibiotic treatment until 14 days of treatment is completed. In this case, it is recommended to take 500 mg Cefalexin orally every 6 hours or 500 mg amoxicillin orally every 8 hours (2).

Table 3. Outpatient empirical treatment of acute pyelonephritis

Antibiotic	Dose

Cefuroxime	250 mg C / 12 h Vo
Cefixime	400 mg C / D Vo
Source: L ó PEZ m, Cobo T, Palacio m, gonc é A. Urinary tract infection and pregnancy. Barcelona, Spain: Barcelona Clinical Hospital; 2017	

– Hospital management

Hospital management includes active hydration and parenteral antimicrobial therapy under the following protocols (7):

- Day 1: 150 ml / h of liquid treatment (e.g. SF 500 ml / 6 hours + SG 5% 500 ml / 8 hours).
- The next day: Liquid Treatment 100ml / h (e.g. SF 500ml / 8h + SG 5% 500ml / 12h)

Conversely, empirical antimicrobial therapy should be started and vital signs and diuresis should be strictly monitored. The proposed scheme is shown in **Table** *4.*

For patients with suspected sepsis, multidrug resistant microorganisms or long-term use of probes, it is recommended to treat Pseudomonas aeruginosa with broad-spectrum antibiotics, *such* as *intravenous* injection of 1G ceftazidime every 8 hours or amikacin 15mg / kg every 24 hours. For patients previously cultured by Enterococcus *faecalis,* 1 *g* ampicillin should be injected intravenously every 6 hours or 1 g vancomycin should be injected intravenously every 12 hours; Piperacillin tazobactam monotherapy can consider intravenous injection of 4 g every 8 hours and requires infection assessment (7).

Table 4. Hospital empirical treatment of acute pyelonephritis

Antibiotic	**Dose**
Cefatriaxone	1-2g IV C/12h
Ampicillin + gentamicin	1g IV C / 6h + 160 mg im C / D
Cefazolin + gentamicin	1-2g IV C/8H+160 mg IM C/D

Source: Cuyuch Hern á ndez J, l ó PEZ Rosa V, Mej í a s á nchez D. Urinary tract infections and obstetric and perinatal complications of pregnant women aged 15 to 30 in specialized family health units in the community of chalguapa, Santa Ana, from January to December 2015. San Salvador, El Salvador: University of El Salvador; 2016.

In addition, maternal and infant monitoring is emphasized, and vitality is evaluated by noninvasive and stress-free fetal monitoring (NST) and biophysical profile. In addition, signs of the threat of preterm birth should be excluded by monitoring uterine dynamics, cervical dilatation, fetal movement and water leakage (2). Urine culture was performed 15 days after treatment and then monthly to ensure resolution. Prevention should be considered after a single attack in patients with recurrent pyelonephritis or nephropathy (7). As shown in Table 5, preventive treatment should start after the completion of the previous plan and continue until the rest of pregnancy and 4-6 **weeks postpartum.** Continuous daily administration is the most commonly used, however, for women with a history of ITU related to sexual activity, it can also be administered 2 hours after sexual intercourse (2.7).

Table 5. Antibiotic prevention of nephropathy or recurrent pyelonephritis

Antibiotic	**Dose**
Fosfomycin	3G VOC / week
Furantoin	100 mg VO HS (avoid labor because of the risk of fetal hemolysis caused by immature enzyme)
Cephalexin	250 mg voc/d HS

Source: Cuyuch Hern á ndez J, l ó PEZ Rosa V, Mej í a s á nchez D. Urinary tract infections and obstetric and perinatal complications in pregnant women aged 15-30 in the community family health unit of chalcuapa, El Salvador: University of El Salvador; 2016.

L ó PEZ m, Cobo T, Palacio m, gonc é A. Urinary tract infection and pregnancy. Barcelona, Spain: Barcelona Clinical Hospital; 2017

Complication

Asymptomatic bacteriuria and untreated cystitis are considered risk factors for pyelonephritis, a pathology, except for the first reason for non obstetric hospitalization during pregnancy; It is closely related to septic shock, perinatal and obstetric complications (1, 6, 15).

The most common perinatal complications are low birth weight, premature delivery, respiratory distress, sepsis

and fetal or neonatal death. Studies have shown that arachidonic acid, phospholipase A and prostaglandins produced by pathogens are the main mechanism of cervical maturation. In addition, the increase of free calcium concentration in uterine myometrium will stimulate uterine tension and early contraction, which will eventually threaten preterm birth and its complications (2, 6, 11, 15).

Obstetric complications include premature rupture of membranes, intrauterine growth restriction, anemia, abortion, preeclampsia and maternal and infant death (2, 6, 15).

After maternal infection, collagenase and estomelisin are produced in the hypoxic decidual segment, which is related to the induction of metalloproteinases on the chorion and amnion, resulting in the weakening and decomposition of extracellular matrix proteins, resulting in premature rupture of the egg membrane. This may lead to chorioamnionitis, neonatal hyaline membrane, early neonatal sepsis, pelvic manifestations, umbilical cord prolapse, head and / or umbilical cord compression, and increased cesarean section rate (2).

Pyelonephritis in pregnant women appears to increase the susceptibility to anemia because of reduced erythropoietin production. The causal relationship between anemia and ITU susceptibility is unclear, but the reduction of defense mechanisms contributes to the colonization of pathogens (2).

Aldosterone can activate the renal vascular system and cause damage to the renal vascular system. Elevated circulating renin increases maternal blood pressure, initially offset by progesterone. However, glomerular injury is associated with decreased filtration rate and accumulation of nitrogen products, resulting in increased serum creatinine, uric acid and urea. The activation of systemic inflammatory response after maternal infection and the resulting endothelial injury are considered to increase the risk of placental hypoxia and uteroplacental atherosclerosis by 1.3 times; Thus contributing to the development of preeclampsia (2, 15).

Conclusion

Urinary tract infections during pregnancy increase the morbidity of mothers and fetuses. It is considered important to implement preventive measures, such as correcting urination habits and managing comorbidities prone to urination habits. However, since simple pregnancy status is a risk factor, screening and optimal prenatal control are essential.

It is recommended that urine analysis screening be carried out 16 weeks before pregnancy and reactive strip follow-up in subsequent prenatal consultation for diagnosis. In addition, when there are symptoms or signs suggestive of ITU, relevant confirmatory studies should be carried out. This is because early detection is essential to avoid complications and adverse events associated with this pathology.

The clinical manifestation will depend on the anatomical site involved, that is, in the infection affecting the lower urinary tract, dysuria, bladder rigidity and polychirality can be expected without systemic symptoms. However, with the rise and involvement of the upper urinary tract, fever, general discomfort, nausea, vomiting and flank pain are expected, accompanied by suprapleural allergies.

After diagnosis, rapid and appropriate treatment through antibiotic treatment can reduce the risk of complex situations that may damage the mother and fetus. The rapid recognition and management of its complications can minimize the impact of mother and baby and achieve successful full-term pregnancy. The economic impact on public health is also decreasing.

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