INFECÇÕES URINÁRIAS EM PACIENTES AMBULATORIAIS: PERFIL MICROBIOLÓGICO E RESISTÊNCIA ANTIMICROBIANA

Urinary infection in outpatients: microbiological profile and drug resistance

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Abstract: The urinary tract infection (UTI) is one of the most common infections and the second most prevalent bacterial infection in the population. The study aimed to determine the prevalence of UTI in outpatients, its etiology and to characterize the profile of antimicrobial resistance. A retrospective and cross-sectional study of the requested urocultures was performed in the clinical analysis laboratory of the Center for Health Care and Professional Practices in Montes Claros/MG, from January to December 2018. The microbiological analysis followed the recommendations of the National Sanitary Surveillance Agency and the Clinical and Laboratory Standards Institute. Of the 153 analyzed urine cultures, 38 (24.8%) showed positive results for UTI. Among the positive, 94.7% patients were female, and aged 41-64 years (44.7%). The most frequent etiological agent was *E. coli* (68.4%), followed by *Enterobacter* sp. (13.2%) and *Staphylococcus* sp (7.9%). High resistance rate of *E. coli* was identified for some antibiotics of choice for the treatment of UTI such as tetracycline (54.54%), nalidixic acid (52.17%), cephalexin (50%), ampicillin 45,45%), sulfazothrin (42.1%) and ciprofloxacin (31.8%). The highest resistance indices for both *E. coli* and other agents were attributed to ampicillin and tetracycline. Conclusion: These data demonstrate the need to know the reality of each region, contributing to the safe and effective empirical antibiotic choice, when it is not possible to perform antimicrobial susceptibility culture and test, as well as to reduce morbimortality, costs and the development of multiresistance bacterial.

Keywords: Urinary tract infection; *Escherichia coli*; Antibiotics.

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Resumo: A infecção do trato urinário (ITU) é uma das infecções mais frequentes e a segunda infecção de origem bacteriana mais comum na população. **Objetivos:** Determinar a prevalência de ITU em pacientes ambulatoriais, sua etiologia e caracterizar o perfil de resistência aos antimicrobianos. **Metodologia:** Realizou-se estudo retrospectivo e transversal das uroculturas solicitadas no laboratório de análises clínicas de uma clínica escola da cidade de Montes Claros/MG, no período de janeiro a dezembro de 2017. **Resultados:** Foram avaliadas 153 uroculturas, das quais 38 (24,8%) eram positivas, com predomínio do sexo feminino (94,7%) e com idade entre 41 e 64 anos (44,7%). O agente etiológico mais frequente foi *E. coli* (68,4%), seguido por *Enterobacter* sp. (13,2%) e *Staphylococcus* sp (7,9%). Identificou-se alta taxa de resistência de *E. coli* a alguns antibióticos de escolha para o tratamento da ITU, como tetraciclina (54,54%), ácido nalidíxico (52,17%), cefalexina (50%), ampicilina (45,45%), sulfazotrin (42,1%) e ciprofloxacina (31,8%). Os maiores índices de resistência, tanto para *E. coli* quanto para os demais agentes, foram atribuídos a ampicilina e tetraciclina. **Conclusão:** Esses dados demonstram a necessidade de conhecer a realidade de cada região, contribuindo para a escolha antibiótica empírica segura e eficaz, quando não é possível realizar cultura e teste de susceptibilidade antimicrobiana, além de diminuir a morbimortalidade, os custos e o desenvolvimento de multirresistência bacteriana.

Palavras-chave: Infecção do Trato Urinário; *Escherichia coli*; Antimicrobianos.

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INTRODUCTION

The urinary tract infection (UTI) is characterized by the presence of micro-organisms, mainly bacteria, and the tissue invasion in any structure of the urinary tract (urine, bladder, kidneys), and may lead to serious complications[1].

