

Etiological and susceptibility profile of microorganisms causing urinary tract infection in pregnant women in the city of Palmas, Brazil

Perfil etiológico e de susceptibilidade de microrganismos causadores de infecção do trato urinário em gestantes no município de Palmas, Brasil

Perfil etiológico y de susceptibilidad de los microorganismos causantes de infección del tracto urinario en mujeres embarazadas en la ciudad de Palmas, Brasil

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Abstract

Urinary tract infections (UTIs) are inflammatory pathologies resulting from the multiplication of microorganisms in the urinary tract. The risk group includes pregnant women, due to physiological changes caused by pregnancy, and such conditions are related to a greater risk of maternal-fetal complications. Treatment is based on the most likely etiology and should consider microbial sensitivity to antimicrobials, given the increasing emergence of resistance. Given the need to monitor the pathogenic epidemiology and its susceptibility, the study aims to determine the etiological and susceptibility profile of the microorganisms that cause UTI in pregnant women in the city of Palmas, Brazil. This is a descriptive observational study, based on the exploration of data made available by the clinical analysis laboratory of the Dona Regina Hospital and Maternity, located in Palmas. Urine culture and antibiogram results of pregnant women attended over a 12-month period (July/2021 - June/2022) were evaluated. The project was registered on Plataforma Brasil, for appreciation and analysis by the CEP/UFT, thus being adequate to the current regulations. It was found that the etiology of infections was predominantly associated with *Escherichia coli* (34.75%) and *Enterococcus faecalis* (23.73%). The drugs with the highest resistance rate were ampicillin (53.47%) and sulfamethoxazole with trimethoprim (41.56%); nitrofurantoin had the lowest rate (3.39%). It is concluded that the etiological profile corresponds to bacteria colonizing the gastrointestinal tract, which have some degree of resistance, especially to ampicillin, and have considerable sensitivity to nitrofurantoin.

Keywords: Urinary tract infections; Pregnant women; Anti-Infective agents.

Resumo

As infecções do trato urinário (ITUs) são patologias inflamatórias consequentes à multiplicação de microrganismos na via urinária. O grupo de risco inclui gestantes, devido a alterações fisiológicas ocasionadas pela gravidez, sendo que tais afecções estão relacionadas a maior risco de complicações materno-fetais. O tratamento baseia-se na etiologia mais provável e deve considerar a sensibilidade microbiana aos antimicrobianos, dado o crescente surgimento de resistência. Haja vista a necessidade de monitorar a epidemiologia patogênica e sua susceptibilidade, o estudo visa determinar o perfil etiológico e de susceptibilidade dos microrganismos causadores de ITU em gestantes no município de Palmas – TO. Trata-se de um estudo observacional descritivo, baseado na exploração de dados disponibilizados pelo laboratório de análises clínicas do Hospital e Maternidade Dona Regina, localizado em Palmas – TO. Foram avaliados resultados de urocultura e antibiograma de gestantes atendidas no período de 12 meses (julho/2021 - junho/2022). O projeto foi cadastrado na Plataforma Brasil, para apreciação e análise do CEP/UFT, sendo assim adequado às normas vigentes. Constatou-se que a etiologia das infecções estava associada predominantemente a

Escherichia coli (34,75%) e *Enterococcus faecalis* (23,73%). As drogas com maior índice de resistência foram ampicilina (53,47%) e sulfametoxazol com trimetoprim (41,56%); nitrofurantoína teve a menor taxa (3,39%). Conclui-se que o perfil etiológico corresponde a bactérias colonizadoras do trato gastrointestinal, as quais possuem algum grau de resistência, sobretudo a ampicilina, e têm sensibilidade considerável a nitrofurantoína.

Palavras-chave: Infecções do trato urinário; Gestantes; Antimicrobianos.

