

Microorganisms causing urinary tract infections in a teaching hospital in northeastern Brazil

Microorganismos causantes de infecciones del tracto urinario en un hospital universitario en el noreste Brasil

Microorganismos causadores de infecções do trato urinário em um hospital universitário do nordeste do Brasil

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ABSTRACT

Objective: to study the UTI-causing bacteria frequency and sensitivity profiles in a teaching hospital in northeastern Brazil. **Method:** A retrospective cross-sectional study was conducted based on the review of 279 patients for whom uroculture and urinary catheter cultures were routinely processed in the Microbiology Laboratory of São Vicente de Paulo Hospital. **Results:** For the catheter culture group, the most frequent microorganism was *Staphylococcus epidermidis* (47%), while in urine culture group *Escherichia coli* was the microorganism most frequently isolated (52%). *E. coli* showed 76.46%, 70%, and 86.36% resistance to ampicillin, amoxicillin and Sulfamethoxazole/trimethoprim respectively. *S. epidermidis* showed high resistance to most drugs used, demonstrating that these drugs should not be used to treat UTIs in this institution. **Conclusion:** This study represents the first study evaluating bacterial resistance in this institution and since data involving epidemiological surveillance and microbiological are limited in this region and due

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to its importance in the national context, the results may reflect important information to the body of research/data on bacterial resistance in the world.

Descriptors: Infection; Urine; Anti-Bacterial Agents.

RESUMEN

Objetivo: estudiar los perfiles de frecuencia y sensibilidad de las bacterias causantes de ITUs en un hospital universitario del nordeste brasileño. **Método:** Se realizó un estudio retrospectivo de corte transversal, con base en la revisión de 279 pacientes, para los cuales las culturas de urocultura y catéter urinario fueron analizadas en el Laboratorio de Microbiología del Hospital São Vicente de Paulo.

Resultados: En el grupo de cultivo de catéteres, el microorganismo más frecuente fue el *Staphylococcus epidermidis* (47%), mientras que en el grupo de la urocultura la *Escherichia coli* fue el microorganismo más aislado (52%). La *E. coli* mostró 76,46%, 70% y 86,36% de resistencia a la ampicilina, amoxicilina y sulfametoxazol/trimetoprima, respectivamente. *S. epidermidis* mostró una alta resistencia a la mayoría de los fármacos utilizados indicando que los medicamentos en cuestión no deben ser usados en el tratamiento de ITUs en esa institución.

Conclusión: Este estudio representa el primer estudio que evalúa la resistencia bacteriana en esa institución y una vez que los datos que involucran vigilancia epidemiológica y microbiológica son limitados en esta región y debido a su importancia en el contexto nacional, estos resultados pueden reflejar informaciones importantes para el cuerpo de búsqueda/datos sobre resistencia en el mundo.

Descriptor: *Infección; Orina; Antibacterianos.*

RESUMO

Objetivo: estudar os perfis de frequência e sensibilidade das bactérias causadoras de ITUs em um hospital universitário do nordeste brasileiro. **Método:** Foi realizado um estudo retrospectivo de corte transversal, com base na revisão de 279 pacientes, para os quais as culturas de urocultura e cateter urinário foram analisadas no Laboratório de Microbiologia do Hospital São Vicente de Paulo.

Resultados: no grupo de cultura de cateteres, o microrganismo mais frequente foi o *Staphylococcus epidermidis* (47%), enquanto no grupo da urocultura a *Escherichia coli* foi o microrganismo mais isolado (52%). A *E. coli* mostrou 76,46%, 70% e 86,36% de resistência à ampicilina, amoxicilina e sulfametoxazol/trimetoprima, respectivamente. *S. epidermidis* mostrou uma alta resistência à maioria dos fármacos utilizados indicando que os medicamentos em questão não devem ser usados no tratamento de ITUs nessa instituição. **Conclusão:** Este estudo representa o primeiro estudo que avalia a resistência bacteriana nessa instituição e uma vez que os dados que envolvem vigilância epidemiológica e microbiológica são limitados nesta região e devido a sua importância no contexto nacional, estes resultados podem refletir informações importantes para o corpo de pesquisa/dados sobre resistência no mundo.

Descritores: *Infecção; Urina; Antibacterianos.*

INTRODUCTION

Exponential advances in healthcare technology has led to an increase in the sensitivity of disease detection and as a result, overtreatment, which has invariably led to increased hospitalization and complications, infections secondary to instrumentation being common¹. The hospital infection rates vary from 5% to 20% and are associated with increased morbidity, mortality and hospital costs².