ITU is the third infection most commonly found in the population, with an overall annual incidence estimated at 250 million in developing countries[2]. It occurs in both sexes and all ages, producing considerable morbidity mainly among individuals prone to recurrent infections. ITU's in men occur in extreme age (infants and the elderly), while among women, the number of cases increases with age. Studies show that at least 5% of women, 5 to 18 years have already had a UTI. The risk factors for UTI in women varies according to the patient's age. In school age girls, the most common ones are congenital abnormalities followed by the beginning of sexual life, in which nephrogenic bacteria migrate to the periurethral area causing ITU[3]. In menopausal women, the risk factors are vaginal atrophy, hypoestrogenism, incomplete emptying of the bladder, inadequate perineal hygiene, among others[4].

Approximately 50% or more of the women have at least one episode of ITU during their lives[5]. With high costs to society, the direct costs include outpatient medical consultations, diagnosis, use of antimicrobials and expenses with hospitalization, as well as the costs associated with lost time from work and morbidity[6]. It is estimated that 3.6 million episodes of acute cystitis occur annually in the USA with a cost of US$1.6 billion[7].

Women are more vulnerable than men to occurrence of urinary tract infection. Studies show that women have 50 times more chances of acquiring UTI than men and 30% of women present symptomatic ITU throughout life. The ascendant path is the main route of infection of the urinary tract, for this reason, the high prevalence in females is related to a shorter anatomic extension of the female urethra and the greater proximity

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between the vagina and anus, characteristic of the female genitalia[8].

The etiology of ITUs and the resistance pattern of isolated pathogens of that site, has been undergoing changes with the passing of time and vary according to certain regions. These changes have a direct influence on the main standardized therapy, the so-called empirical treatment[1].

The diagnosis of UTI is determined by the appearance of bacteria in the urine and have as minimum limit the existence of 100,000 bacterial colony-forming units per milliliter of urine (CFU/mL). In the absence of symptoms, the infection is called asymptomatic bacteriuria. ITU can be classified as low (cystitis) or high (pyelonephritis)[9].

Urinary tract infection can affect patients without structural anomalies that interfere with the flow of urine, and complicated when it occurs with lesions in the urinary tract or with systemic diseases. The Gram-negative bacteria are the most frequent and due to genetic plasticity, these micro-organisms propagate and easily acquire resistance to antimicrobial agents[10].

Among the clinical occurrences, the most prevalent are the cystitis, whose most common complaints are the increase of trips to the bathroom, dysuria, urinary urgency, suprapubic pain, hematuria and fetid odor in the urine. Pyelonephritis, however, is a systemic infection, with the presence of fever and lumbar pain. Constant pains and changes in urine are historical assessments for signs and symptoms related to urinary tract infection[11.12].

The most frequently involved etiologic agents with ITU are in order of frequency: *Escherichia coli, Staphylococcus saprophyticus*, species of *Proteus* of *Klebsiella* and *Enterococcus faecalis*. *E. coli*, alone, is responsible for 70% to 85% of infections of the urinary tract and by 50% to 60% in elderly patients admitted in institutions. However, when the ITU is acquired in the hospital, in hospitalized patients, the etiologic agents are diverse, predominating the enterobacteria, with reduction in the frequency of *E. coli* (although still remains usually as the first cause), and a growth of *Proteus sp*, *Pseudomonas aeruginosa*, *Klebsiella sp*., *Enterobacter sp*., *Enterococcus faecalis* and fungi, especially *Candida sp*[10].

The diagnosis of urinary UTI involves clinical and laboratory findings, but it is not always easy. Laboratory tests increase the accuracy of diagnosis, identifying the cause of

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the infection and the profile of sensitivity/resistance of bacterial agent to antimicrobial agents. Initially, urine examination is requested (Urine type I) which, in the majority of cases, confirms the diagnosis. The urine culture (from medium urine jet plane and aseptically harvested) is required to identify the agent determinant of infection, and the antibiogram distinguishes the susceptibility to antibiotics[12].

