Study of variables involved in hospital-acquired urinary tract infections at a university hospital

Estudo de variáveis envolvidas em infecção do trato urinário nosocomiais em um hospital universitário

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ABSTRACT

OBJECTIVE: Analyze bacteria involved in urinary tract nosocomial infections (UTIs), their sensitivity profile, and other correlated clinical variables. **METHODS:** This was a retrospective study, based on the analysis of positive urine culture reports (from 100,000CFU/ml) for nosocomial infection covering the years 2009, 2010 and 2011, and on medical records. Statistical analysis was performed through SPSS 19.0 software, using chi-square tests with Yates correction and Pearson's correlation coefficient. $p<0.05$ was considered statistically significant. **RESULTS:** The sample consisted of 74 positive urine cultures, 64.9% of which from females, and 58.1% of which from patients above 50 years of age. Medical conditions accounted for 87.8% of cases, and nervous and gastrointestinal problems were the most prevalent. Hospital stay ranged from 56.7±35.7 days; 51.4% of the patients used indwelling urinary catheter, 54% of whom over a 30 day period. *Klebsielle pneumoniae* and *Escherichia coli* together accounted for 60.8% of cases. Amikacin, Gentamicin, Cefoxitin, Piperacillin-tazobactam, Imipem, Meropenem and Ertapenem showed ≥50% sensitivity. There were correlations between symptoms associated to UTI and antibiotic use after urine culture (p=0.02), and catheter use and duration of hospital stay (p=0.04). **CONCLUSIONS:** Female patients over 50 years of age with underlying clinical conditions originated in the nervous system or the gastrointestinal apparatus making use of indwelling urinary catheters for over 30 days and a hospital stay period of 56.7±35.7 days are more likely to develop nosocomial UTIs. Amikacin, Gentamycin and Cefoxitin are feasible options for empirical antibiotic therapy against the two most prevalent bacteria.

Keywords: Cross Infection; Urinary tract infection/epidemiology; Urinary tract infection/quimioterapia; Cefoxitin/therapeutic use; Gentamicins/therapeutic use

RESUMO

OBJETIVO: Analisar as bactérias envolvidas nas infecções do trato urinário (ITUs) nosocomiais, perfil de sensibilidade, e outras variáveis clínicas correlacionadas. **MÉTODOS:** Estudo retrospectivo, com base na análise dos laudos de urocultura positiva (a partir de 100 mil UFC/ml) para infecção nosocomial abrangendo os anos 2009, 2010 e 2011, em prontuários médicos. A análise estatística foi realizada no SPSS 19.0, utilizando os testes do qui-quadrado com correção de Yates e coeficiente de correlação de Pearson. Considerou-se estatisticamente significativo p<0,05. **RESULTADOS:** A amostra constitui-se de 74 uroculturas positivas, sendo 64,9% do sexo feminino, com 58,1% acima de 50 anos. As patologias clínicas corresponderam a 87,8% dos casos, sendo sistema nervoso e gastrointestinal os de maiores prevalências. Tempo de permanência hospitalar foi de 56,7±35,7 dias, 51,4% fizeram uso de SVD, sendo 54% destes com uso acima de 30 dias. As bactérias *Klebsielle pneumoniae* e *Escherichia coli* representaram juntas 60,8% dos casos. Os antibióticos Amicacina, Gentamicina, Cefoxitina, Piperaciclina-tazobactam, Imipem, Meropenem e Ertapenem apresentaram sensibilidade ≥50%. Houve correlação entre sintomas associados à ITU e uso de antibiótico após urocultura (p=0,02); tempo de uso de sonda e tempo de permanência hospitalar (p=0,04). **CONCLUSÕES:** Pacientes femininos com mais de 50 anos e doença de base clínica, de origem no sistema nervoso ou gastrointestinal, em uso de SVD por mais de 30 dias e tempo de permanência hospitalar de 56,7±35,7 dias, estão entre as mais propensas a desenvolverem ITU nosocomial. A Amicacina, Gentamicina e Cefoxitina apresentaram opções factíveis para a antibioticoterapia empírica as duas bactérias mais prevalentes.