Resumen

Las infecciones en el tracto urinario (ITU) son patologías inflamatorias consecuentes a la multiplicación de microorganismos en la vía urinaria. El grupo de riesgo incluye gestantes, debido a alteraciones fisiológicas causadas por el embarazo, y tales afecciones están relacionadas con un mayor riesgo de complicaciones materno-fetales. El tratamiento se fundamenta en la etiología más probable y debe considerar la sensibilidad microbiana a los antimicrobianos, considerando el crecente surgimiento de la resistencia. Debido a la necesidad de monitorizar la epidemiología patogénica y su susceptibilidad, el estudio visa a determinar el perfil etiológico y de susceptibilidad de los microorganismos causadores de ITU en gestantes en la ciudad de Palmas – TO. Se trata de un estudio observacional descriptivo, basado en los datos puestos a disposición por el laboratorio de análisis clínicas del Hospital y Maternidad de Dona Regina, en Palmas – TO. Fueron evaluados resultados de urocultivo y antibiograma de gestantes atendidas en el período de 12 meses (julio/2021 – junio/2022). El proyecto fue registrado en la Plataforma Brasil para la evaluación y análisis del CEP/UFT, adecuándose a las normas vigentes. Se constató que la etiología de las infecciones era asociada predominantemente a *Escherichia coli* (34,75%) e *Enterococcus faecalis* (23,73%). Las drogas con mayor índice de resistencia fueron ampicilina (53,47%) y sulfametoxazol con trimetoprim (41,56%); nitrofurantoína tuvo la menor tasa (3,39%). Se concluye que el perfil etiológico corresponde a bacterias colonizadoras del tracto gastrointestinal, las cuales poseen algún grado de resistencia, sobretudo a ampicilina y tienen sensibilidad considerable a nitrofurantoína.

Palabras clave: Infecciones del tracto urinario; Gestantes; Antimicrobianos.

1. Introduction

Urinary tract infections (UTIs) correspond to an inflammatory process resulting from the invasion and consequent multiplication of microorganisms in the urinary tract (Durán Chávez et al., 2018; Oliveira et al., 2021). The clinical spectrum generated is broad and comprises acute, recurrent, and chronic infections, as well as asymptomatic bacteriuria (Asadi Karam et al., 2019), which may or may not present with dysuria, frequency, irritability, chills, and fever (Geerlings, 2016). UTIs, therefore, are among the most common causes of infectious diseases, second only to those of a respiratory nature, and constitute an important public health problem, due to their high prevalence and high economic cost (Alviz-Amador et al., 2018).

The risk group, in turn, is composed of multiple populations and includes pregnant women, due to physiological changes caused by pregnancy (Oliveira et al., 2021). The combination of factors, such as suppression of the immune system and changes in the urinary tract, which determine stasis and vesicoureteral reflux, compromise pregnant women and add to the proliferation of uropathogens (Belete & Saravanan, 2020). An aggravating factor is that such conditions are related to a higher risk of maternal-fetal complications, such as preeclampsia, maternal anemia, abortion, and premature birth, with a high rate of perinatal morbidity and mortality. This justifies the need for screening by urine culture in the aforementioned contingent (Ndamason et al., 2019).

In pregnant women, as in other populations, UTIs are mainly caused by germs from the perineal region, with *Escherichia coli* representing the absolute majority of cases, both symptomatic and asymptomatic (Campo-Urbina et al., 2017). The common agents related to these infections are *Klebsiella pneumoniae*, *Proteus mirabilis*, *Citrobacter* spp, *Enterobacter* spp, *Pseudomonas aeruginosa*, and gram-positive *Staphylococcus* spp, *Streptococcus* sp, enterococci and eventually *Candida albicans* fungi (Kot, 2019).

Treatment must consider the susceptibility of microorganisms to drug therapy, given the increasingly expressive emergence of resistant pathogens. In this context, the importance of urine culture and antibiogram results are highlighted, which denounce the sensitivity of the isolated pathogen to each antimicrobial, thus directing the choice of the correct drug for effective therapy (Miranda et al., 2019). This is a fundamental issue, especially in developing countries, such as Brazil, where

the abusive use of antimicrobials, lack of therapeutic adherence, poor preventive practices, and inadequate control over the sale of medicines are common (Nigussie & Amsalu, 2017).

