ORIGINAL ARTICLE

Characterization of the health-care-associated urinary tract infections at the Hospital das Clínicas de Ribeirão Preto, São Paulo, Brazil

Caracterização das infecções do trato urinário relacionadas à assistência médica no Hospital de Ribeirão Preto - SP

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ABSTRACT

Urinary tract infections (UTIs) are the most common health-care-associated infections (HCAIs) and one of the top-ranking microbial infections. In the community, about 80% of UTIs are caused by uropathogenic *Escherichia coli* (UPEC), but there is a high variability of etiological agents involved in hospital-acquired UTIs. With this context in mind, the current study aimed to evaluate the prevalence of the main etiological agents responsible for UTIs and their susceptibility profile at the Hospital das Clínicas de Ribeirão Preto, a high complexity reference hospital in the Southeast region of Brazil. This retrospective and descriptive study analyzed all positive inpatient cultures [100,000 colony-forming unit (CFU)/mL] from November 2016 to April 2017. The most prevalent microorganism was *Klebsiella pneumoniae* (23 isolates), equivalent to 37.7% of positive urocultures. The second most prevalent agent was UPEC, with 19 isolates (31.1%). The risk factors evaluated in these inpatients showed that 17.5% underwent a urological procedure on admission, 31.6% were using a urinary catheter; 26.2% were using immunosuppressive drugs during the period in which the clinical diagnosis was made. Our results demonstrate the prevalence of UTI causes in the hospital context and the main risk factors for them and will be pretty helpful in guiding empirical treatment in severe UTIs inside the hospital as well as reflect on the actual need and time duration of invasive procedures in the hospital environment.

KEYWORDS: Health-care associated infections, Catheter-associated urinary tract infections

RESUMO:

As infecções do trato urinário (IU) são a terceira causa principal de infecções associadas ao ambiente hospitalar, logo após as infecções pulmonares e da corrente sanguínea. Na comunidade, cerca de 80% das IU são causadas por E. coli, mas há uma alta variabilidade de agentes etiológicos envolvidos nas IU hospitalares. Este estudo visa avaliar a prevalência dos principais agentes etiológicos e perfil de suscetibilidade envolvidos em IU em um ambiente hospitalar de referência de alta complexidade no sul do Brasil. Este é um estudo retrospectivo e descritivo que analisou todas as culturas positivas (100.000 ufc/ml) de pacientes nas enfermarias de um hospital terciário no período entre novembro de 2016 a abril de 2017. O microorganismo mais prevalente foi Klebsiella pneumoniae (23 isolados), o que equivale a 37,7% das uroculturas. O segundo agente mais prevalente foi Escherichia coli, com 19 isolados (31,1%). Os fatores de risco avaliados nestes pacientes mostraram que 17,5% foram submetidos a um procedimento urológico na admissão, 31,6% estavam usando um cateter urinário; 26,2% estavam usando drogas imunossupressoras no período em que o diagnóstico clínico foi feito. Nossos resultados demonstram uma mudança importante na prevalência das causas de IU no contexto hospitalar e os principais fatores de risco para elas e serão bastante úteis para orientar o tratamento empírico em IU grave dentro do hospital, bem como refletir sobre a real necessidade e a duração dos procedimentos invasivos no ambiente hospitalar.

Palavras-chave: Infecção do tracto urinário, Infecção cruzada, Resistência antimicrobiana

INTRODUCTION

Health-care-associated infections (HCAIs) are among the most common types of adverse events affecting hospitalized patients. Internationally, UTIs represent around 40% of HCAIs, with significant consequences for morbidity and mortality and substantial financial implications (1).

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Urinary tract infection (UTI) is the most common nosocomial infection, accounting for more than 40% of all nosocomial infections (10).

In Brazil, UTIs are considered one of the most common infections. A study that investigated through a literature review the most prevalent bacterial species, as well as their resistance profile concerning the treatments of choice in UTIs at hospitals in North and Northeast Brazil, showed that *Escherichia coli* is the most significantly prevalent bacterium in all groups analyzed, regardless of sex and age group, followed by *Klebsiella pneumoniae* (*K. pneumoniae*) and *Proteus mirabilis* (*P. mirabilis)* (2).