The ITU treatment is performed with antimicrobial agents, chosen preferably after the results of urine culture and antibiogram. The antibiotic of choice for ITU should obey the variables as: presentation of infection (cystitis and pyelonephritis, community, hospital, complicated or uncomplicated), host (children, adults, pregnant women or elderly) and agent (Gram positive and Gram negative). Strategies involving different regimens in accordance with specific groups of patients maximizes the therapeutic benefits, in addition to reducing costs, the incidence of adverse effects and the emergence of resistant microorganisms[10].

The urinary infection is especially a community growing problem of great prominence in our environment and its management is usually empirical, based on the foreseeable spectrum of the etiological agents and their patterns of susceptibility[12]. Due to the emergence of antimicrobial resistance among the uropathogens, the effectiveness of empirical therapy was affected[3]. In Montes Claros MG the antimicrobial susceptibility among pathogens involved in infections of the urinary tract is poorly investigated. Therefore, it is important to obtain information about the rates of antimicrobial resistance site to provide suitable treatment to community infections. In this study, we investigated the microbiological profile and patterns of antimicrobial susceptibility of isolates of urine culture among outpatients treated by clinical analysis laboratory of a clinic school of the city of Montes Claros - MG.

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METHODOLOGY

The research was performed at the Center of Attention to Health and Professional Practices (NASPP) in the period from January to December of 2017, through a documentary history research based on laboratory reports of the sector of the Microbiology Laboratory of Clinical Analysis (LAC) of NASPP. The inclusion criteria were those patients of both genders, without limit of age, skin color and social class. Patients whose reports were not available were excluded. Only the data that are indispensable to the study were collected from medical records and transcribed to an individual form developed specifically for this research analysis.

Microbiological analyzes were performed according to the Standard Operating Procedure (POP) from the laboratory of NASPP. The samples were seeded by the method of calibrated loop, quantitative culture, in which a volume of 0.01 mL (10 μL) was sown in CLED Agar (Cystine Lactose-Electrolyte-Deficíent) and MacConkey agar, incubation in a bacteriological greenhouse at a temperature of 35ºC ±

1°C for 24-48 hours. When necessary, bacteria screen was also performed for Gram staining. In the period studied all urine cultures performed in LACb were analyzed , adopting as the criterion of positivity to count colonies of the same type, in a number equal to or greater than 10^5 CFU/mL of urine. The colonies were identified according to the observed characteristics of morphology, type of wall and appropriate biochemical series. The qualitative method of disk diffusion (Kirby-Bauer technique) was used for analysis of antimicrobial susceptibility.

The quantitative variables were subjected to a statistical analysis on the basis of epidemiological investigation through the construction of tables, graphs and frequencies, using the program *Statistical Package for Social Science* (SPSS®), version 20.0 for Windows®. Discrete variables were expressed as frequencies and percentages.

The research followed the Resolution 466/2012 of the Ministry of Health and was approved by the Committee for Ethics in Research with

the opinion o number 2.449.563.

RESULTS

During the period from January to December 2017, 153 urine cultures were performed in the Laboratory of Clinical Analysis. Among these a total of 38 urine cultures (24.8%) presented a positive result (score $\geq$ 105 CFU/mL). Of the positive samples, 36 (94.7%) were female and 2 (5.3%) of the male sex.

Women are more susceptible to Bacteriuria by several factors, among them we can include the presence of anatomical and functional changes of bladder related or not to multiparity, active sexual life, menopause and recurrent infections that end up increasing the incidence of ITU[12]. The length of the urethra and its location near the anal opening, facilitating, thus, the ascension of enterobacteria are factors that may also be involved in Bacteriuria[12]0.

The indexes of positivity of urine cultures vary greatly according to the region. In our study, the positivity rate was 24.8%. This is similar to other studies performed in Brazil[14, 15.16].

Among women, the most prevalent age group was 41 to 64 years (44.7%), already in men, age above 65 years (5.2%), which can be observed in table 1. This proves that the increase of age is related to the decrease of body defenses against the colonization by pathogens. Thus, aging is directly associated with the increase of urinary tract infections in both men and women[12].

