

# Urinary tract infections in pregnancy

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## ABSTRACT

**Background.** Urinary tract infections (UTI) are the most common infections during pregnancy. The fetomaternal complications linked to this pathology can be severe if untreated and the treatment has been a subject of interest hence the multiple drugs contraindications in pregnancy, the restraint panel of antibiotics that can be used and the antimicrobial resistance that is constantly increasing. The purpose of this article is to review the latest data from literature and guidelines regarding the best management of the urinary tract infections in pregnancy.

**Methods.** It was undertaken a systematic electronic search for articles, reviews and guidelines using Cochrane Date Base, PubMed and the international protocols in use recommended by the Obstetrics and Gynecology societies (ACOG - American College of Obstetricians and Gynecologists, CNGOF – Collège National des Gynécologues et Obstétriciens Français, RCOG – Royal College of Obstetricians and Gynecologists).

**Results and conclusions.** Special consideration should be given to urinary tract infections developed during pregnancy because they are related to serious fetal and maternal complications. Routine screening is recommended and the antibiotic therapy properly individualized. Emotional impact on the future mothers is particularly important and non-pharmacologic prophylaxis should always be discussed at the begging of pregnancy. Future research should be focused on finding the actual mechanism of pathogenesis that link UTI and the complications they associate.

**Keywords:** urinary tract infections, pregnancy, diagnosis, treatment, antibiotics

## INTRODUCTION

Urinary tract infections (UTI) are the most frequent infections during pregnancy. This pathology can be at the origin of multiple fetomaternal complications (acute pyelonephritis, maternal sepsis, premature birth, intrauterine growth restriction – IUGR), fact that justifies the systematic screening during pregnancy. Common symptoms of UTI include high frequency of urination and pain associated with burn sensation when discharging urine [1]. Severe UTI forms can also associ-

ate fever, nausea, vomiting and chills. The actual difficulty is represented by treating the pregnant women with a reduced arsenal of antibiotics, due to their contraindications and taking into account the antibiogram result [1,2].

The pathogens that cause UTI in pregnancy are the same as in the general population, especially bacteria of bowel provenance. Dominantly involved are Gram-negative bacilli as *Escherichia coli* (75-90%), *Proteus mirabilis*, *Klebsiella pneumoniae* and Gram-positive cocci (5%) as Enterococcus, Group B Streptococcus,

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Staphylococcus. The treatment and the prognosis differ according to the gravity, as UTI can be divided in asymptomatic bacteriuria, acute cystitis and acute pyelonephritis [1,3,4].

## METHODS

It was undertaken a systematic electronic search for articles, reviews and guidelines using Cochrane Date Base, Pub Med and the international protocols in use recommended by the Obstetrics and Gynecology associations (ACOG – American College of Obstetricians and Gynecologists, CNGOF – Collège National des Gynécologues et Obstétriciens Français, RCOG – Royal College of Obstetricians and Gynecologists). The publications were selected taking in account the originality, the year of publication, the novelty they came with, and also the accessibility and attainability of the full text. Search words were “urinary tract infections”, “pregnancy”, “diagnosis”, “treatment”, “infections”, “cystitis”, “pyelonephritis”, “pregnancy-associated infections”, “antibiotherapy”. All the publications used can be found as mentioned in the references section.

## RISK FACTORS

Risk factors of UTI in pregnancy can be divided according to their origin as mechanical, hormonal or of other nature. In pregnancy, the augmented volume of the uterus compresses the urinary bladder (causing an incomplete voiding of the urine with an associated post urinary residue) and the ureters (which determines urinary stasis, preponderant on the right side due to the physiologic uterine dextro-rotation). Moreover, the stretching of the ureters can be associated with the vesicoureteral reflux and increases the incidence of pyelonephritis, frequently located on the right side. As hormonal factors the progesterone causes a decrease in the ureteral peristalsis and a hypotonia of the urinary tract with subsequent urine reflux and stagnation, while the estrogens induce a bladder congestion associated with increased adherence of the germs to the urothelium [5].

Medical conditions associated to pregnancy like gestational diabetes, malformations of the urinary tract, recurrent UTI in the patient’s history, vaginal infections, can also influence the onset and the gravity of UTIs. Physiological changes in pregnancy that diminish the renal reabsorption of glucose causing glycosuria and urine alkalinization contribute furthermore to the high frequency of these infections [6].