Multivariate analysis indicates the risk factors for UTIs, including prolonging the duration of the catheter, female sex, older age, diabetes mellitus, the absence of systemic antibiotics, catheter insertion outside the operating room, and a breach in the closed system of catheter drainage (3).

The typical UTIs are identified when the organism is isolated in quantitative counts of at least 100,000 colony-forming units per mL (CFU/mL) of urine, collected by medium jet and with adequate asepsis plus clinical manifestation. Patients catheterized and performing rigorous asepsis counts above 100 CFU/mL can be considered significant (4). This infection may be accompanied by the classic signs and symptoms of UTIs such as dysuria, gross haematuria, and new or worsening urinary incontinence. In addition, HCAIs are infections that first appear 48 hours or more after hospitalization or within 30 days after having received health care (5).

UTI can be classified as symptomatic, presenting the clinical picture previously described, or asymptomatic. The threshold for asymptomatic bacteriuria from a clean-catch voided urine specimen is the isolation of a single organism in quantitative counts $\geq 10^5$ (CFU)/mL (6). As for the localization, it can be classified as low (cystitis) when it reaches the lower urinary tract or high UTI (pyelonephritis) when it reaches the upper and lower urinary tracts concomitantly. In pyelonephritis, symptoms such as fever above 38 ºC, chills, and low back pain are much more frequent than in cystitis, forming the triad of classic symptoms of this comorbidity (5).

Considering the UTIs acquired in the hospital environment, a decrease in the prevalence of UPEC occurred compared with the etiology of community cases, although it is still the first cause. Catheter-associated UTIs were reported by acute care hospitals and long-term acute care facilities to the US National Healthcare Safety Network (NHSN) between 2011 and 2014, the most common causative pathogens identified were *E. coli* (24%), *Candida* spp. (24%), *Enterococcus* spp. (14%), *P. aeruginosa* (10%), and *Klebsiella* spp (10%) (6).

The repetitive inappropriate administration of antimicrobials often leads to greater bacterial resistance. CAUTIs habitually lead to biofilm formation on the extraluminal and intraluminal portal catheter surface, mainly from extraluminal microorganisms (7).

A recent Australian study compared the susceptibility of bacteria isolated from urine specimens submitted by nursing-home residents with that of elderly subjects in the community. There was a significantly higher prevalence of multi-drug resistant isolates in the nursing home urine specimens for all *Enterobacteriaceae* (12.4% v. 6.1%), for UPEC (8.3% v. 3.9%), and *P. mirabilis* (27.4% v. 8.1%) (8). The presence of indwelling devices, including chronic urethral catheters, is also a risk for colonization with resistant bacteria. Globally, extended-spectrum β-lactamase (ESBL)-producing *Enterobacteriaceae* (9) and carbapenemase-producing *Klebsiella pneumoniae* and other *Enterobacteriaceae* (10) have been increasingly reported in residents of long-term care facilities.

Thus, the collection of data regarding the prevalence of possible etiological agents of HAUTI services becomes research of great relevance for the health center to be analyzed. From this, there is more information on microorganisms that cause nosocomial infections, aiding in targeting therapeutic behaviors based on the profile of the antimicrobial susceptibility test. Considering that there is no previous work that tries to raise the profile of the microorganisms that cause nosocomial urinary tract infections in a tertiary hospital, it is believed that the development of this research is to analyze the characteristics of HAUTI and can contribute both to the production of knowledge and the clinical management of these infections.

METHODS

A descriptive and retrospective study of all patients with positive urocultures, from 18 to 95 years old and of both gender, hospitalized in any ward of the Hospital das Clínicas de Ribeirão Preto from November 2016 to April 2017, was performed. This retrospective study was carried out by reviewing patient records and followed the inclusion criteria mentioned below.

