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Original Article

Urinary tract infection: study of bacterial sensitivity and resistance in hospitalized patients

Infecção do trato urinário: estudo de sensibilidade e resistência bacteriana em pacientes internados

Maria Leopoldino Stinghel[1], Dhiessika Kreitlow[2], Carlos Franz Benz[3], Orlando Chiarelli Neto[4]

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ABSTRACT: Urinary tract infection (UTI) is a bacterial disease that mainly affects females, with a higher prevalence in children and the elderly. Antibiotics have the ability to inhibit growth and destroy bacteria that cause UTI. The use of antibiotics without conducting antibiograms increased the number of resistant isolates. The focus of this study was to investigate the incidence and antibiotic resistance of bacteria that cause UTIs in Colatina hospitals. Uroculture reports of patients hospitalized between 2015 and 2019 were investigated. Statistical evaluation was performed using Origin 8.0 at $p < 0.05$. The results showed a higher incidence of UTI in children and the elderly, with a greater number of female patients (56%). *Klebsiella pneumoniae* (31%), *Escherichia coli* (29%), *Enterococcus sp.* (20%), *Pseudomonas aeruginosa* (7%), *Proteus* (7%), and *Staphylococcus sp.* (6%) were the most prevalent. *Klebsiella pneumoniae* was resistant to 41% of the antibiotics administered. The other bacteria showed 38% resistance to *Staphylococcus sp.*, 30% to *Pseudomonas aeruginosa*, 29% to *Proteus*, 21% to *Escherichia coli*, and 19% to *Enterococcus sp*. Amikacin, gentamicin, imipenem, and vancomycin were the most effective antibiotics for the treatment of UTIs. Patients admitted to Colatina hospitals with UTI showed a bacterial resistance of approximately 40% for most antibiotics administered. Therefore, it is necessary to use antibiograms to avoid increasing bacterial resistance in hospital environments in Colatina, ES.

Keywords: Urinary tract infection; Microbial resistance; Antibiotic Antibiogram.

RESUMO: Infecção do Trato Urinário (ITU) é uma doença bacteriana que acomete principalmente o sexo feminino com maior prevalência em crianças e idosos. Os antibióticos possuem uma capacidade de inibir o crescimento bem como destruir as bactérias que causam a ITU. O uso de antibióticos sem condução do antibiograma tem aumentado o número de isolados resistentes. O foco deste estudo foi investigar a incidência e a resistência aos antibióticos das bactérias causadoras da ITU em hospitais de Colatina. Laudos da urocultura dos pacientes hospitalizados no período de 2015 a 2019 foram investigados. Faixa etária, sexo, agentes etiológicos mais freqüentes e resistência aos antibióticos foram analisados. A avaliação estatística foi realizada pelo programa Origin 8,0 a $p<0,05$. Os resultados mostraram maior incidência de ITU em crianças e idosos com acometimento maior em pacientes do sexo feminino (56%). *Klebsiella pneumoniae (*31%), *Escherichia coli (*29%), *Enterococcus sp (*20%), *Pseudomonas aeruginosa* (7%)*, Proteus* (7%) *e Stapylococcus coagulase negativa* (6%) foram as bactérias mais prevalentes. *Klebsiella pneumoniae* mostrou-se resistente em 41% dos antibióticos administrados, *Stapylococcus coagulase negativa* 38%, *Pseudomonas aeruginosa* 30%, *Proteus* 29%, *Escherichia coli* 21% e *Enterococcus sp* 19%. Amicacina, gentamicina, imipenem e vancomicina foram os antibióticos mais eficazes para o tratamento da ITU. Pacientes internados em hospitais de Colatina com ITU apresentaram resistência bacteriana em torno de 40% para a maioria dos antibióticos administrados. Portanto faz-se necessário o uso do antibiograma para evitar o aumento da resistência bacteriana nos ambientes hospitalares de Colatina – ES.

Palavras–chave: Infecção do trato urinário; Resistência microbiana; Antibiótico; Antibiograma.