The prostatic disease in the elderly man is a factor that correlates with ITU. In addition, the urethral stricture and other anatomic abnormalities are also relate

Table 1. Percentage distribution of urine cultures positive for the different age groups and sex.

Sex		Age range		
Percentage (n)	**1-13 years**	**14-40 years**	**41-64 years**	**$\geq$ 65 years**

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Female	5.2 (2):	23.7 (9):	44.7 (17):	21.2 (8):
Male				5.2 % (2)

Of the bacterial isolate agents in this study (Table 2), the gram-negative *E. coli* (68.4%) and *Enterobacter* sp. (13.2%) stood out. Still in the group of Gram-negative bacteria, *Ewardsiella* sp was isolated. (2.6%), *Klebsiella* sp. (2.6%) and *Gardnerella vaginallis* (2.6%). These data corroborate with other published epidemiological data in studies with the same profile of objectives[15,16,17]. *E. coli* is the main etiological agent involved in infections of the urinary tract, being responsible for up to 90% of cases[2]. This fact is related to the presence of bacteria in the intestinal microbiota and eventually can cause extra-intestine infections. Unlike another study in which the second isolate reported was *K. pneumoniae*[3], in this study was *Enterobacter* sp., followed by *Staphylococcus* sp. (7.9%).

The Gram-positive bacteria, in our study, corresponded to 10.5% of the identifications. Among these bacteria, *Staphylococcus* sp. was the most prevalent agent (7.9%) occupying the third place among the pathogens most isolated in the ITUs. *Streptococcus* sp. was responsible for 2.6% of the positive urine cultures. Similar results were observed in similar studies[16.17].

Infecções Urinárias Em Pacientes Ambulatoriais:
Perfil Microbiológico e Resistência
Antimicrobiana

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**Table 2. Prevalence of etiologic agents causing UTI
in patients treated in LAC in the period from
January to December 2017.**

Micro-organism.	**Number of isolates (%)**
Escherichia coli	26 (68.4):
Enterobacter sp.	5 (13.2):
Staphylococcus sp.	3 (7.9):
Edwardsiella sp.	1 (2.6):
Klebsiella sp.	1 (2.6):
Gardnerella vaginallis	1 (2.6):
Streptococcus sp.	1 (2.6):
Total	100% (n = 38)

The resistance of isolated bacteria to antimicrobial agents is shown in table 3.

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Table 3. Profile of in vitro susceptibility to antimicrobial agents of the main bacteria isolated in patients with ITU met in LAC, in the period from January to December 2017.

Antimicrobial agent		*E. coli*	*Enterobacter* sp.	*Staphylococcus* sp.	*Gardnerella vaginalis*	*Klebsiella* sp.	*Edwarsiela* sp.
Amoxicillin + clavulanic acid	Sensitive	68%	66.66%	100%	-	100%	100%
	Resistant	32%	33.33%	-	100%	-	-
Cephalexin	Sensitive	50%	*	*	*	100%	*
	Resistant	50%	*	*	*	-	*
Ceftriaxone	Sensitive	87.5%	66.66%	50%	-	*	100%
	Resistant	12.5%	33.33%	50%	100%	*	-
Ciprofloxacin	Sensitive	68.1%	75%	-	*	*	100%
	Resistant	31.8%	25%	100%	100%	*	-
Nitrofurantoin	Sensitive	87.5%	20%	50%	*	100%	100%
	Resistant	12.5%	80%	50%	*	-	-
Norfloxacin	Sensitive	80.76%	75%	33.33%	-	100%	100%
	Resistant	19.2%	75%	66.66%	100%	-	-
Sulfazotrin	Sensitive	57.9%	100%	50%	*	*	100%
	Resistant	42.1%	-	50%	*	*	-
Nalidixic Acid	Sensitive	47.82%	75%	-	100%	*	100%
	Resistant	52.17%	25%	100%	-	*	-
Amikacin	Sensitive	90.9%	100%	100%	*	*	100%
	Resistant	9.1%	-	-	*	*	-
Ampicillin	Sensitive	54.54%	75%	-	*	*	100%
	Resistant	45.45%	75%	100%	*	*	-
Cefazolin	Sensitive	85%	75%	100%	*	*	100%
	Resistant	15%	75%	-	*	*	-
Gentamicin	Sensitive	77.27	100%	100%	*	*	100%
	Resistant	22.72	-	-	*	*	-
Levofloxacin	Sensitive	75%	33.33%	-	-	*	100%
	Resistant	25%	66.66%	100%	100%	*	-
Tetracycline	Sensitive	45.45%	66.66%	66.66%	100%	*	100%
	Resistant	54.54%	33.33%	33.33%	-	*	-
Meropenem	Sensitive	100%	100%	100%	*	*	100%
	Resistant	-	-	-	*	*	-
Cefepime	Sensitive	90.47%	75%	66.66%	*	*	*
	Resistant	9.52%	25%	33.33%	*	*	*