A urinary tract infection (UTI) is one of the most prevalent causes of infections related to health care, and can occur in patients without typical UTI symptoms. It is also preventable as most UTIs are related to catheterization³.

Catheterization of the urinary tract is the introduction of a catheter through the urethra, allowing the flow of urine into a disposal plastic bag. This device is used in various situations, such as urinary retention, urine volume control during major surgery, or in ICU patients, particularly those with severe burns⁴.

About 80% of urinary tract infections related to health care are attributable to the use of a urinary catheter, so these patients should be the priority for epidemiological surveillance⁵.

The etiological agents responsible for UTIs usually belong to the natural flora of the patient, though the use of antibiotics and the lack of proper aseptic catheter care can modify the endogenous microbiota. Gram-negative bacteria such as Enterobacteriaceae are the most common, but the gram-positive bacteria also have their epidemiological relevance⁵.

The pathogen most commonly isolated in UTIs is Escherichia coli, though other bacteria are also often isolated including Proteus mirabilis, Klebsiella pneumoniae, Pseudomonas aeruginosa, Enterococcus spp., Enterobacter spp., Group B Streptococcus, and Staphylococcus saprophyticus. Previous use of antibiotics and variations in the local susceptibility spectrum are important predictors of resistance⁶.

Antibiotic treatment takes into consideration the efficacy, urinary excretion, toxicity, cost, and the dosage schedule of the drug. The delay in diagnosis of infections and the indiscriminate, empirical, or erroneous prescription of antibiotics are currently seen as responsible for the development of bacterial resistance, which is becoming a global concern⁷.

Studies show that the microbial resistance level is increasing worldwide, both in hospitals and in the community. Therefore, it is extremely important to monitor the resistance of microorganisms against antibiotics in clinical practice, so that empirical treatment can still result in elimination of these pathogens⁸. Antibiotic resistance poses a serious threat to infection control complicating patient management and treatment strategy, contributing significantly to increase morbidity rates and mortality.

Thus, this work aims to study the UTI frequency and sensitivity profiles of the causative agents in a teaching hospital in northeastern Brazil, The hospital under study is a 270 bed Hospital, and it is part of the Unified Health System (UHS) in Brazil and is one of the major teaching hospitals of the interior of the Brazilian Northeast. HMSVP receives patients from the Cariri Metropolitan Region of Ceará and the surrounding states, serving more than 12 thousand patients monthly. Therefore, the bacterial resistance data collected at this hospital may reflect the bacterial resistance in Brazil and thus may contribute, along with other Brazilian studies, to the body of research/data on bacterial resistance in the world.

METHOD

A retrospective cross-sectional study was conducted based on the review of records of 279 patients for whom uroculture and urinary catheter cultures were processed in the Microbiology Laboratory of São Vicente de Paulo Hospital (HMSVP).

For the susceptibility test of microorganisms to antimicrobials, the samples were identified and processed following the protocols of the microbiology laboratory and the Control Center of Infections (CCIH) of the aforementioned hospital, based on the standardization proposed by the National Committee for Clinical Laboratory Standards (NCCLS) and adopted by ANVISA.

In this study, the results considered reliable were only those where antibiotics were tested in more than 50% of the bacterial strains. For resistance and susceptibility of the microorganisms was used the margin of 70% to classify the sensitive microorganisms or resistant to antibiotics. The study included all

cultures from inpatients with a urinary tract infection, and who had their urinary cultures evaluated from January to December 2012.

The data were analyzed using SPSS version 9 and Excel. The results were summarized using tables and figures.

Ethics approval for research involving human participants was obtained according to Resolution 466/12 of the Ministry of Health and the National Health Council of Brazil⁹, under number 863.557 in 04/11/2014.

RESULTS AND DISCUSSION

In the period from January to December 2012, 279 samples were cultured, of which 84 were positive. Of the 55 catheter samples, 69.90% had microbial growth. Of the 225 urine culture samples, 21% had microbial growth (Figure 1). 41 of these patients had a community-acquired UTI, and 43 had a hospital-acquired UTI.

Most hospital-acquired urinary tract infections are closely related to catheter use, Catheter-associated (CA)-bacteriuria is the most frequent health care-associated infection worldwide, Being responsible for up to 40% of hospital-acquired infections in US hospitals each year¹⁰. A study in Brazil showed that 35% to 45% of nosocomial infections in Brazilian hospitals are UTIs¹¹, and of these 80% are related to catheterization, which is the main risk factor and transmission vehicle.