Descritores: Infecção hospitalar; Infecções urinárias/epidemiologia; Infecções urinárias/drug therapy; Cefoxitina/uso terapêutico; Gentamicinas/uso terapêutico

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INTRODUCTION

Urinary tract infections (UTIs) are frequent pathologies, both in community and hospitalized patients, being one of the major causes of nosocomial infection. Nosocomial UTIs are estimated to have a three billion dollar annual cost in the USA alone[1]. Infection risk factors include the use of indwelling urinary catheters (IUC) and their duration of use, underlying diseases, and duration of hospital stay. Of these, the major risk factor is IUC duration of use[2-5].

Nosocomial UTIs caused by bacteria show sensitivity profiles that vary according to the hospital under analysis. According to Merle et al., *Pseudomonas aeruginosa* and *Enterococcus* spp. were the main pathogens at the Charles Nicolle University Hospitalin in the city of Rouen, France[6]; Olowu et al.,[7] in turn, reported *Klebsiella* spp. and *Staphylococcus aureus* as being the most frequent agents in a study done at the Obafemi Awolowo University Hospital in Nigeria; Almeida et al.,[8] mentioned *Escherichia coli* and *Klebsiella* spp as the most frequent bacterial agents at the Presidente Prudente University Hospital in the state of São Paulo, Brazil. Almeida et al., [8] argue that each institution should have its own map of UTI etiologic agents, as well as their sensitivity profile to antimicrobials, for an improved therapeutic assistance.

UTIs can affect both the lower urinary tract, causing cystitis that may be associated with dysuria, urinary frequency, urinary urgency and suprapubic pain, as well as the upper urinary tract, causing pyelonephritis with high fever, chills, nausea, vomiting and kidney pain; they may also be asymptomatic[4,9]. In the face of a clinical suspicion, urine culture with antibiogram is the gold standard complementary exam for etiology and sensitivity diagnosis, guiding the choice of antibiotics. However, sensitive antibiotics are often not used, even after the urine culture results have been obtained[10].

This study aims to analyze the bacteria involved in nosocomial UTIs and their sensitivity profile, in addition to other variables such as sex, age, symptoms, indwelling urinary catheter (IUC) duration of use, cause of hospitalization, use of sensitive antibiotics according to the antibiogram report, and duration of hospital stay.

METHODS

A retrospective study based on the analysis of positive urine culture reports (from 100,000CFU/mL) for nosocomial infection was performed, covering the years 2009-2011, which had been previously selected by the Hospital Infection Control Committee at Lauro Wanderley University Hospital in the city of João Pessoa, Paraíba State, Brazil. Nosocomial infection was defined as the onset of infection after 48 hours of hospitalization. Repeated urine cultures from the same patient with the same bacteria and sensitivity profiles were excluded. After patient selection, the study variables were obtained from medical records. The symptoms were defined according to the presence or absence of UTI-related symptoms. Reasons for hospitalization were grouped according to the ICD-10 of the International Classification of Symptoms. Ceftazidime, Cefepime Cefotaxime were classified as broad-spectrum cephalosporins. Ciprofloxacin, levofloxacin and norfloxacin were classified as fluoroquinolones.

Statistical analysis was performed through the SPSS 19.0 software for Windows. The chi-square test with Yates correction was used to evaluate the relation between the variables symptoms associated to UTI and antibiotic use after urine culture. Pearson's correlation coefficient was used to assess the time of indwelling urinary catherer (IUC) use and duration of hospital stay, as well as age and duration of hospital stay. $p < 0.05$ was considered to be statistically significant.

RESULTS

The sample included 74 patients with positive urine cultures, 64.9% of whom female and 35.1% male, with a mean of 51±22 years; 58.1% of the patients were over 50 years of age. The reason for hospitalization which showed the highest hospital UTI frequency was either related to the nervous system or the gastrointestinal apparatus, each amounting to 23% (Table 1). Clinical pathologies (87.8%) prevailed over those of surgical nature (Table 2). The average hospital stay was 56.7 days. 51.4% of the patients used indwelling urinary catheters (IUC), averaging 31.6±26.3 days of use, 54% of whom used them for over a 30 days period; 41.9% of patients were symptomatic and 52.7% of patients were prescribed antibiotics, according to the report. *K. pneumoniae* and *E. coli* represented, respectively, 32.4% and 28.4% of cases (Table 3). Amikacin, Gentamycin, Cefoxitin, piperacillin-tazobactam, Imipem, Meropenem and Ertapenem showed ≥50% sensitivity (Table 4).

