Prospective study analyzing risk factors and characteristics of healthcare-associated infections in a Urology ward

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Purpose: Healthcare-associated infections (HAIs) in urological patients have special features due to specific risk factors. Our objective was to evaluate the characteristics and risk factors for HAIs in patients hospitalized in a Urology ward.

Materials and Methods: We evaluated prospectively, from 2012 to 2015, the incidence, types and risk factor for HAIs, microbiological and resistance patterns.

Results: The incidence of HAIs was 6.3%. The most common types were urinary infections (70.5%) and surgical site infections (22.1%). Univariate analysis showed an increased risk of HAIs among patients with American Society of Anesthesiologists physical status classification system III–IV (odds ratio [OR], 1.39; p<0.001), immunosuppression (OR, 1.80; p=0.013), previous urinary infection (OR, 4.46; p<0.001), and urinary catheter before admission (OR, 1.74; p<0.001). The surgical procedures with the highest incidence of HAIs were radical cystectomy (54.2%) and renal surgery (8.7%). The most frequently isolated microorganisms were Escherichia coli (25.1%), Enterococcus spp. (17.5%), Klebsiella spp. (13.5%) and Pseudomonas aeruginosa (12.3%). Enterococcus sp was the most common microorganism after radical cystectomy and in surgical site infections, E. coli showed resistance rates of 53.5% for fluoroquinolones, 9.3% for amikacin. The percentage of extended-spectrum betalactamase producing E. coli was 24.7%. Klebsiella spp. showed resistance rates of 47.8% for fluoroquinolones, 7.1% for amikacin and 4.3% for carbapenems. Enterococcus spp showed resistance rates of 1.7% for vancomycin and; P. aeruginosa of 33.3% for carbapenems and 26.2% for amikacin.

Conclusions: Comorbidities, previous urinary infections, and urinary catheter are risk factors for HAIs. The microorganisms most commonly isolated were E. coli, Enterococcus and P. aeruginosa. Prospective monitoring may decrease the incidence of infections.

Keywords: Hospital Urology Department; Infection control; Multiple drug resistance; Surgical wound infections; Urinary tract infections

INTRODUCTION

Healthcare-associated infections (HAIs) are those infections in patients receiving medical treatment in a healthcare facility. HAIs include hospital-acquired infections and some patients receiving healthcare treatment...
on an outpatient basis. These 2 types of infections have different microbiological patterns and report higher resistance rates than community-acquired infections [1-3]. Finally, a worrisome aspect is the increasing isolation of Enterobacteriaceae producing extended-spectrum beta-lactamases (ESBL) and others multidrug-resistant microorganisms [4].

Patients hospitalized in a Urology ward showed a higher prevalence of urinary catheterization in comparison with those in other department and urologic surgery is performed in most of them. Urinary catheter and surgery are well-established risk factors for infections [5]. Furthermore, surgery that requires manipulation of the urinary tract is commonly performed. Therefore, infections in patients hospitalized in a Urology ward may show specific characteristics regarding type of infections, microbiological patterns, and resistance rates.

Our purpose was to analyze the incidence, risk factors and characteristics of HAIs in patients hospitalized in a Urology ward.

**MATERIALS AND METHODS**

We carried out a prospective observational study for four years (2012 to 2015) to review HAIs. A database was designed to collect and analyzed the infections in our Urology Department. The database included comorbidities, risk factors and microbiological characteristics of all patients admitted in the Urology ward. Our objectives were stated at the beginning of the study and the research was initiated in 2012.

The study excludes patients younger than 16 years old and those admitted for a renal transplantation because they are hospitalized in the Pediatric and Nephrology ward, respectively.

The study analyzed the incidence, type and risk factors for HAIs, the microbiological characteristics and resistance to antibiotics. Moreover, we evaluated the appropriateness of antibiotic and the death rate.

We used the definition of HAIs according to Friedman criteria as an infection that occurs 48 hours after hospital admission and those in patients receiving dialysis, chemotherapy, outpatient intravenous therapy, resided in a long-term care facility or, hospitalized in the preceding 90 days [23,6]. Both HAIs and hospital-associated infections differ to community-associated infections in term of microbiological data and susceptibility to antibiotics [7]. Our article focused on hospital-acquired infections in a Urology Ward. We also included in our study patients admitted from emergency with an infection related to a previous hospitalization in urology.

Patients with negative or contaminated cultures were considered as HAIs if there were symptoms compatible with infection such as fever, dysuria, lumbar or suprapubic tenderness for urinary infections. Surgical site infections (SSI) were defined as those infections that occurred after surgery in the place where the surgery took place and included superficial incisional, deep incisional or organ space SSI according to CCD criteria [8]. Pathogen identification and antimicrobial susceptibility testing were performed according to Clinical and Laboratory Standard Institute recommendations [9].