Inclusion criteria

Positive urine cultures from patients diagnosed with urinary tract infection through medical record review.

Exclusion Criteria

Positive urocultures from patients with a value lower than 100,000 CFU/mL, which did not match the UTI criteria according to the NHSN/CVE 2017, with or without the use of chronic indwelling catheters. In addition, patients who had asymptomatic bacteriuria who were not hospitalized for more than 48 hours or who were admitted to the hospital with UTIs were considered in this study.

RESULTS

From November 2016 to April 2017, 57 patients were selected according to the inclusion and exclusion criteria previously described, totaling 61 positive urocultures recorded in 4 months. Considering the patients selected, 32 (56.1%) were female, and 25 (43.9%) were male. In addition, they presented a mean age of 55.71 years, the highest recorded age being 95 years and the lowest age of 18 years. The main comorbidities found in these patients were systemic arterial hypertension, with 25 patients (43.86%); malignant neoplasms in general, with 14 patients (24.50%); diabetes mellitus with 13 patients (22.80%); and chronic kidney disease - dialytic or not - with 11 patients (19.30%) (**Table 1**).

These 57 patients were hospitalized with a diagnosis of UTI at least 48 hours after admission to various hospital wards. Among the units, there were 8 patients in Neurology, 6 in Gynecology and Obstetrics, 5 in the Renal Transplant Unit, 3 in the Intensive Care Unit, 4 in Proctology, 4 in Cardiology, 3 in Gastric Surgery, 3 in Gastroclinical, 3 in Infectious Diseases, 2 in Neurosurgery, 2 in Urology and only one patient in Orthopedics, Hematology, Thoracic Surgery, Nephrology, Oncology, Coronary Unit, General Practice and Psychiatry units (**Figure 1**). In addition, these patients were hospitalized for an average of 41.84 days, with the shortest admission time being 4 days and the longest 210 days. The time of hospitalization up to the clinical diagnosis of UTI was, on average, 20.82 days, with the lowest evaluated being 2 days and the highest of 84 days.

Regarding the risk factors evaluated in these patients, it was found that 17.5% of the patients underwent a urological procedure on admission, 31.6% were using a urinary catheter; 26.2% were using immunosuppressants during the period in which the clinical diagnosis was made; 70.5% used antibiotic in the 90 days before the diagnosis; and 36.8% had some previous hospitalization in the last 90 days (**Table 1**). According to the literature, the risk factors of CAUTI are female sex, older age, diabetes mellitus, bacterial colonization of the drainage bag, and errors in catheter care (e.g., errors in sterile technique, not maintaining a closed drainage system) (9).

About the bacteria found in the analyzed urocultures, the most prevalent was *K. pneumoniae*, corresponding to the 23/57 or 61 (37.7%) clinical samples. The second most prevalent agent was UPEC, the primary etiological agent of UTI in the community, corresponding to 19/57 or 61 (31.1%) samples. In the other samples, 5 *Enterococcus faecalis* (8.2%) were found; 3 *P. aeruginosa*, *Acinetobacter baumannii*, and *Proteus mirabilis* corresponding to 4.9% of each bacterium; 2 samples of *Enterobacter cloacae* (3.3%); and a sample of *Providencia stuartii*, *Citrobacter koseri,* and *Morganella morganii*, equivalent to 1.6% of the cultures each.

Concerning the prevalence of the etiological agents of HAUTI, the antibiotic susceptibility testing of these bacteria was also analyzed. Of the

significant antimicrobials used for the treatment of hospital UTI, the most resistant, regardless of the causative bacteria, was Cephalexin, with a resistance rate of 79%. The less resistant antibiotic was Amikacin, which showed a resistance rate of 12%. Second-generation quinolones, such as ciprofloxacin and norfloxacin, are widely prescribed to treat community UTIs and showed, respectively, the resistance rate of 54% and 58% (**Table 2**).