Furthermore, it is estimated that patients catheterized for more than 30 days (long-term catheterization) nearly all of them will experience bacteriuria^{3,12}, despite adequate aseptic technique and closed drainage systems. The risk of acquiring bacteriuria occurs between 3% and 8% per day of catheterization, demonstrating the cumulative risk of infection over the days of catheterization³. The high percent of positive cultures (69.90%) in our samples support the findings of the study.

Our findings can also be compared to similar studies carried out in other Brazilian territories by authors Vieira et al.¹³ in the state of Pará, Kazmirczak, Giovelli and Goulart¹⁴ in the state of Rio Grande do Sul, Costa et al¹⁵ in the state of Paraíba.

For the adequate treatment of urinary infections it is essential to identify the causative bacteria, which aids in antibiotic selection¹⁶.

Figure 2 shows that there was a different predominant etiologic agent between the investigated regions. In urinary catheter cultures the most frequent microorganism was Staphylococcus epidermidis (47%), accompanied by Klebsiella pneumoniae (21%). However, in non-catheterized patients Escherichia coli was the most frequent microorganism (52%), accompanied by Pseudomonas aeruginosa (13%), Klebsiella pneumoniae (9%), and Staphylococcus saprofiticus (9%).

Such findings may be justified by the fact that Staphylococcus epidermidis is a microorganism that is naturally found in the skin. However, S. epidermidis has been increasingly associated with critical infections due to the formation of bacterial biofilms in medical devices such as prostheses, valves, and catheters¹⁶. While Escherichia coli is a commensal bacterium in the intestines of humans, the anatomical proximity of the anus to the urethra, the main entry point of urinary pathogens, causes this organism to be a significant source of UTIs¹⁷. Moreover, E. coli has several attachment factors, such as several adhesins and pili that allow it to better adhere to uroepithelium. While adherence to epithelial cells is essential for successful colonization and establishment; its virulent capacity is expressed by other encoding toxins, lipopolysaccharide (LPS), capsule, and invasins¹⁸.

With regard to the contamination of vesical catheters by Staphylococcus epidermidis, it currently ranks the first among the causative agents of biofilm-related nosocomial infections, where the organism promotes extraluminal colonization of catheters with high antibiotic resistance. Moreover, the mechanism involved in the accumulation of staphylococcal biofilms remains not yet fully understood, it varies by strain as well as environmental conditions, which hinders the effectiveness of a specific treatment^{16,19-22}. However, it is important to mention that Klebsiella pneumoniae, a gram-negative pathogen, was the second most frequent bacterium in patients using catheters. Furthermore, this correlates well with literature, as it the second most frequently isolated pathogen in cases of nosocomial UTIs²³.

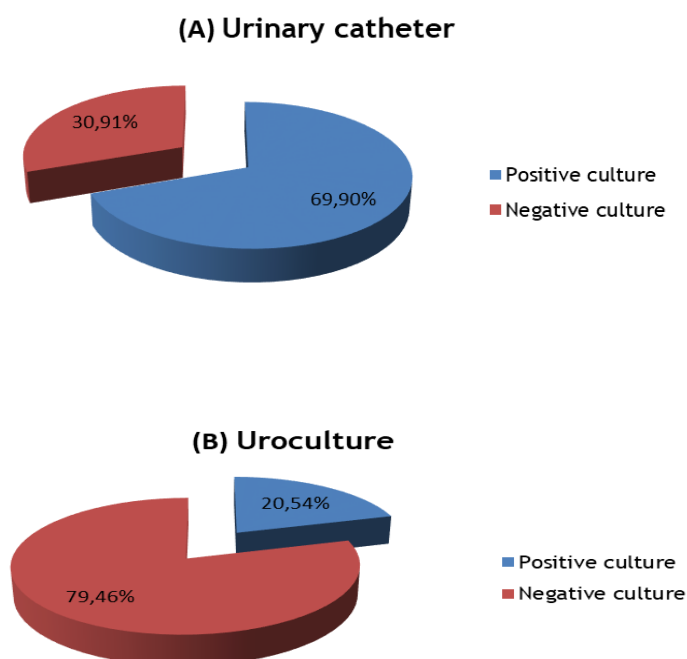


Figure 1 - Number of positive samples in urinary catheters (A) and urocultures (B).