Antibiotic prophylaxis was routinely used before surgical procedure according to a protocol approved by our center. In brief, we used cephalosporins in the induction of anesthesia before open, laparoscopic or endourologic clean-contaminated surgery in the urinary tract such as transurethral resections and prostatectomies. In patients with an indwelling urinary catheter or risk factors, we recommended perioperative treatment for one day. When the surgery required bowel management, we used gentamicin and vancomycin. In case implantation of prosthetic devices such as artificial urinary sphincter or penile prosthesis, we recommend antibiotic treatment during at least 3 days.

We collected demographic characteristic and risk factors for infections such as age, sex, hypertension, diabetes mellitus, heart disease, liver disease and immunosuppression and American Society of Anesthesiologists (ASA) physical status classification. We also reviewed urological factors such as prior urinary infection, urinary catheterization, and surgery during the hospitalization.

The research was a prospective investigation, and it does not affect the daily management. Therefore, informed consent was not required. However, informed consent was required for any diagnostic or surgical procedure. The study was approved by the Ethic Committee of Instituto de Investigación Hospital 12 de Octubre.

Categorical variables were reported as frequencies and percentages. Continuous variables are expressed as mean and standard deviation. The association between demographic variables and risk factors for HAIs was assessed using chi-square test or Fisher exact test for qualitative variables. Continuous variables were compared using the Student t-test or analysis of variance with Bonferroni as a posthoc test. All possible risk factors were examined by univariate analysis. A multivariable analysis using a binary logistic regression was performed to analyze factors associated with a higher risk of HAIs, including those variables with a p-value less than 0.05.
than 0.05 in the univariate analysis. The results are shown as odds ratio (OR) and 95% confidence intervals (95% CI). Statistically significance was defined as a 2-tailed p-value less than 0.05. Statistical analysis was carried out using the IBM SPSS Statistics ver. 23.0 (IBM Co., Armonk, NY, USA).

RESULTS

Among 6,546 patients hospitalized in our Urology ward, 415 (6.3%) reported some type HAI. The incidence of HAIs decreased from 7.3%–65% in 2012–2014 to 4.8% in 2015. Table 1 summarizes the demographic characteristic and risk factor.

In 70.6% cases the type of HAI was urinary tract infection. SSI and venous catheter-associated bacteremia accounted 22.2% and 6.3%, respectively. The percentage of urinary infections among HAIs increased from 66% in 2012 and 2013 to 80% and 71.2% in 2014 and 2015, respectively. Conversely, SSI decreased from 30% and 24% in 2012 and 2013 to 14.2% and 18% in 2014 and 2015. Four hundred twenty-eight HAIs were reported in 415 patients, more than one type of HAIs was more commonly found after cystectomy (The evolution of each type of HAIs over the time is summarized in Table 2).

The univariate analysis showed that higher incidence of infections among patients with older age (OR, 1.01; 95% CI, 1.004–1.016; p=0.001), ASA physical status classification III–IV (OR, 1.45; 95% CI, 1.25–1.69; p<0.001), arterial hypertension (OR, 1.26; 95% CI, 1.03–1.54; p=0.020), immunosuppression (OR, 2.08; 95% CI, 1.44–3.00; p<0.001), previous urinary infection (OR, 3.44; 95% CI, 2.32–5.12; p<0.001), and indwelling urinary catheter before admission (OR, 2.31; 95% CI, 1.87–2.86; p<0.001) or during the hospitalization period (OR, 1.62; 95% CI, 1.25–2.10; p<0.001). Multivariate logistic regression analysis showed that higher ASA physical status classification (OR, 1.39; 95% CI, 1.15–1.67; p<0.001), immunosuppression (OR, 1.80; 95% CI, 1.13–2.88; p=0.013), prior urinary tract infection (OR, 4.46; 95% CI, 2.32–8.57; p<0.001), and indwelling urinary catheter prior admission (OR, 1.74; 95% CI, 1.32–2.30; p<0.001) were independent risk factors for HAIs (Table 3).