The antimicrobials susceptibility was also analyzed according to the etiological agent. For the 23 *K. pneumoniae* isolates analyzed, the most active antibiotic was Amikacin (84%), and the less active was Cephalexin (14%). For UPEC, the most active antibiotics were Amikacin, nitrofurantoin, and meropenem, showing 100% susceptibility for the 19 cultures. The Figure below shows the susceptibility of each antibiotic according to the etiological agent. Still, on the resistance rate of these bacteria, it was found that of the 61 samples studied, 17 were ESBL-producers, equivalent to 28% (**Table 3**).

DISCUSSION

Catheter-associated UTIs reported by acute care hospitals and long-term acute care facilities to the US National Healthcare Safety Network (NHSN) between 2011 and 2014, the most common causative pathogens identified were 24%.

According to the NHSN, between 2011 and 2014, the most common causative pathogens identified were *E.coli* (24%), *Enterococcus* spp. (14%), *Pseudomonas* (10%), and *Klebsiella* (10%) (4). In our study, *K. pneumoniae* was the most prevalent, corresponding to 23 samples, equivalent to 37.7% of urocultures, followed by UPEC.

Regarding antimicrobial resistance, our results indicate a high resistance rate for cephalosporins, and the lowest resistant were aminoglycosides (Amikacin with 12% resistance). However, quinolones presented a resistance rate ranging from 54% and 58%. This fact contributed because 70.5% used antibiotics in the 90 days before diagnosis and 36.8% had previous hospitalization in the last 90 days. According to NHSN, 35% of UPEC were resistant to quinolones and 16% to advanced generation anti-pseudomonal cephalosporins (i.e., cefepime and ceftazidime) (4). Of 4700 *Klebsiella* isolates, 9.5 percent were resistant to carbapenems.

Regarding the risk factors, our study shows similarity with the literature, and most of these patients with UTIs had invasive procedures such as urological procedures and the use of immunosuppressants.

With these results, the use of quinolones and cephalosporins, including the fourth generation, should be better evaluated in its therapeutic indication for critically-ill patients in the hospital, given the high resistance rate for these two antimicrobial classes. The use of aminoglycoside or carbapenems seems to be the safest and better choice.

Thus, the collection of data on the prevalence of possible etiological agents of health services becomes research of great relevance for the establishment of institutional therapy protocols. There is more information on microorganisms that cause hospital-acquired infections, aided by local epidemiological data, from the sensitivity profile of clinical samples. Considering that no previous work has tried to raise the profile of the microorganisms that cause HAUTI in the Hospital das Clínicas de Ribeirão Preto, Brazil, we believe that this study will contribute to a better understanding of the hospital context and the clinical management of these infections.

CONCLUSION

This study demonstrates the change in microbiologic prevalence in the hospital context. Regarding antimicrobial resistance, there was a high prevalence of ESBL-producing strains. The change in microbiological prevalence in the hospital context may be due to risk factors such as urological procedures. Thus, we should reevaluate for each patient the real need for these procedures in the hospital environment, especially concerning the time of use of invasive devices.