The relationship of etiological agents isolated from urocultures presented in Figure 2B showed results similar to those of the SENTRY Antimicrobial Surveillance Program by Sader et al.²⁴, which studied the resistance of the main pathogens isolated from 12 Brazilian hospitals in four Brazilian states in a period of three years. Their results showed UTI frequency as follows: 47.6% *E. coli*, 12.6% *P. aeruginosa*, 9.8% *Klebsiella pneumonia* and 5.8% *Enterobacter spp.* It is important to mention that in our study *Pseudomona aeruginosa* and *Klebsiella pneumonia* appear colonizing both catheterized and non-catheterized patients (Figure 2), this finding may be an indicator of alertness, given the increasing mortality related to them and their high resistance rates to multiple antimicrobial drugs. Thus, only an appropriate antibiotic treatment of these infections, based on sensitivity testing and adjusting empirical antimicrobial therapy, will determine a suitable clinical evolution^{25,26}.

It is clear that the rational use of antimicrobials should be based on the antibiogram, which allows physicians to make the correct choice of antibiotic based on its sensitivity profile. This approach reduces the rates of bacterial resistance and facilitates the correct choice of antibiotic for each patient.

For the prudent choice of antibiotic agents, some factors must be taken into account, such as clinical efficacy against a particular group of bacteria, local resistance, and costs. Such selection has been quite effective in controlling infection, whether at the community or hospital level.

Escherichia coli was the most resistant bacterium in this study, with a resistance of 76.46% to the use of ampicillin, 70% to the use of amoxicillin, and 86.36% to the use of sulfametazol/trimetoprim (SMZ-TMP) (Table 1). It is important to say that this high resistance associated with Escherichia coli would be expected since this bacterium represented 52% of all the microorganisms isolated in the uroculture samples (Figure 2B). These results were confirmed in part by Blatt and Miranda et al.²⁷, where Escherichia coli resistance was 60.4% for ampicillin and 54.7% for SMZ-TMP.

Regarding the highest resistance index of E. coli to SMZ-TMP in our study, a similar study carried out in northern Utah, USA, showed a resistance of 71.6%^{28,29}, while another study carried out in the city of São Paulo, Brazil, showed that 58.3% of the strains analyzed were resistant to this medication²⁸, demonstrating the ineffectiveness of this drug for this type of treatment.

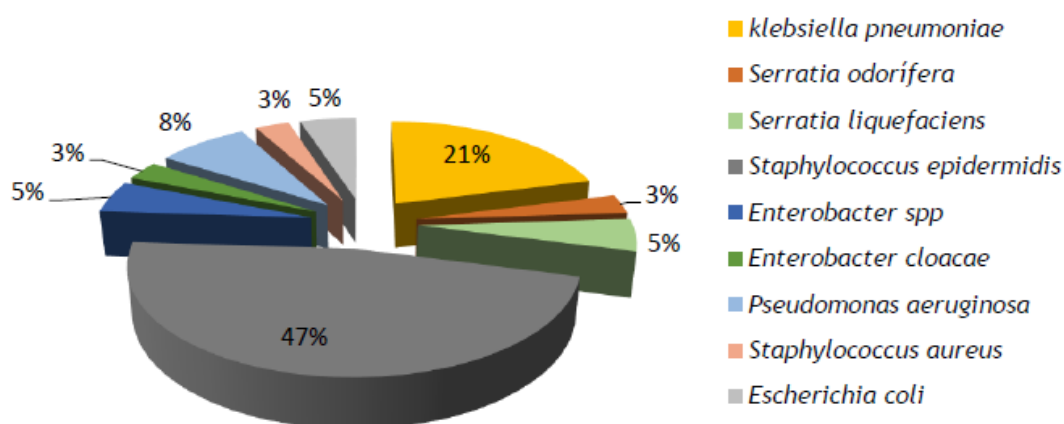
Tavares, in 2009³⁰, reported that the indiscriminate use of SMZ-TMP in Brazil for the treatment of cystitis would become one of the main factors for the increasing resistance of UTI pathogens, due to change of the endogenous microbiota.

