

URINARY TRACT INFECTION IN PREGNANT WOMEN A LITERATURE REVIEW

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ABSTRACT

Urinary tract infection (UTI) is the second most common complication during pregnancy. Because it is seen as an urgent matter, the treatment of UTIs is often done in an empirical way, which may not always be efficient and provoke resistance from these bacteria. This study aims to collect information about urinary tract infection and its treatment. The articles included in the work were published between 2016 and 2019, totaling 25 files, which after being found were evaluated for their relevance to the work, using 18 works for the production of the study. This literature review reinforces the importance of early diagnosis of urinary tract infections in pregnant women. The treatment of this disease is another key point for the absence of complications with the mother and the fetus. Since not all antibiotics can be used in this period, and the sensitivity of microorganisms to some predilection drugs is low. Thus, the combination of early diagnosis with appropriate and immediate therapy is essential during pregnancy.

KEYWORDS: INFECTION, PREGNANT WOMAN, URINARY TRACT INFECTION.

INTRODUCTION

Urinary tract infection (UTI) is the second most common complication in the gestational period, with a prevalence of 20%, being only behind anemia.¹ It is associated with increased pre-delivery, low birth weight newborn, pre-eclampsia and perinatal death.²

These infections can be classified as asymptomatic or symptomatic, according to the presence or absence of signs, symptoms and complaints, even with a simple positive urine test (>10⁵ organisms/mL). Symptomatic UTIs include cystitis (lower urinary tract) or pyelonephritis (upper urinary tract).^{3,4}

The most common etiologic agent is the uropathogen *Escherichia coli*, followed by *Proteus mirabilis* (ranging from second to fifth place), *Klebsiella pneumoniae*, *Enterococcus* spp, *Staphylococcus saprophyticus* and *Streptococcus agalactiae*.³

The occurrence of urinary infections is more common in women, due to the shorter extension of the urethra and the greater proximity of the anus with the urethra and vaginal vestibule. In the gestational period there are anatomical, physiological and hormonal transformations that contribute to the occurrence of UTI by favoring bacterial proliferation, reducing the antibacterial activity of urine and the adhesion of strains to the urinary tract.⁴

During this period, urinary infections can cause several consequences for the mother and fetus, ranging from pre-

mature labor to perinatal death.²

Considering the frequency of UTI during pregnancy and its complications for the mother and fetus, treatment may require urgency, starting without confirmation by culture and antibiogram. However, this empirical treatment can further increase the prevalence of resistant strains, since not all antibiotics can be offered to this woman.⁵

In order for the antibiotic used to be more sensitive when the empirical treatment is performed, the prescriber must have knowledge of the main etiological agents and the antibiotic resistance profile. This monitoring must be periodic and regional, since it has been noticed the reduction of more employed antimicrobials.⁶

In Brazil, there are few studies on this topic, making it difficult to decide on an outpatient basis, thus resorting to international guidelines, which are inadequate for developing countries.⁶

Based on this need, the present study aims to conduct a literature review on urinary tract infection in pregnant women, the prevalence of etiologic agents, sensitivity to antibiotics and the use of norfloxacin in this period, since inadequate treatment can bring serious complications. .

METHODOLOGY

This research included scientific publications of national and international scope published between 2016 and 2019. The methodology adopted in this work was a biblio-

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graphic review, through search of articles and journals published in the database of SCIELO (Scientific Electronic Library Online), NCBI (National Center for Biotechnology Information) and LILACS (Latin American and Caribbean Literature) to survey and analyze what has already occurred about urinary tract infections in pregnant women.

The research topics were Urinary infection in pregnant women, urinary infection, treatment of urinary infection in pregnant women, microorganisms urinary infection in pregnant women, use of norfloxacin in pregnant women, norfloxacin and urinary infection in pregnant women and norfloxacin.

The search resulted in 25 files that after being found were evaluated for their relevance to the work, using 18 files for the production of the study.

LITERATURE REVISION

3.1. URINARY TRACT INFECTION IN PREGNANT WOMEN

Urinary tract infection (UTI) is more prevalent in women. During pregnancy it is the second most common complication, after anemia. In this period, the UTI has an estimated prevalence between 17 and 20%, according to the Ministry of Health, causing maternal and fetal complications.^{1; 5; 4}

Many pregnant women with UTI participate in high-risk prenatal care due to the maternal and fetal complications of this condition. High-risk pregnancy occurs when the pregnant woman has a socio-biological condition or disease, which impairs the evolution of the pregnancy and can lead to maternal death (COSTA et al, 2016).

In a study by Costa et al. (2016)⁷ 14.8% of the 61 pregnant women participated in high-risk prenatal care due to UTI. Of the pregnant women interviewed, 52.5% stated that they had previous chronic diseases or recurrent urinary infections.