## SCREENING METHODS

Although asymptomatic bacteriuria in non-pregnant women does not require treatment, both sympto-

matic and asymptomatic UTIs in pregnancy are linked to severe complications and need prompt treatment with antibiotics. Clinical vigilance is therefore necessary and acquired by systematic screening for bacteriuria. The French society of obstetricians and gynecologists recommends monthly screening with urinary dipsticks which detect the nitrites and leukocyturia. If the dipstick result is positive for these two markers there is a high possibility that a UTI is present [4]. A midstream urine sample and urine culture, which represents the gold standard in detection of UTI, is therefore required [3]. The RCOG and the ACOG sustain the UTI screening by repeating the urine culture in each trimester of pregnancy [6].

## THE COMPLICATIONS OF URINARY TRACT INFECTIONS IN PREGNANCY

### UTI and preeclampsia

It has long been a subject of debate if urinary tract infections influence the occurrence of preeclampsia in pregnancy. Preeclampsia (PE) represents a multisystemic vascular syndrome that arise frequently after 20 weeks gestation and is defined by tensional values equal or exceeding 140 mmHg for systolic and 90 mmHg for diastolic. Even though the actual etiology of PE has not yet been established, it is highly believed that the systemic inflammatory response plays a key role in this pathology, so each trigger of the immune system can be at the origin of its occurrence in pregnancy [7,8].

There is evidence showing that the systemic inflammation has a negative influence on placentation by favoring uteroplacental acute atherosclerosis, which affects the spiral arteries and is defined by intramural deposits of lipids, with high incidence in PE [21]. As the most frequent infection that occurs in pregnancy, UTI is probably one of the main activators of the immune system, making the screening and rapid treatment of UTI in pregnancy a priority of a good medical practice [4,7].

### UTI and preterm birth

Preterm birth or delivery under 37 weeks of gestation represents a great public health issue with a prevalence of 11-12% in United States. Even though the exact mechanism of pathogenesis is not known, recent studies have shown there is a direct correlation between untreated UTI in pregnancy and preterm birth. Theoretically it is believed that genetic and environmental influences, combined with infections can modify the vaginal flora favoring amniotic inflammation which conducts to preterm birth [5].

## UTI and low birth weight / Intrauterine growth restriction

Abnormal placentation associated with systemic inflammation caused by infections may slow the rate of fetal growth and influence the future wellbeing after birth. The risk of preterm birth, also detected in untreated UTI, is related with low birthweight newborns [3,9].

The emotional impact of UTI in pregnancy is very high and it is based on the prenatal attachment to the fetus and the knowledge that untreated, it could harm the future baby [10]. The prevention of genitourinary infections in pregnancy implies informing the patient that drinking water (>2L), frequent voiding, wiping techniques from front to back and a good local personal hygiene are recommended [11]. Adequate treatment and prophylaxis of UTI have the potential to diminish the incidence of premature birth and low birth weight and have a beneficial effect on the welfare of the mother and child [9,12].

## MANAGEMENT

As previously mentioned, all UTI in pregnancy need to be treated adequately [2]. UTI during pregnancy are divided in three classes, according to their clinical gravity: asymptomatic bacteriuria, acute cystitis, acute pyelonephritis. There are numerous antibiotics that can safely be used taking in account the urine culture result and the necessity of urgent treatment initiation. While asymptomatic bacteriuria can wait the antibiogram result, acute cystitis and acute pyelonephritis need rapid start of therapy with subsequent adjustment [13].

### Lower UTI

The first-choice antibiotic in lower UTI in pregnant women (acute cystitis and asymptomatic bacteriuria) is nitrofurantoin. Nitrofurantoin should be avoided in the first trimester or in pregnancy at term, in the few weeks before birth, because it is related to the risk of neonatal hemolysis. The treatment should be administrated for a period of 7 days, with a dosage of 100 mg given twice a day [3,22].

Other antibiotics, recommended as second-line choice, are penicillins (amoxicillin) and cephalosporines (cefalexin). They have to be indicated if the first-line choice antibiotic does not relieve the symptoms or if the symptoms worsen after at least 48 hours of treatment. The advised antibiotherapy is 7 days, with Amoxicillin 500 mg administrated three times a day and Cefalexin 500 mg twice a day [22].