*New resistant strains would lead to even greater therapeutic challenges. Resistance to ciprofloxacin remains low in some areas (0% in nova scotia, Canada), but is found in 72% of isolates in Mexico and 5-10% in the USA³¹. Also troubling is the emergence among patients with community-acquired UTI of E. coli possessing the extended spectrum *B*lactamase enzymes, which confer resistance against penicillins, third generation cephalosporins, and monobactams.*

In a given region, the prevalence of antibiotic resistance can not exceed 20%, according to Warren et al.³² However, this study shows a resistance rate above 20% for E.coli to cephalosporins and quinolones, making its use non-viable for this population. More recent studies have shown that E. coli presents high resistance rates (>45%) to wide-spectrum penicillins, cephalosporins, aztreonam, and ciprofloxacin²⁵.

However in this study, *E. coli* showed 100% sensitivity to aminoglycosides (amikacin and tobramycin), and carbapenems (meropenem and imipenem). Similar data were reported in the Lago, Fuentefria, and Fuentefria study³³ showing 95% sensitivity, and the Miranda et al. study³⁴ showing a sensitivity of 100% for the same drugs. These studies suggest that the use of carbapenems and aminoglycosides are well indicated in severe cases, such as chronic infections, nosocomial outbreaks, hospital-acquired infections.

(A) Urinary catheter



(B) Uroculture

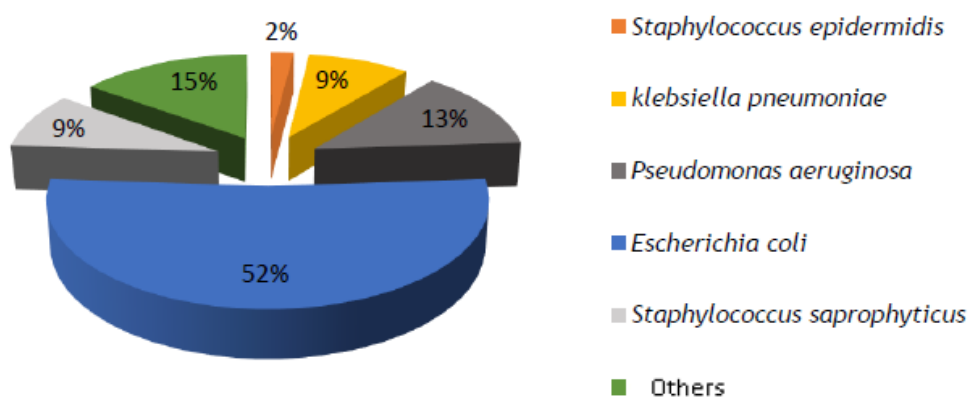


Figure 2 - Frequency of uropathogens in urinary catheter (A) and uroculture (B).

Table 1 - Antibiogram pattern of E.coli isolated from urocultur.

| Antimicrobial agents | Studied samples | Sensitiv (S) | %(S) | Resistant (R) | %(R) |
|--------------------------------------|------------------------|---------------------|-------------|----------------------|-------------|
| <i>imipenem</i> | 24 | 24 | 100,0 | 0 | 0 |
| <i>meropenem</i> | 24 | 24 | 100,0 | 0 | 0 |
| <i>amikacin</i> | 24 | 24 | 100,0 | 0 | 0 |
| <i>gentamicin</i> | 24 | 21 | 87,50 | 3 | 12,50 |
| <i>tobramycin</i> | 23 | 23 | 100,0 | 0 | 0 |
| <i>ceftazidime</i> | 24 | 23 | 95,84 | 1 | 4,16 |
| <i>ceftriaxone</i> | 24 | 19 | 79,17 | 5 | 20,83 |
| <i>cefotaxime</i> | 24 | 19 | 73,22 | 5 | 26,78 |
| <i>cefoxitin</i> | 21 | 20 | 95,24 | 1 | 4,76 |
| <i>aztreonam</i> | 23 | 18 | 78,27 | 5 | 21,73 |
| <i>norfloxacin</i> | 22 | 17 | 77,28 | 5 | 22,72 |
| <i>ciprofloxacin</i> | 21 | 16 | 76,20 | 5 | 23,80 |
| <i>trimethoprim-sulfamethoxazole</i> | 22 | 3 | 13,64 | 19 | 86,36 |
| <i>ampicillin</i> | 17 | 4 | 23,53 | 13 | 76,47 |
| <i>amoxicillin</i> | 20 | 6 | 30,00 | 14 | 70,00 |

As previously mentioned, *Staphylococcus epidermidis* was the most frequent bacterial agent in urinary catheter cultures, which presented high resistance to most of the drugs used, as seen in Figure 2A and Table 2. This is due to the increase in the acquisition of resistance by the genus *Staphylococcus* to most of currently available antimicrobial agents with anti-staphylococcal activity, such as aminoglycosides, lincosamides, macrolides, quinolones, and tetracycline. Therefore, glycopeptides, especially vancomycin, have become one of the few effective therapeutic alternatives in the treatment of infections caused by *Staphylococcus*, alone or in combination³⁵.