1. Centro Universitário do Espírito Santo, Faculdade de Enfermagem. ORCID: https://orcid.org/0000-0002-8253-174X. E-mail: m.stingnel@yahoo.com.br.
2. Centro Universitário do Espírito Santo, Faculdade de Farmácia. ORCID: https://orcid.org/0000-0003-2026-1294. E-mail: dhiessika.kreitlow@hotmail.com.
3. Laboratório de Análises Clínicas Santa Maria - LAC. ORCID: https://orcid.org/0000-0001-5615-0743. E-mail: carlosbenz@hotmail.com.
4. Centro Universitário do Espírito Santo; Faculdade de Medicina. ORCID: https://orcid.org/0000-0002-8685-1185. E-mail: ochiarelli@unesc.br.
Endereço para correspondência: Orlando Chiarelli Neto. Av Fioravante Rossi, 2930 Bairro Martinelli - Colatina – ES, Brasil. E-mail: ochiarelli@unesc.br.

INTRODUCTION

Urinary tract infection (UTI) is a microbiological pathology caused by bacteria that affects the urinary system. Although it occurs at all ages, it is most frequent in children and female patients[1]. When not treated correctly, the infectious condition generates dysfunction in other organs, leading to sepsis[2].

Worldwide, approximately 150 million people are diagnosed with UTI per year[3]. A European multicenter study showed that *Escherichia coli, Enterococcus sp., Candida sp., Klebsiella sp., and Pseudomonas aeruginosa* are the most common bacteria that affect patients admitted to hospitals[4]. Brazilian studies have shown rates close to international ones, with cases caused by *Escherichia coli* ranging from 60% to 90%[3,5,6,7]. Bacterial infections account for 8% of all clinical consultations held in Brazil[6]. These data show the importance of the correct use of antibiotics and proper UTI treatment approaches.

The indiscriminate and incorrect use of antibiotics has led to the development of multidrug-resistant bacteria[7,8]. Besides *Enterococcus faecalis*, *Escherichia coli*, and *Staphylococcus aureus*, *Klebsiella pneumoniae* has shown 90% antibiotic resistance to ampicillin, cotrimoxazole, and cephalothin[5]. The main form of treatment for UTI is the prescription of antibiotics; therefore, it is necessary to know the type of bacteria for correct treatment, and an antibiogram is a method for identifying the appropriate antibiotic[9].

Bacterial resistance has grown in Brazil and Espirito Santo State, and there are no reports in the literature on the epidemiology and degree of microbial resistance in patients with UTI. Colatina town has eight (8) emergency care hospitals, and investigating cases of UTI in this niche is necessary not only to expand the state of the art but also the best therapeutic approach.

This study aimed to identify the most frequent etiological agents for UTI and correlate bacterial resistance with cases in the population of the Northern Center of the Espirito Santo State.

MATERIAL AND METHODS

A total of 196 reports of urine samples from patients admitted to the School Hospital (HMSJ) of the University Center of Espírito Santo (UNESC), from 2015 to 2019, were analyzed. Cultures and antibiograms were performed with the co-participant Laboratory of Clinical Analyses Santa Maria (LAC) according to the guidelines of the Brazilian Committee on Antimicrobial Susceptibility Testing (BrCAST).

Exclusion criteria were reports that presented unaltered results or descriptions of fungal microorganisms, which do not fit the interest of this research. Age groups, patient sex, types of bacteria, and antibiotics administered in the treatment of UTI were evaluated. Data were collected using tables in percentages to illustrate the main determinant agents of the infection and its resistance to the antimicrobials chosen.

The study was approved by the Ethics Committee on Research with Human Beings of the UNESC under protocol number 3733275. The data were analyzed using the Student's t-test with $p<0.05$, using the Origin 8.0.

RESULTS

The reports evaluated as positive for UTI showed the prevalence of 110 female patients (56%), 71 males (36%), and 15 children up to 3 years (8%). In 60 of the samples analyzed in this study (31%), *Klebsiella pneumoniae* was the most prevalent causative agent of UTI. Among the other bacteria found, in 133 samples, UTI was caused by the following: *Escherichia coli* (29%), *Enterococcus sp*. (20%), *Pseudomonas aeruginosa* (7%), *Proteus* (7%), and *coagulase-negative Staphylococci (*6%) (Table 1).