This infection presents itself as a clinical syndrome of acute infection that occurs when enterobacteria colonize and replicate in the vagina and ascend to the urinary tract. They are classified as asymptomatic bacteriuria, acute urethral syndrome, prostatitis, cystitis, pyelonephritis and recurrent infections.^{1; 8; 4}

In the pregnancy period, the most common UTIs are asymptomatic bacteriuria, low urinary tract infection (cystitis), acute pyelonephritis and chronic pyelonephritis. In this period, it is important to note that urinary tract infection can cause several complications, such as premature labor, premature rupture of amniotic membranes, restriction of intrauterine growth, low birth weight newborns, premature delivery, pre-eclampsia and perinatal death, being responsible for 10% of hospitalizations during pregnancy.^{1; 2; 4}

Regarding the correlation between the incidence of UTI during pregnancy and an increased rate of prematurity Veiga et al. (2017)⁹ observed that of the 10.1% of pregnant women participating in the study who had UTI, 18.2% had premature delivery. Of these, 10.4% of babies were born with low weight and 33.3% were born while pregnant

women had a urinary tract infection.

The classification of asymptomatic bacteriuria is due to the absence of signs, symptoms and complaints of urinary infection by the patient, even with positive urine culture, thus considered when exceeding the limit of 100,000 units forming bacterial colonies per milliliter of urine (CFU/mL). It is found in 4 to 7% of pregnant women, and if not treated properly it can progress to pyelonephritis.^{2; 1; 5}

When urinalysis reports the presence of bacteriuria or pyuria, it is advisable to request urine culture with a test of sensitivity to antimicrobials in vitro, which will guide more effective therapy. Since bacterial resistance to antibiotics used frequently is increasing significantly.^{3; 10; 6}

Symptomatic infections are defined when the pregnant woman has complaints, having different symptoms according to the location of the infection. When the infection is in the lower urinary tract (cystitis) the most frequent symptoms are dysuria (difficult, painful and urgent urination) and pyuria (leukocytes). Pregnant women with upper urinary tract infections (pyelonephritis) commonly present with fever, chills, flank or lumbar pain, nausea and vomiting.⁵

Urinary tract infections are more common in women due to their shorter length of the urethra and the greater proximity of the anus to the urethra and vaginal vestibule. Other situations that make it more prevalent in women are previous cystitis, sexual intercourse, use of spermicidal jellies, pregnancy, diabetes, age over 35, multiparous women, malnutrition, anatomical abnormalities of the urinary system and poor hygiene.^{2; 4; 5}

These characteristics and the anatomical and physiological changes in the urinary system contribute to the occurrence of UTI in pregnant women. In which the changes of the period favor the bacterial proliferation, the reduction of the antibacterial activity of the urine and the adhesion of strains to the urinary tract.⁴

Changes related to favoring bacterial proliferation include pelvic and urinary tract dilation and increased uterine size, as it partially obstructs the ureter, creating conditions to stop urinary flow, reducing the amount of potassium excreted and increasing the excretion of glucose and amino acids, urine with alkaline pH and change of bladder position to abdominal, reduction of bladder tone and relaxation of bladder and ureter smooth muscles.^{11; 5}

The reduction in the antibacterial activity of the urine occurs due to the greater production of urine and lower concentration of it. While it is gestational hyperestrogenism that favors the adhesion of *Escherichia coli* strains carrying type 1 adhesins to uroepithelial cells.⁵

Another situation that increases the susceptibility to both urinary infection and other infections is immunological changes, since in this period the cellular immunity decreases.¹¹

The UTI during pregnancy, according to Ramos et al. (2016)⁴ occurs with a prevalence of 8.33% in the first trimester and increases to 14.58% and 15.47% in the second

and third trimesters, respectively. Of the 432 pregnant women participating in this study, 25.46% had UTI in at least one of the trimesters of pregnancy, 5.32% in two trimesters and 0.93% in the three trimesters.

3.2 MOST PREVALENT MICROORGANISMS IN URINARY INFECTIONS IN PREGNANT WOMEN

ard for the diagnosis of urinary tract infection, being considered positive (significant bacteriuria) when the bacterial count is greater than 100,000 colony-forming units per milliliter of urine (CFU/mL). When symptomatic bacteriuria, bacterial counts between 100 to 10,000 CFU/mL can represent a true bacterial infection.⁵

The most common etiologic agent is the uropathogen *Escherichia coli*, followed by *Proteus mirabilis* (ranging from second to fifth place), *Klebsiella pneumoniae*, *Enterococcus* spp, *Staphylococcus saprophyticus* and *Streptococcus agalactiae*.³

The bacterium *Escherichia coli* commonly found in UTI episodes has a frequency of 63-85% of cases, a result observed by Ramos et al. (2016) and Pigosso et al. (2016). In these studies, the *E. coli* bacterium was diagnosed with a frequency of 98.2% and 77.8%, respectively. This bacterium inhabits the intestinal tract where it leads to an innocuous existence, until it finds a favorable niche for its replication, where it can cause diseases, such as the urinary tract.^{12; 2}

Other bacteria are also identified in these infections, with variable prevalence between studies. In the study by Ramos et al. (2016)⁴ in addition to *E. Coli*, the bacteria *Klebsiella pneumoniae*, *Enterococcus faecalis* and *Staphylococcus saprophyticus* were identified with a frequency of 0.6%. In comparison, the study by Pigosso et al. (2016)¹³ also performed in Brazil, presented *Streptococcus agalactiae* and *Enterococcus faecalis*, both with 11.1%. In a study carried out in Colombia by Amador et al. (2016)¹ the prevalence was equal to 46.7% *E. coli*, 17.93% *E. coli* positive for β -lactamase of the extensive spectrum and 10.86% aeruginous *Pseudomonas*.