There was a correlation between UTI-associated symptoms and antibiotic use following urine culture (p=0.02), so that symptomatic patients were given antibiotics. There was a correlation between IUC period of use and duration of hospital

Table 1. Reasons for Hospitalization of patients with nosocomial UTI at the Lauro Wanderley University Hospital, João Pessoa, Paraíba State, Brazil

ICD-10	Percent (%)
Diseases of the Nervous System	23.0
Diseases of the Gastrointestinal Apparatus	23.0
Diseases of the Genitourinary Apparatus	16.2
Endocrine, Nutritional and Metabolic Diseases	12.2
Disease of the Musculoskeletal and Connective Tissue System	12.2
Diseases of the Circulatory System	9.5
Diseases of the Blood and Hematopoietic Organs	4.1

Table 2. Nosocomial UTI-related pathologies at the Lauro Wanderley University, Hospital, João Pessoa, Paraíba State, Brazil

Pathology	Percent (%)
Clinical	87.8
Surgical	12.2

stay (p=0.04), (rho=0.3), inasmuch as ICU use prolonged hospital stay. There was no correlation between age and duration of hospital stay (p=0.1).

DISCUSSION

The epidemiological profile of patients with community-acquired UTIs is different from those of nosocomial origin, though there are some similarities. As to the former, it is known

Table 3. Bacteria associated to nosocomial UTIs at the Lauro Wanderley University Hospital, João Pessoa, Paraíba State, Brazil

Bacteria	Percent (%)
Klebsiella pneumoniae	32.4
Escherichia coli	28.4
K. oxytoca	6.8
Enterobacter spp.	6.8
Pseudomonas aeruginosa	5.4
Acinetobacter spp.	5.4
Proteus mirabilis	5.4
Providencia spp.	4.1
Proteus vulgaris	2.7
Staphylococcus aureus	1.4
Morganella morganii	1.4

Table 4. *Klebsiella pneumoniae* (n=24) and *Escherichia coli* (n=21) sensitivity profile to antibiotics tested in the 2009-2011period at the Lauro Wanderley University Hospital, João Pessoa, Paraíba State, Brazil

Antibiotic	*K. pneumoniae*	*E. coli*
Ampicillin	0/13	21.4/14
Amikacin	70/20	93/14
Gentamycin	50/16	50/10
Tobramycin	16.7/6	83.3/6
Aztreonam	33.3/18	58.3/12
Imipenem	93.3/15	100/19
Meropenem	95.5/22	100/21
Ertapenem	88.9/9	100/9
Cefazolin	25/4	50/4
Cefalotin	26.7/15	27/13
Cefoxitin	68.4/19	100/15
Ceftazidime	42.9/7	57.1/7
Cefotaxime	31.3/16	60/15
Cefepime	33.3/15	57.1/7
Nalidixic acid	18.2/11	22.2/9
Ciprofloxacin	41.7/12	26.7/15
Norfloxacin	52.6/19	40/20
Levofloxacin	58.8/17	44.4/9
Nitrofurantoine	22.2/18	80/15
Sulfamethoxazole- trimethoprim	18.8/16	44.4/9
Tetracyclin	16.7/6	45.5/11
Piperacillin-tazobactam	60/15	91/11
Chloramphenicol	50/2	26.7/15
Polymyxin-B	-	-

Percent/Total testing.

that women over 50 years of age bearing underlying clinical diseases are the main risk group for UTIs[11]. However, hospital originated UTIs may be either more frequent in men[5,6,8,12] or in women[3,13], depending on the study, although these infections have a greater prevalence in patients over 50 years in both sexes, as well as in patients with clinical pathologies[2,3,5,8]. Despite the fact that the latter are more closely related to nosocomial UTIs than surgical pathologies, which was confirmed by this study and is also in agreement with Stamm's (1999) findings, no associations with the severity of the condition were found[2]. In the present study, most nosocomial UTI cases were related to females over 50 years of age and the occurrence of clinical underlying diseases.

IUC use and duration of use are the main risk factors for nosocomial UTIs (2). A single catheterization is associated with a risk of UTI development of up to 2%, and the cumulative risk is as much as 5% per day[5]. When a patient gets a UTI, daily costs can be as high as US $ 558 per patient[14]. An alarming fact is that up to 38% of physicians may be unaware that their patients are being catheterized, which contributes for the catheter to be kept longer than necessary[5]. Therefore, hospitalized patients may be catheterized for an unnecessary period of time, with a greater risk of infection, increased hospital costs and mortality[14,15].