Table 1 - Prevalence of bacteria causing UTI in patients admitted to the HMSJ between 2015 and 2019

Microorganism	Prevalence
Klebsiella pneumoniae	31,08% (n=60)
Escherichia coli	29,53% (n=57)
Enterococcus Sp.	19,69% (n=38)
Pseudomonas aeruginosa	7,25% (n=14)
Proteus	6,73% (n=13)
Coagulase-negative Staphylococci	6,21% (n=12)

After evaluating the prevalent bacteria in this study, antibiotics administered to patients hospitalized with UTIs were also investigated.

Imipenem (n=56) and amikacin (n=57) showed total efficacy against Klebsiella pneumoniae and regarded as the most effective antibiotics for the treatment of UTI. Gentamicin (n = 43) was also considered an antibiotic of choice for treatment in 81% of cases. Klebsiella pneumoniae was resistant to antibiotics levofloxacin (n=15), nalidixic acid (n=17), ceftriaxone (n=33), and trimethoprim-sulfamethoxazole (n=40) (Table 2).

Table 2 - Sensitivity and resistance profile of *Klebsiella Pneumoniae* strains isolated in patients with UTI from 2015 to 2019

Antimicrobial	Sensitive	Resistant
Imipenem	100% (n=56)	--
Amikacin	100% (n=57)	--
Gentamicin	81,35% (n=43)	18,64% (n=11)
Levofloxacin	74,14% (n=43)	25,86% (n=15)
Nalidixic acid	65,30% (n=32)	34,7% (n=17)
Ceftriaxone	43,10% (n=25)	56,41% (n=33)
Trimethoprim+ sulfamethoxazole	28,57% (n=16)	71,43% (n=40)

The sensitivity and resistance profile of *Escherichia coli* strains isolated from hospitalized patients showed a more efficient scenario for the treatment of UTI.

Amikacin (n=54), gentamicin (n=54), and nitrofurantoin (n=52) showed an efficacy of approximately 98% against *Escherichia coli* strains. In contrast, cefepime (n=43), ceftriaxone (n=42), and ciprofloxacin (n=37) have an increased resistance (Table 3).

Table 3 - Sensitivity and resistance profile of *Escherichia Coli* strains isolated in patients with UTI from 2015 to 2019

Antimicrobial	Sensitive	Resistant
Amikacin	98,18% (n=54)	1,81% (n=1)
Gentamicin	96,42% (n=54)	3,57% (n=2)
Nitrofurantoin	98,11% (n=52)	1,81% (n=1)
Cefepime	89,58% (n=43)	10,42% (n=5)
Ceftriaxone	76,36% (n=42)	23,63% (n=13)
Ciprofloxacin	66,07% (n=37)	30,35% (n=17)

Vancomycin and cefepime showed 100% efficacy (n=31) compared to *Enterococcus sp.* strains. Tetracycline (n=27), ampicillin (n=29), and gentamicin (high-level disc) (n=29) showed efficacies of 82%, 83%, and 78%, respectively. In norfloxacin (n=25) and erythromycin (n=20), *Enterococcus sp.* resistance above 30% was noted (Table 4).

Table 4. - Sensitivity and resistance profile of *Enterococcus sp*. strains. Patients with UTI from 2015 to 2019

Antimicrobial	Sensitive	Resistant
Vancomycin	100% (n=31)	--
Cefepime	100% (n=31)	--
Tetracycline	81,81% (n=27)	18,18% (n=6)
Ampicillin	82,85% (n=29)	17,14% (n=6)
Gentamicin (High Level)	78,37%(n=29)	21,62% (n=8)
Norfloxacin	67,57% (n=25)	32,43% (n=12)
Erythromycin	60,06% (n=20)	39,39% (n=13)

Although sensitivity and resistance data were presented for the most prevalent bacteria, antibiotic resistance data were investigated for all bacteria in this study (*Klebsiella pneumoniae, Escherichia coli, Enterococcus sp., Pseudomonas aeruginosa, Proteus, and coagulase-negative Staphylococci*) (Table 5).

Table 5 shows the percentage of bacterial resistance to antibiotics administered during the internment. Among them, amikacin presented a more effective treatment against the bacteria detected in patients. Gentamicin and imipenem also showed high efficiency with few variations in treatment (Figure 1). The other antibiotics varied in the efficiency of bacterial combat (Table 5).