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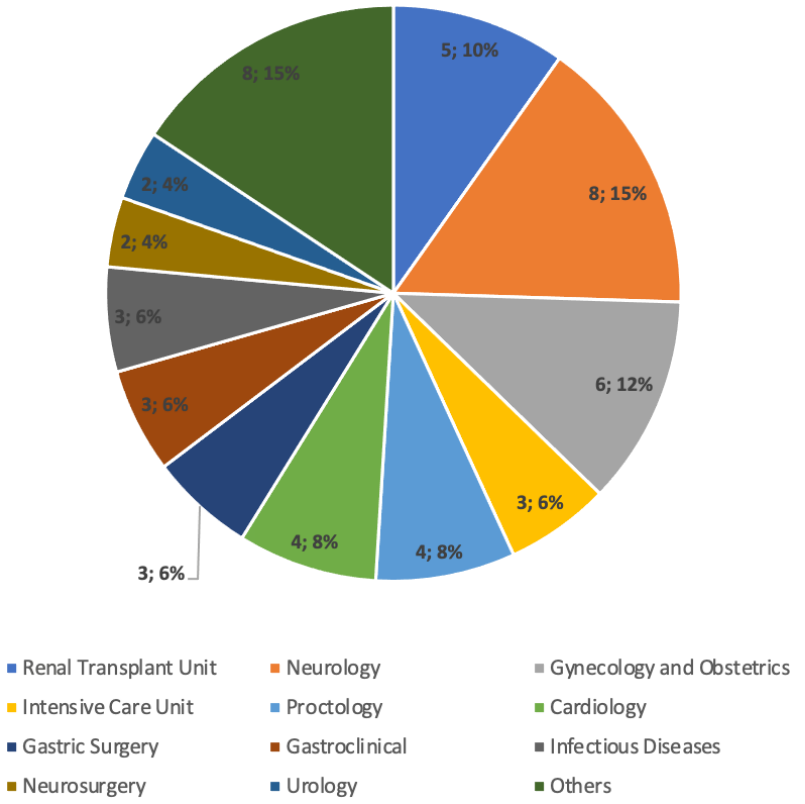

Figure 1: Distribution of the patients studied with Urinary Tract Infection concerning the medical specialty from November 2016 to April 2017.

Table 1

Characterization of the study population with Urinary Tract Infection from November 2016 to April 2017.

Distribution Age (years)	Number of patients	Percentage (%)
18-30	6	10.5%
30-60	19	33.3%
> 60	32	56.2%
Distribution by gender	Nº. of patients	Percentage(%)
Male	25	43.9%
Female	32	56.1%
Comorbidities	Nº of patients	Percentage (%)
Arterial Hypertension	44%	44%
Neoplasms	26%	26%
Diabetes mellitus	23%	23%
Chronic kidney disease	20%	20%
Risk factor	Nº of patients	Percentage (%)
Urological procedures	10	17.5%
Use of SVD*	18	31.6%
Current use of immunosuppressants	16	26.2%
Prior use of antibiotics	43	70.5%
Previous Hospitalizations	21	36.8%

* urinary catheter

Table 2

Geral sensibility profile of total microorganisms involved in urinary tract infections from November 2016 to April 2017.

Antibiotic	Sensitivity	Nº of strains tested
Cephalexin/ Cephalothin	21%	38
Cefuroxime	42.85%	49
Ceftriaxone	43.50%	46
Cefepime	44.40%	54
Nalidixic Acid	35.10%	37
Norfloxacin	41.70%	36
Ciprofloxacin	46%	61
Amoxicillin/clavulanate	35.30%	34
Piperacillin/tazobactam	57.40%	54
Meropenem	76.37%	55
Amikacin	88.23%	51
Gentamicin	75%	60
Nitrofurantoin	61%	41
Sulfamethoxazole / Trimethoprim	46.15%	39

Table 3:

Sensitivity profile of the main antibiotics prescribed for urinary tract infection, regardless of the etiological agent, from November 2016 to April 2017.

	Klebsiella pneumoniae		Escherichia coli	
Antibiotic	Sensitivity	No. of tested strains	Sensitivity	No. of tested strains
Cephalexin/Cephalothin	14%	14	25%	16
Cefuroxime	29%	21	63%	19
Ceftazidime	33%	9	NA	NA
Ceftriaxone	25%	20	71%	17
Cefepime	29%	21	74%	19
Nalidixic acid	25%	12	35%	17
Norfloxacin	25%	12	47%	17
Ciprofloxacin	39%	23	53%	19
Ampicillin	NA	NA	25%	16
Amoxicillin/clavulanate	25%	12	43%	14
Piperacillin/tazobactam	40%	20	84%	19
Meropenem	71%	21	100%	18
Amikacin	84%	19	100%	17
Gentamicin	68%	22	84%	19
Nitrofurantoin	23%	13	100%	19
Sulfamethoxazole / Trimethoprim	33%	12	50%	18
TOTAL	-	23	-	19

NA: Not Applicable