Siqueira et al. (2016)¹⁴ when evaluating the microorganisms that cause UTI in pregnant women in Mato Grosso, found a result similar to other studies. The bacterium *Escherichia coli* was diagnosed in 75% of the samples, while *Enterococcus faecalis* in 16.67% and *Streptococcus agalactiae* in 6.25% of the samples.

3.3 ANTIBIOTIC THERAPY IN URINARY INFECTIONS IN PREGNANT WOMEN

The pathogens that cause urinary infections have different patterns of sensitivity and resistance to antibiotics for each region. Due to the urgency of treatment when pregnant, it is empirically prescribed by the doctor. This practice contributes significantly to the increase in the prevalence of antibiotic resistant strains, reason that reinforces the importance of performing urine culture to support microbiological confirmation regarding the etiological agent

and its resistance pattern in addition to the importance of the health professional being updated on the topic and the possible antibiotics to be used.⁵

According to Oliveira (2016)¹⁰ the drugs recommended by the Ministry of Health (MS) during pregnancy are: amoxicillin, cephalexin nitrofurantoin and ampicillin. In research carried out by Muanda et al (2017)¹⁵ on the use of antibiotics during pregnancy and the risk of malformation, the relationship between amoxicillin, cephalosporin, nitrofurantoin and penicillin with fetal malformations was not observed, in concordance with what was published by the MS.

In contrast, there are recommendations made by the American College of Obstetricians and Gynecologists on the non-use of nitrofurantoin and sulfonamides in the first trimester of pregnancy, due to the potential risk of birth defects, such as anencephaly, heart defects and orofacial fissures.¹⁶

Oliveira et al. (2016)¹⁰ when performing the bacteria sensitivity test in relation to antibiotics commonly used in treatments during pregnancy, found low sensitivity of *E. coli* and *P. aeruginosa* in relation to penicillin (ampicillin and amoxicillin).

This sensitivity relationship has been observed in other studies. Ferreira et al. (2017)¹⁷ researched the resistance of *E.coli*, *Klebsiella sp* and *Proteus sp*, finding results of 49.7%, 84.3% and 58.1%, respectively. A similar result was found by Gomes et al. (2017)³, who found ampicillin resistance of 43%, 100% and 27%, of *E.coli*, *K. pneumoniae* and *Pseudomonas mirabilis* bacteria.

The tests carried out by Oliveira et al. (2016)¹⁰ showed as a result the good sensitivity of gram negative bacteria to nitrofurantoin, a result consistent with that found by Gomes et al. (2017)³ in relation to *E. coli* samples where 4% showed resistance, but it differs from the results of this study for *K. pneumoniae*, which presented 55% resistance to this antibiotic.

An antibiotic commonly used by doctors in the empirical treatment of urinary tract infections in non-pregnant adults is norfloxacin. According to Ferreira et al. (2017)¹⁷, 56.1% of the 57 doctors interviewed prescribe this medication as the first antimicrobial choice and 19.3% prescribe sulfamethoxazole with trimethoprim.

According to a document by the Health Surveillance Agency (ANVISA) containing information on the drug, it is in risk category C due to the absence of studies carried out in pregnant women. Therefore, the safety of this medicine has not been established for this group.

Previous studies have detected this antibiotic in the umbilical cord and in the amniotic fluid. Even without authorization for use in pregnant women, a study carried out in the United States in 2014, by Ailes et al. (2018)¹⁶ analyzed Truven's health database and found a total of 34.7% of pregnant women with UTI with norfloxacin prescriptions.

Despite the few studies that bring the use of norfloxacin by pregnant women when evaluating forums for pregnant women, as is the case of the forum <https://brasil>.

babycenter.com and <https://medicoresponde.com.br> there are questions from women in the pregnancy period who received a prescription for the drug and do not know if they should use it.

CONCLUSION

This literature review reinforces the importance of early diagnosis of urinary tract infections in pregnant women with urine and urine culture tests which are recommended since the first trimester of pregnancy, from which the treatment of this infection will be effective, avoiding possible maternal and fetal complications.

The concern of health professionals about this disease is expressed in the appropriate classification of this pregnancy, thus starting to assist pregnant women as high-risk prenatal care when necessary.

The treatment of this disease is another key point for the absence of complications with the mother and the fetus. Since not all antibiotics can be used in this period, and the sensitivity of microorganisms to some predilection drugs is low.

The reduced sensitivity for some antibiotics is related to the excessive, uncontrolled and inappropriate use of these drugs, impacting the increase in microbial resistance. Therefore the appropriate choice of medication implies in reducing maternal and fetal complications of these infections.

Thus, the combination of early diagnosis with appropriate and immediate therapy is essential during pregnancy.

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