Table 5 - Percentage (%) of bacterial resistance. # means percentages below 2%. n/a means not administered. * represents statistical significance at $p<0.05$

Antibiotics	Bacteria					
	Klebsiella	*E coli*	*Enterococcus*	*Staphylococcus*	*Proteus*	*Pseudomonas*
Amikacin*	#	2	#	#	8	#
Ampicillin	41	23	16	50	#	29
Cefaclor	50	51	n/a	50	23	14
Cefepime	47	12	#	#	23	#
Ceftriaxone	55	35	13	33	38	64
Ciprofloxacin	48	26	29	42	46	36
Gentamicin *	17	4	18	8	8	14
Imipenem *	#	#	#	8	#	14
Levofloxacin	22	33	37	42	23	21
Nitrofurantoin	73	2	5	*#	31	57
Norfloxacin	47	32	26	42	46	21
Tetracycline	23	14	13	42	15	7
Trimethoprim+sulfamethoxazole	67	35	13	67	62	50
Vancomycin	n/a	n/a	#	n/a	n/a	n/a

Although *Klebsiella pneumoniae, Escherichia coli,* and *Enterococcus sp.* were more prevalent in this study, most of the bacteria detected showed resistance to the antibiotics administered. The mean resistance values were 41%, 38%, 30%, 29%, 21%, and 19% *for Klebsiella pneumoniae, coagulase-negative Staphylococci, Pseudomonas aeruginosa, Proteus, Escherichia coli, and Enterococcus sp.*, respectively. The graph in Figure 1 shows the variability in resistance as a function of the antibiotics administered. Resistance variations were observed among the strains investigated, with values above 40% in the vast majority of antibiotics (Figure 1). Amikacin, gentamicin, and imipenem were the antibiotics with the lowest variation in resistance, with nitrofurantoin having a high variety (Figure 1). Remarkably, nitrofurantoin was efficient for *coagulase-negative Staphylococci* (< 2% for resistance), and *Klebsiella pneumoniae* showed 73% resistance to the same antibiotic (Table 5).

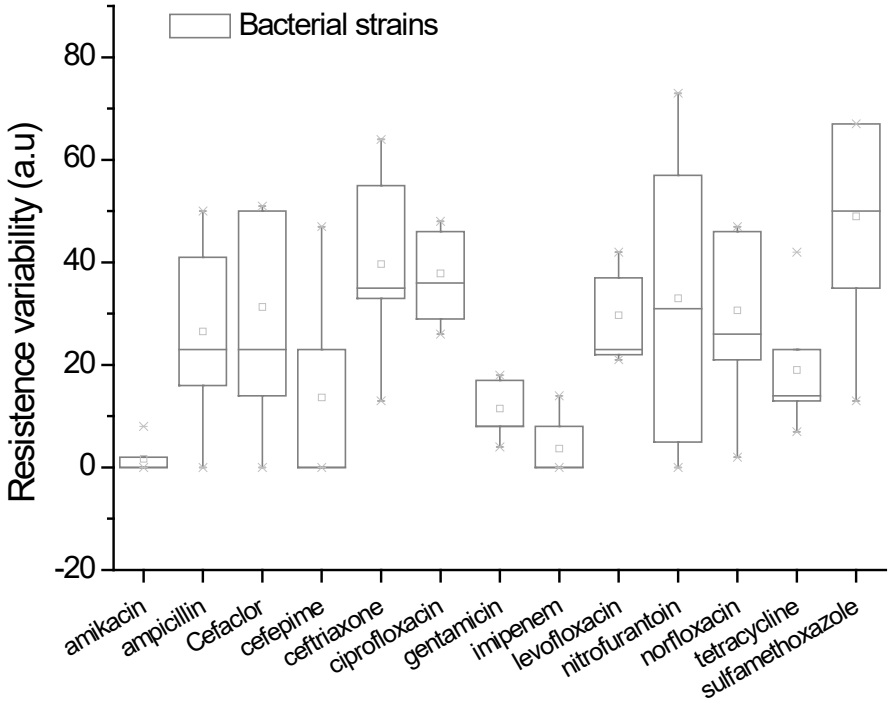

Figure 1: Variability of resistance of the six strains investigated according to the antibiotics administered

DISCUSSION

Bacterial resistance is defined as a high probability of therapeutic failure even when there is increased exposure and has become a clinical and public health problem[9]. The isolation and identification of microorganisms in the laboratory is a definitive proof for the diagnosis and control of resistance. However, the minimum susceptibility has not been adequately followed[10]. *Enterococcus sp., Escherichia coli, Klebsiella pneumoniae, Proteus,* and *Pseudomonas aeruginosa* are prevalent bacteria in the literature that affect the urinary tract and are resistant to various antibiotics[4,5,9].