Gram negative bacteria account for most UTIs. Of these, *E. coli* is most often connected with UTIs of varied origins[2,3,11,16]. However, *K. pneumoniae* is becoming more and more relevant as the main etiology of nosocomial UTIs[7,8,16,17]. The alternating etiologic pattern has practical implications, once the selection of empirical antibiotic coverage prior to the urine culture report should cover *K. pneumoniae* strains. Nevertheless, antibiotic selection should be carefully assessed, as a major concern over these bacteria lies in the selection of KPC-producing ones (carbapenemase-producing *K. pneumoniae*), which are associated with increased morbidity and mortality rates[18].

In a study performed in Spain with community and hospital urine cultures, Piñero-Acin et al.,[19] reported that 52.8% of positive urine cultures were from symptomatic patients, and that 51.3% of the patients had received suitable antibiotics according to the reports. Although the present study included only hospitalized patients, the data of the two studies are similar, inasmuch as in the present study 41.9% of the patients were symptomatic and 52,7% of the patients were administered antibiotics according to reports. Therefore, it becomes evident that the non-use of sensitive antibiotics, even after the results of the urine culture have been obtained, is common[10].

In relation to broad-spectrum cephalosporins for *E. coli*, Leblebicioglu, Esen[20] from Turkey reported a 75.4% sensitivity; Almeida et al., from São Paulo, Brazil, 100%, and this study, 78.6%[8]. However, when antibiotics from the broad-spectrum cephalosporin group were evaluated isolatedly, Cefotaxime showed a 60% sensitivity in our study, as contrasted to a 92% sensitivity obtained in a study by Dias Neto et al.,[21] from São Paulo, Brazil. Upon analyzing fluoroquinolones for *K. pneumoniae*, Leblebicioglu, Esen[20] reported 59.4 sensitivity, Almeida et al.,[8] 14.4%, as compared to the 50% sensitivity found in this study. In the present study, Levofloxacin obtained the highest sensitivity within its group - 58.8% - as contrasted

to 60% reported in a study by Dias Neto et al.[21]. As it can be perceived, the sensitivity profile varies according to the hospital under analysis. Studies conducted in Brazil, however, point out that *E. coli* is quite sensitive to broad-spectrum cephalosporins, while fluoroquinolones show wide variance for *K. pneumoniae*, ranging from 14.4% to 60%.

As the selection of empiric antibiotic therapy for nosocomial UTIs should take into account the etiologic and sensitivity profile in each hospital, and as there are hospitals where this profile is not analyzed, and in view of the fact that *K. pneumoniae* has increased its prevalence in nosocomial UTIs, better therapeutic care is recommended while the urine culture result is being awaited. In community-acquired infections, there is the recommendation to use fluoroquinolones when *E. coli* strains - the most frequent pathogen in UTIs - show >22% resistance to trimethoprim-sulfamethoxazole[22]. Nevertheless, there is no recommendation for the nosocomial UTI cut-off point. The authors of this study have chosen to establish a ≥50% sensitivity cut-off point to recommend empirical antibiotic therapy. Thus, the antibiotics which could cover both bacteria are Amikacin, Gentamycin, Cefoxitin, Piperacillin-tazobactam, Imipem, Meropenem and Ertapenem. Due to KPC concern, the use of Amikacin, Gentamycin, Piperacillin-tazobactam and Cefoxitin is recommended. Except for Piperacillin-tazobactam, which has only been tested in the present study, the other suggested antibiotics have also obtained ≥50% sensitivity in a study by Dias Neto et al.,[21] correspondence, ie, the same as that in this study.

CONCLUSION

Female patients over 50 years of age with clinical disease originated in the nervous system or the gastrointestinal apparatus using IUCs for over a 30 day period with an average duration of hospital stay of 56.7 days are more likely to develop nosocomial UTIs. Among the most frequent bacteria related to nosocomial UTIs at Lauro Wanderley University Hospital are *Klebsiella pneumoniae* and *Escherichia coli*. amikacin, gentamycin and cefoxitin are feasible and possible options for empirical antibiotic therapy the two most prevalent bacteria. Because patients who have symptoms will certainly be prescribed antibiotics, asymptomatic patients having such epidemiological characteristics should get more attention from the medical team.

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