Indeed, given the complexity of the aspects associated with UTIs, continuous and periodic monitoring of the epidemiology of the main causative germs and their sensitivity to the most frequently prescribed drugs is necessary (Woldemariam et al., 2019). Such surveillance makes it possible to prevent complications and, therefore, reduce death rates, especially in vulnerable populations, such as pregnant women.

Therefore, considering the scarcity of research on UTI in the city of Palmas, above all concerning pregnant women, the present research aims to determine the etiological and susceptibility profile of the microorganisms that cause UTI in pregnant women in Palmas. Thus, the paper aims to contribute to the optimization of therapeutic measures, preventing the production of resistance and reducing public spending resulting from this pathology.

2. Methodology

This is a descriptive observational study carried out in the city of Palmas, state of Tocantins, Brazil. Secondary data regarding the results of urine cultures and antibiograms were collected from the hospital's clinical laboratory database in order to verify the prevalence of pathogens and their resistance profile (Estrela, 2018). The sample included is that of pregnant women treated at the Dona Regina Hospital and Maternity (HMDR). Data were collected in the hospital's clinical analysis laboratory. The laboratory collected urine samples with medical orders and performed the analysis by culture and antibiogram.

All cultures requested in the HMDR from July 1, 2021, to June 30, 2022, were verified. The inclusion criteria were positive results of urine cultures from pregnant patients, aged 18 to 35 years. According to the exclusion criteria, results indicative of probable contamination were discarded, as well as analyzes that were not completed due to errors in the system or the processing of the sample.

The choice of drugs to be tested for each agent was determined following NCCLS standards. The proposed investigation only determined the outcome of susceptibility to class B, C, and D antimicrobials recommended for the treatment of UTI during pregnancy, according to the guideline of the Brazilian Federation of Gynecology and Obstetrics Associations (Febrasgo, 2018). Namely: amoxicillin with clavulanate, ampicillin, cefuroxime, nitrofurantoin, gentamicin, sulfamethoxazole with trimethoprim, ciprofloxacin, and chloramphenicol. Cephalexin and norfloxacin are not included in the laboratory tests, so they are absent from the study.

The project was registered on Plataforma Brasil, for consideration and analysis by the CEP/UFT, under CNS Resolution No. 466/12 in line with the Tocantins State Department of Health and was approved with CAAE: 48416621.0.0000.5519.

3. Results and Discussion

Several bacterial species of variable resistance have been identified as causative agents of urinary tract infections in pregnant women - a group vulnerable to this type of infection. Therefore, the research is important to qualitatively delineate the prevalence of strains present in this population and the resistance profile, to outline strategies.

During the period considered, 862 urine cultures and antibiogram analyzes were requested for pregnant women treated at the HMDR. Of the total results, 218 were excluded, as the patients did not meet the stipulated exclusion criteria.

Urine culture and antibiogram are essential to verify strain profiles and their susceptibility to antimicrobials. Therefore, it is essential that such tests are requested for all pregnant women, even with the need for initial empirical treatment, to verify the resistance profile of the identified species (Matuszkiewicz-Rowińska et al., 2015).

Thus, 584 results were included in the study - 118 (20.48%) with isolation of microorganisms and 466 (79.52%) with

no biological growth. July/2021 was the month with the highest incidence (47.05%); October/2021, on the other hand, presented the lowest (6.06%). Regarding the prevalence, December was the month with the highest number of positive urine cultures, adding up to 25 results (13.29%).

The most isolated pathogens were *Escherichia coli* and *Enterococcus faecalis*, totaling 41 (34.75%) and 28 (23.73%) cases, respectively (Table 1). Other agents found were: *Citrobacter* sp; *Klebsiella pneumoniae*; *Salmonella enterica*; *Pseudomonas* sp.; *Proteus mirabilis*; *Acinetobacter baumannii* complex; *Enterobacter* sp.; *Kluyvera ascorbata*; *Yokenella regensburgei*; *Hafnia alvei* and *Candida* sp.

Table 1 - Microorganisms isolated in urine culture of pregnant women at the Dona Regina Hospital and Maternity in the city of Palmas. AF - Absolute frequency, RF - Relative frequency.