Similar to the data in the literature, the highest prevalence of UTI in this study was in females and children in pediatric age[9,11]. Recurrences in hospitalized patients were also common due to limitations in movements, diaper use, and inadequate hygiene, which reflect the increased incidence of these infections[12].

Klebsiella pneumoniae was the major causative agent of UTI in this study (31%), with an average resistance of 41% to the antibiotics administered. Imipenem and amikacin showed 100% treatment efficiency, and gentamicin showed good treatment potential (Table 2). The literature also shows that *Klebsiella pneumoniae* not only reveals an increase in antibiotic resistance in patients with UTI, but also a high resistance in domestic and wild animals[13]. The data here show that *coagulase-negative Staphylococci* and *Pseudomonas aeruginosa* presented 8% and 14% resistance, respectively, to imipenem (Table 5). This may indicate the possibility of resistance against carbapenems, among other strains, such as *Klebsiella pneumoniae.*

Escherichia coli, in turn, is quite incident in regions of Brazil and worldwide, with variable proportions above 50% of cases of UTI[3,4,5]. Table 3 shows that *Escherichia coli* showed sensitivity to amikacin, nitrofurantoin, and

gentamicin at approximately 100%, but there was increased resistance to other antibiotics administered (Table 3).

It is important to note in Table 5 an increase in resistance of *Escherichia coli* to antibiotics in recent years. The resistance of the bacterium to ceftriaxone was 23.6% in the sample observed between 2015 and 2016 (Table 3). Conversely, the reports of the most recent samples from this study showed an increase in resistance to 35% (Table 5). It is important to note that the chronology between 2015 and 2019 showed an increase in resistance of 11.4% of *Escherichia coli* to the antibiotic ceftriaxone. A study on the identification of *Escherichia coli* pathotypes in tributaries of the Dooce River basin has also been shown to be growing in samples collected in 2015. It is important to highlight that Colatina is a town that uses fresh river water. With ore tailings spilled into the sweet river bed in 2015, many residents of the region have sought alternatives to capture water in springs and tributaries of the basin without any care or application of water treatment protocols. This procedure may corroborate the increase in the infection rates.

Enterococcus sp. has also shown variables that require care to prevent the growth of resistance[15]. Our data showed that vancomycin and cefepime had 100% sensitivity against *Enterococcus spp.* (Table 4).

Trimethoprim-sulfamethoxazole is an example of bacterial resistance (Table 5) caused by the inadequate use of antibiotics and without an antibiogram. The authors report that the drug was developed early in the history of antibiotics and is considered a first-line drug for the treatment of acute cystitis. Its indiscriminate use over the years has been one of the main factors responsible for resistance by microorganisms causing UTI[16,17]. This shows the severity of public health when adequate protocols are not applied.

Some authors have shown high rates of bacterial resistance to ceftriaxone and ciprofloxacin[18]. The data in Table 5 also show resistance around 50%, 30%, and 20% for *Klebsiella pneumoniae*, *Escherichia coli,* and *Enterococcus sp.*, respectively, for the antibiotics ceftriaxone and ciprofloxacin (Table 5). The *coagulase-negative Staphylococci* showed 33% resistance to ceftriaxone, even with the high exposure guidelines recommended by BrCAST. International protocols have recommended the administration of ceftriaxone (2 g/day) associated with other drugs for the treatment of coronavirus disease 2019[19]. This methodology has been applied in protocols of numerous Brazilian hospitals, and this approach can leverage the resistance process of *coagulase-negative Staphylococci* and other bacteria, as already highlighted for *Escherichia coli* in Table 5.

CONCLUSION

Klebsiella pneumoniae, Escherichia coli, and *Enterococcus* were the most prevalent bacteria for UTI in patients hospitalized in Colatina, ES. Although imipenem and amikacin are the most effective in combating UTI-causing bacteria, there is an increase in bacterial resistance that affect the urinary tract. Therefore, it is necessary to use an antibiogram to avoid increased bacterial resistance in the hospital niche of Colatina, ES.

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