Trimethoprim is not recommended in pregnancy because being a folate antagonist, it has a teratogenic risk in the first trimester. However, when there is no

other option for treatment of UTI, but Trimethoprim, this could be offer together with folic acid 5mg daily in the first trimester [4,23].

There is a high debate regarding the use of Fosfomycin trometamol in pregnancy because there are insufficient data available on the safety of the product. Fosfomycin is a broad-spectrum antibiotic, that succeeds in maintaining high urinal concentrations for a long period of time (approx. 3 days) and which comes as a single dose therapy, versus the other recommended drugs that need to be taken for up to 7 days [14,15]. Although there have been made several trials which concluded there are no adverse effects of the drug in pregnancy, adequate research is to be made taking in account the ethical considerations [1,6,24].

The follow up of the case implies repeating the urine culture one week after termination of treatment, with subsequent bacteriuria clearance. If the bacterial growth is present (more than 105 CFU/ml) and if the pathogen remains the same, it can be reinitiated the initial antimicrobial therapy for a longer time, or the antibiotic can be changed with the conventional length of treatment.

### Upper UTI (acute pyelonephritis)

Acute pyelonephritis is associated with symptoms like high fever (>38°C), chills, flank ache (positive Giordano's sign), sickness, vomiting and costovertebral soreness. The clinical diagnosis is confirmed by the presence of bacteriuria [27]. When pyelonephritis is diagnosed, parenteral broad-spectrum antibiotics need to be given rapidly and implies hospitalization for at least 48 hours. If there are no signs of gravity, the treatment can be initiate with cephalosporines (ceftriaxone, cefepime, cefotaxime), aztreonam or amoxiclav [25]. Severe forms of pyelonephritis associated with obstacle, septicemia, or immunosuppression, need a more aggressive therapy with ticarcillin associated with clavulanic acid, piperacillin associated with tazobactam, meropenem, ertapenem or doripenem [6]. After 48 hours without fever, the therapy should be adapted to the antibiogram result and pass to oral administration. The duration of the treatment should be 2 weeks [4,6,27]. If there is no clinical improvement after 24 to 48 hours of parenteral antibiotic, it is necessary to perform a renal ultrasound and to collect a new sample for the urine culture, in order to exclude a pathology of the urinary tract or an infection with a resistant pathogen to the antimicrobial therapy [27].

## RISKS AND PROGNOSIS

Urinary tract infections if mismanaged increase the risk of systemic maternal infection and severe acute pyelonephritis. These maternal complications influence the evolution of the pregnancy and could result in af-

fecting the fetus as well by preterm birth, low birth weight, preeclampsia [16]. A positive urine culture for Group B Streptococcus should not be overlooked, as it is closely associated with fetal infection, premature rupture of membranes and going in labor before term [17]. Once identified this pathogen, peripartum antibiotic is required for preventing a neonatal infection [16,18]. Antibiotic treatment given in pregnancy for UTI is necessary and its administration has good prognostic value for the maternal and fetal outcome, reducing the prevalence of preterm labor and low birth weight infants [19,20,26].

## CONCLUSIONS

Special consideration should be given to urinary tract infections developed during pregnancy because they are related to serious fetal and maternal complications. Routine screening by urine culture, in each trimester, is recommended by the British and American societies of obstetrics and gynecology or by monthly urinary dipsticks according to the French society. Antibiotic

therapy is always required in the presence of a urinary tract infection, even though asymptomatic. The risks of leaving untreated a UTI are severe as in acute pyelonephritis, maternal septicemia, premature birth, low birth weight. The range of antibiotics used in pregnancy is limited and has to be concordant to the antibiogram result. The antimicrobial treatment should be individualized and should not neglect the aspect of increasing antimicrobial resistance. There are important emotional aspects that the future mother experience when discovering an ITU, regarding the well-being of the fetus and the perceived risks associated with the required antibiotherapy, that have to be taken in consideration by the medical personnel and adapt the case management properly. The importance of behavioral changes in the prophylaxis of urinary tract infections should not be overlooked and the future mother should be given appropriate advice. Future research should be focused on finding the actual mechanism of pathogenesis that link UTI and the complications they associate as preeclampsia, premature delivery and low birth weight.

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