Pathogen	AF	RF
<i>Escherichia coli</i>	41	34,74%
<i>Enterococcus</i> sp.	28	24,56%
<i>Citrobacter</i> sp.	12	10,16%
<i>Klebsiella pneumoniae</i>	10	8,47%
<i>Candida</i> sp.	9	7,62%
<i>Salmonella enterica</i>	5	4,23%
<i>Pseudomonas</i> sp.	3	2,54%
<i>Proteus mirabilis</i>	2	1,69%
<i>Acinetobacter baumannii</i> complex	2	1,69%
<i>Enterobacter aerogenes</i>	2	1,69%
<i>Kluyvera ascorbata</i>	1	0,84%
<i>Yokenella regensburgei</i>	1	0,84%
<i>Hafnia alvei</i>	1	0,84%
Total	118	100%

The most isolated pathogens were *Escherichia coli* and *Enterococcus faecalis*, totaling together almost 60% of the cases. Source: Authors.

Regarding susceptibility to the antibiotics tested, the class B drug with the highest resistance rate was ampicillin (53.47%), followed by amoxicillin with clavulanate (29.11%) (Table 2). Nitrofurantoin, on the other hand, had the lowest rate (3.39%), both among class B and class C/D drugs. In the case of the latter, in turn, sulfamethoxazole with trimethoprim (41.56%) and ciprofloxacin (16.33%) were the antimicrobials with the highest resistance rates (Table 3).

Table 2 - Susceptibility to Class B drugs in antibiograms of pregnant women at the Dona Regina Hospital and Maternity in the city of Palmas.

	AMOXICILLIN / CLAVULANATE	AMPICILLIN	CEFUROXIME	NITROFURANTOIN
NOT TESTED	39	17	74	59
TESTED	79	101	44	59
SENSITIVE	56 (70,89%)	47 (46,53%)	24 (54,55%)	56 (94,92%)
RESISTANT	23 (29,11%)	54 (53,47%)	9 (20,45%)	2 (3,39%)
SENSITIVE, INCREASING EXPOSURE	0	0	11 (25%)	1 (1,69%)

Regarding class B drugs, ampicillin was the drug with the highest resistance rate (53,47%); nitrofurantoin had the lowest (3,39%). Source: Authors.

Table 3 - Susceptibility to Class C/D drugs in antibiograms of pregnant women at the Dona Regina Hospital and Maternity in the city of Palmas.

	GENTAMICIN	SULFAMETHOXAZOLE / TRIMETHOPRIM	CIPROFLOXACIN	CHLORAMPHENIC OL
NOT TESTED	43	41	20	48
TESTED	75	77	98	70
SENSITIVE	64 (85,33%)	41 (53,25%)	76 (77,55%)	63 (90%)
RESISTANT	6 (8%)	32 (41,56%)	16 (16,33%)	7
SENSITIVE, INCREASING EXPOSURE	5 (6,67%)	4 (5,19%)	6 (6,12%)	0

Regarding class C/D drugs, sulfamethoxazole with trimethoprim was the drug with the highest resistance rate (41,56%), followed ciprofloxacin (16,33%). Source: Authors.

Pregnant women are part of the group of patients at higher risk of developing urinary tract infections, both because of their female anatomical condition and because of physiological changes that occur during pregnancy. In this context, the pathology is also more serious, since it is associated with a considerable rate of maternal and fetal complications (Silva et al., 2021).

In the present study, urine cultures were positive in 20.48% of the tests. It was found that the etiology of urinary infections was predominantly associated with *Escherichia coli* and *Enterococcus faecalis*. The aforementioned etiological agents follow the pattern observed in the already established literature (Ramos et al., 2016; Pagnonceli & Colacite, 2016; Pigosso et al. 2016). This occurs as a consequence of the anatomy of the human organism, which favors the microbiota of the digestive tract in the pathogenesis of UTIs, mainly due to its proximity to the urinary tract (Arruda et al., 2021). Other microorganisms isolated were *Klebsiella pneumoniae*, *Citrobacter* sp., and *Proteus mirabilis*, which are also colonizing bacteria of the gastrointestinal tract.