A surgical procedure was performed in 4,952 (75.6%) of patients. Among them, the incidence of HAIs was 4% (110 out of 2,737) after transurethral surgery, 7.4% (23/312) after

| Table 1. Descriptive analysis of demographic characteristics and risk factors of patients admitted to the Urology ward (2012–2015) |
|-----------------|-----------------|-----------------|----------|
|                  | Patients who did not report any HAI during hospitalization (n=6,131) | Patients who reported any HAI during hospitalization (n=415) | p-value |
| Patients admitted to the Urology ward (%) | 93.7 | 6.3 |          |
| Demographics | | | |
| Age (y) | 63.8±16.74 | 66.4±14.89 | 0.001 |
| Sex (%), male:female | 74.7%:25.3% | 77.1%:22.9% | 0.274 |
| ASA | | | |
| I | 613/4,688 (13.1) | 27/291 (9.3) |          |
| II | 2,351/4,688 (50.1) | 114/291 (39.2) |          |
| III | 1,459/4,688 (31.1) | 122/291 (41.9) |          |
| IV | 265/4,688 (5.7) | 28/291 (9.6) |          |
| Comorbidities | | | |
| Arterial hypertension | 2,683/6,131 (43.8) | 206/415 (49.6) | 0.020 |
| Diabetes mellitus | 1,088/6,131 (17.7) | 76/415 (18.3) | 0.770 |
| Heart disease | 1,211/6,131 (19.8) | 96/415 (23.1) | 0.095 |
| Liver disease | 254/6,131 (4.1) | 24/415 (5.8) | 0.109 |
| Immunosuppression* | 260/6,131 (4.2) | 35/415 (8.4) | <0.001 |
| Urologic risk factors | | | |
| Urinary lithiasis | 1,143/6,131 (18.6) | 57/415 (13.7) | 0.012 |
| Prior urinary infection | 145/6,131 (2.4) | 32/415 (7.7) | <0.001 |
| Urinary catheter before admission | 1,105/6,131 (18.0) | 140/415 (33.7) | <0.001 |
| Urinary catheter during hospitalization | 4,553/6,131 (74.3) | 342/415 (82.4) | <0.001 |
| Surgery during hospitalization | 4,652/6,131 (75.9) | 300/415 (72.3) | 0.099 |
| Hospitalization period (d) | 5.3±6.10 | 17.3±16.58 | <0.001 |

Values are presented as means±standard deviation or number (%) unless otherwise indicated.

HAI, Healthcare-associated infection; ASA, American Society of Anesthesiologists physical status classification system.

*Immunosuppression includes patients who suffer hematological neoplasms such as leukemia, lymphoma, multiple myeloma, acquired immunodeficiency syndrome and treatment with immunosuppressant drugs.
open prostatic surgery, 8.7% (33/381) renal surgery and 54.2% (39/72) following radical cystectomy. The highest incidence of HAI s after cystectomy was reported in 2012 and 2013 (78.6%–68.7%) in comparison with 50%–31.8% in 2014–2015.

The most commonly isolated pathogens were Escherichia coli (25.1%), followed by species of Enterococcus (17.5%), Klebsiella (13.5%) and Pseudomonas (12.3%). Staphylococcus aureus and Candida were isolated in a 6.7% and 5.6% of positive cultures, respectively (Fig. 1). No microorganisms were isolated in 31.4% patients. The isolation of Klebsiella spp. increased over the time, representing 17% of positive cultures in 2015. Furthermore, Klebsiella spp. were the most
frequently isolated microorganism in patients with diabetes mellitus, liver disease, immunosuppression and prior urinary infection. In patients with SSI following abdominal or renal surgery, the most commonly isolated microorganism was *Enterococcus*, more frequently after radical cystectomy.

*E. coli* showed resistance rates of 34.9% for amoxicillin+ betalactamase inhibitor, 53.5% for fluoroquinolones, 92.3% for amikacin. All cultures where *E. coli* were isolated showed susceptibility to carbapenems. *Klebsiella* spp. showed resistance rates of 39.3% for third generation cephalosporins and 4.4% for carbapenems. Among cultures where *E. coli* was isolated, 24.7% were ESBL-producing bacteria and 34.7% whether *Klebsiella* was isolated.

*Enterococcus* spp. showed resistance rates of 26.7% for amoxicillin/ampicillin, 47.8% for fluoroquinolones and 1.7% for vancomycin. *Pseudomonas aeruginosa* showed resistance rate of 40.5 for piperacillin/tazobactam, 33.3% for carbapenems and 26.2% for amikacin. Table 4 summarized the resistance rate for the most frequently isolated pathogens.

Empirical treatment was adequate according to antibiogram in 90.7%. However, if ESBL-producing bacteria were isolated, the appropriateness of empirical treatment decreased to 81.2%. Isolation of ESBL-producing bacteria or *Enterococcus* and patients who underwent radical cystectomy showed a higher rate of inappropriate empirical antibiotic treatment.

The mortality rate among patients who suffered from HAIs was 2.4% in comparison with 0.3% in those who no suffer from HAIs. Risk factors for mortality were immunosuppression (OR, 6.7) and inadequate empirical antibiotic treatment (OR, 22). Mortality causes in patients who suffered from HAIs were related to infection in 8 out of 10.