* Antimicrobial agent not tested for the micro-organism.

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High resistance rate of *E. coli* was identified for some antibiotics of choice for the treatment of UTI such as tetracycline (54.54%), nalidixic acid (52.17%), cephalexin (50%), ampicillin 45,45%), sulfazothrin (42.1%) and ciprofloxacin (31.8%). The highest resistance indices for both *E. coli* and other agents were attributed to ampicillin and tetracycline.

The resistance to antimicrobial agents has been noted since the first use of these people and is a growing worldwide problem[18]. In the present study, only the Meropenem (100%) presented satisfactory activity for all isolates of *E. coli*.

The spread of resistant bacteria has expanded rapidly throughout the world, indicating that the systems for continuous monitoring and effective measures for infection control are absolutely necessary. Interactions of health care, including the use of antibiotics and hospital transfers are among the well-defined risk factors for the acquisition of resistant bacteria[19].

The bacterial resistance is set in a major public health problem and is responsible for a significant increase in morbidity and mortality of patients[15]. This resistance is commonly diagnosed in clinical microbiology laboratories by disk-diffusion method, according to criteria established by the *Clinical and Laboratory Standards Institute* (CLSI), which reviews and, where appropriate, updates annually these criteria[12].

Currently, the empirical treatment indicates the norfloxacin or Ciprofloxacin as first choice treatment[9], in this study, 19.2% of the E. coli isolates were resistant to norfloxacin and 31.8% to ciprofloxacin. These indexes justify the therapeutic failure mentioned in various studies. It is important to emphasize that the antibiotics amikacin and meropenem presented high levels of sensitivity in many isolates, 90.0 and 100%, respectively, being precisely these antimicrobials used in the hospital environment, thus increasing the concern, because the options for outpatient use are already reduced

Among the published works related to the profile of bacterial resistance in examinations of urine

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culture, the prevalence of studies related to the hospital environment[1,10,13]. However, it has been observed the presence of multiresistant bacteria in ambulatory patients, this fact can result in failure or even lack of empirical treatment for urinary infections, leading to clinical complications that can

CONCLUSION

The present study demonstrates that the prevalence of ITU and the micro-organisms involved will vary according to the gender and age of patients. Despite this, *E. coli* is notably the most common bacterial pathogen in infections of the urinary tract of the investigated ambulatory patients. The presence of uropathogens resistant to antibiotics as evidenced in this study demonstrates the need to know the

increase the morbidity[20].

The standardization of the empirical treatment is very important, since it starts even before the final outcome of the antibiogram, being essential for the control of bacterial resistance to antibiotics[21]

reality of each region, contributing to the empirical safe and effective antibiotic choice, especially when it is not possible to perform culture and antimicrobial susceptibility test. As the resistance to medicines is an evolving process, studies of surveillance and routine monitoring are conducted continuously in order to provide physicians the knowledge on the most effective empirical treatment of the ITUs, and one must always think in sensitivity to the drug is associated with the lowest since effect for the patient.

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