Escherichia coli are gram-negative bacilli of the *Enterobacteriaceae* family. Most strains are non-pathogenic; but some acquire invasive or enterotoxin-encoding factors, becoming virulent (Makvana & Krilov, 2015). These strains are the main causes of uncomplicated UTI, followed by *Proteus* spp., *Klebsiella* spp., and other *Enterobacteriaceae*. Lower virulence

pathogens such as *Enterococcus* spp. and *Candida* spp. are often more prominent in patients with underlying complicating factors such as diabetes, spinal cord injury, and other comorbidities.

As for the action of the evaluated drugs, there was lower sensitivity to ampicillin (46.53%). In the literature, the association of this pharmacological susceptibility to the frequent choice of this antimicrobial for the prophylaxis and therapy of UTIs in the country is widely discussed (Pigosso et al., 2016). The same applies to the combination of sulfamethoxazole and trimethoprim, which also showed a significant resistance rate (41.56%). It is ratified, therefore, that the indiscriminate use of antimicrobials promotes increased resistance, difficulty in treatment, increased hospitalization costs, and contributes to greater severity of infections.

Overall, pathogens isolated in urine samples were more susceptible to nitrofurantoin (96.61%). In comparison, amoxicillin with clavulanate and cefuroxime - also recommended as first-line treatment for UTIs in pregnant women - showed 29.11% and 20.45% resistance rates, respectively. Thus, the choice of this nitrofuran may be increasingly preferred over the prescription of other class B drugs, as has also been suggested in recent research (Adeep et al., 2022; Hateet, 2022).

All pregnant women diagnosed with UTI should be treated, even if they are asymptomatic, given the risk of maternal and fetal complications and sequelae if therapy is not instituted. Some of the most frequent developments are preeclampsia, intrauterine growth restriction, preterm labor, premature rupture of membranes, low birth weight, and neonatal systemic infection (Szweda & Jóúwik, 2016). Recent studies have also identified other less common associations of UTI in pregnant women with maternal and fetal anemia, chorioamnionitis, developmental delay, mental retardation, childhood epilepsy, and even attention deficit hyperactivity disorder (Kalinderi et al., 2018).

The antibiogram guides the choice of the drug indicated for the treatment. However, while there are several options between classes of antibiotics, the use of any medication during pregnancy is a risk-versus-benefit decision. In addition to maternal and fetal safety, there are physiological changes during pregnancy that can lead to pharmacokinetic changes and impact antibiotic therapy (Jin, 2022). Due to the risk of significant complications in case of non-treatment of infections, drug therapy is always performed, giving preference to class B antibiotics whenever possible, since they did not demonstrate a risk to the fetus in pharmaceutical studies, unlike those of class C/D (Bookstaver et al., 2015).

The study found limitations regarding the collection of more epidemiological variables. At first, a questionnaire was designed to collect information from the patients about clinical, socio-cultural, and economic data. However, there was no adherence from pregnant women to fill out the investigative form. Furthermore, the difficulty of establishing partnerships with other public and private health units, whether in primary, secondary, or tertiary care, also prevented the research from covering a larger population contingent.

4. Conclusion

In this work, became evident the etiological and susceptibility profile of the microorganisms that cause UTI in pregnant women in the city of Palmas as well as the need to seek prevention strategies, continuing education for professionals, and information for pregnant women. The identified profile corresponds to colonizing bacteria from the gastrointestinal tract, which, in general, have some degree of resistance, especially to ampicillin, and have considerable sensitivity to nitrofurantoin - which can be proposed as the first choice in the treatment of UTIs in pregnant women, the public covered in the studies. Furthermore, the high number of positive results of urine culture and resistance of microorganisms to antimicrobials indicated in therapy is alarming and reinforces the need for screening in this population, especially in Primary Care, as well as emphasizes the importance of the rational use of antibiotic therapies. In the meantime, other studies in Primary Care, to track community infections and compare them with hospital infections, would add to the understanding of the incidence of the pathology on an outpatient basis.

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