However, some results have shown a varied efficacy of this antibiotic on the bacterial biofilm, which can be explained by its limited penetration into the biofilm matrix, which means a great challenge for clinicians making it difficult or impossible to treat and detachment from the device may result in systemic infections³⁵.

In this study, *S. epidermidis* showed 100% sensitivity to vancomycin, 82.36% to amikacin, and 81.25% to chloramphenicol. Similar results were found by Michelim et al.³⁶, where *S. epidermidis* was 100% sensitive to vancomycin. However, intermediate resistance to vancomycin has been described³⁷.

Table 2 - Antibiogram pattern of *Staphylococcus epidermidis* isolated from urinary catheters.

| Antimicrobial agents | Studied samples | Sensitiv (S) | %(S) | Resistant (R) | %(R) |
|-------------------------------|------------------------|---------------------|-------------|----------------------|-------------|
| vancomycin | 18 | 18 | 100,00 | 0 | 0 |
| amikacin | 17 | 14 | 82,36 | 3 | 17,64 |
| gentamicin | 19 | 9 | 47,37 | 10 | 52,63 |
| tetracycline | 19 | 13 | 68,43 | 6 | 31,57 |
| chloramphenicol | 16 | 13 | 81,25 | 3 | 18,75 |
| ciprofloxacin | 15 | 11 | 73,34 | 4 | 26,66 |
| imipenem | 19 | 10 | 52,63 | 9 | 47,37 |
| meropenem | 19 | 10 | 52,63 | 9 | 47,37 |
| cephalothin | 18 | 9 | 50,00 | 9 | 50,00 |
| cefoxitin | 18 | 9 | 50,00 | 9 | 50,00 |
| penicillin | 18 | 0 | 0 | 18 | 100,00 |
| erythromycin | 12 | 3 | 25,00 | 9 | 75,00 |
| trimethoprim-sulfamethoxazole | 18 | 7 | 38,89 | 11 | 61,11 |
| ampicillin | 14 | 0 | 0 | 14 | 100,00 |
| amoxicillin | 13 | 0 | 0 | 13 | 100,00 |

The increasing prevalence of highly virulent and multi-drug resistant bacterial strains constitutes a major concern in modern medicine. Biofilm formation adds an additional compounding factor, making therapy extremely difficult when there is antibiotic resistance in a subpopulation of a biofilm-forming species. Pathogenic staphylococci are now regarded in the scientific community as antibiotic-resistant “superbugs,” because they have the capacity to acquire resistance traits.

The difficulties of predicting a clinical infection with *S. epidermidis* in patients with positive blood cultures with this organism may mean management quandary for clinicians, since there are no reliable phenotypic or genotypic algorithms to predict the pathogenicity of an infection of the bloodstream by *S epidermidis*^{38,39}.

Possible targets for drug development include enzymes involved in the biosynthesis of cell envelope structures, such as peptidoglycan, teichoic acids, membrane lipids, or cell wall-associated adhesins³⁸.

Epidemiological research is of fundamental importance for the proper use of antimicrobials, since the use of a particular drug in empirical therapy should not be conducted when the level of local resistance is greater than 20%³⁹. The evolving nature of antibiograms illustrates the importance of repeating work over time, which may demonstrate possible changes either in prevalence or resistance pattern, and can provide data that can update antimicrobial therapy.

CONCLUSION

The study identified the most frequent etiological agents and the antimicrobial susceptibility profiles of microorganisms that cause UTIs in both catheterized and non-catheterized patients while in hospital. We can conclude that 69.09% of the catheter samples had positive cultures, and that 21% of the non-catheterized samples analyzed had positive results. The majority of bacteria isolated were gram-negative enteric bacilli, with Escherichia coli having the largest portion at 52% prevalence in urocultures and with high resistance to betalactamicos and SMZ-TMP. Moreover, Staphylococcus epidermidis is the most frequent bacterial agent isolated from urinary catheters, showing high resistance to most drugs used.

This study represents the first study evaluating bacterial resistance in this Brazilian hospital and since data involving epidemiological surveillance and microbiology are limited in this region and due to its importance in the national context, the results may reflect important information to the body of research/data on bacterial resistance in the world.

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