**DISCUSSION**

HAIs are a worrisome problem for health systems [3,6]. However, few articles evaluated this topic in urological patients. Among these, it should be pointed of the European Society of Infections in Urology (ESIU-EAU) which reviewed HAIs in Urology departments since more than ten years ago [5,10,11]. Such studies are essential as HAIs in urological patients have some special features such as higher incidence of urolithiasis, lower urinary tract symptoms, higher prevalence of previous urinary infections. All these factors suppose higher resistance to antibiotics among urological patients [12]. Furthermore, patients admitted in Urology ward frequently had an indwelling urinary catheter. In patients hospitalized in a general ward, 12%–16% had a urinary catheter in comparison with 74% in our series [13]. On the other hand, among patients in a Urology ward, a surgical procedure is frequently carried out, 75% according to our data. Endourological transurethral procedures constitute 55% of surgeries performed. Therefore, urinary infections are the most common type of HAIs (70%). Data from non-Urology departments showed that urinary infections represent 15%–57% of HAIs [14,15]. Both, urinary infections

| Resistance pattern | Enterobacteriaceae (n=135) | E. coli (n=86) | Klebsiella (n=46) | Enterococcus (n=60) | Pseudomonas (n=40) |
|--------------------|-----------------------------|----------------|-------------------|---------------------|---------------------|
| Ampicillin/Amoxicillin | 80.0%                       | 74.4%          | 93.5%             | 26.7%               | -                   |
| Amoxicillin + beta-lactamase inhibitor | 45.2%                       | 34.9%          | 54.3%             | 7.3%                | -                   |
| Piperacillin/Tazobactam | -                          | -              | -                 | 40.5%               | -                   |
| Cefuroxime | 51.1%                       | 37.2%          | 54.3%             | -                   | -                   |
| Ceftriaxone | 39.3%                       | 29.1%          | 52.2%             | -                   | -                   |
| Ceftazidime | -                          | 22.4%          | 34.9%             | -                   | 40.5%               |
| Cefepime | 30.4%                       | 22.1%          | 50.0%             | -                   | 43.9%               |
| ESBL-producing bacteria | 34.3%                       | 24.7%          | 47.8%             | -                   | -                   |
| Carbapenems | 4.4%                        | 0.0%           | 4.3%              | -                   | 33.3%               |
| Fluoroquinolones | 46.3%                       | 53.5%          | 47.8%             | 50.0%               | 54.8%               |
| Co-trimoxazole | 34.3%                       | 38.7%          | 35.6%             | -                   | -                   |
| Gentamicin | 21.8%                       | 22.1%          | 31.1%             | 44.1%               | 38.1%               |
| Amikacin | 8.6%                        | 9.3%           | 7.1%              | -                   | 26.2%               |
| Fosfomycin | 18.0%                       | 7.1%           | 28.9%             | -                   | -                   |
| Nitrofurantoin | -                          | 6.0%           | 29.5%             | -                   | -                   |
| Vancomycin | -                          | -              | 1.7%              | -                   | -                   |

*E. coli, Escherichia coli; ESBL, extended-spectrum betalactamase.*
catheter, and surgical procedure are well-established risk factors for HAIIs [13]. Surgery of the urinary tract and urinary catheter must be evaluated together. Furthermore, 19% had an indwelling catheter before admission. Indwelling urinary catheter and the duration of catheterization are the main risk factors for healthcare-associated urinary tract infections with the higher incidence among patients with urinary catheter before admission (OR, 1.74). Patients with urinary catheter commonly develop bacteriuria with a daily risk of 5% [16]. Although antimicrobial treatment is not required in case of asymptomatic catheter-bacteriuria, adequate perioperative prophylaxis is needed before surgery. Prior transurethral surgery, a urinary culture should be advised to tailor the antibiotic prophylaxis or treatment before surgery [17].

Apart from, urinary catheter and urological surgery, some characteristics increased the risk of HAIIs. Our results are in concordance with other studies that demonstrated that comorbidities such as immunosuppression, diabetes, obesity, liver dysfunction, malnutrition are related to an increased risk of HAIIs [16,18]. In our series, higher ASA physical status classification is associated with higher incidence of HAIIs, 45% among ASA I–II and 8% in ASA III–IV. Moreover, longer hospital stay is a risk factor for HAIIs [17]. Previous antibiotic treatment and urinary infections are also risk factors to focus due to a higher incidence of infection and a different microbiological pattern. According to our data, in patients with previous urinary infection, the most frequently isolated microorganism is Klebsiella. It has been described that when several risk factors are associated, there is an increased risk of isolation pathogens with higher resistance rate such as Klebsiella spp. or Pseudomonas spp. or Candida spp. [16].

Our study demonstrated a reduction in the incidence of infection from 7.3% in 2012 to 4.8% in 2015. Several reasons may explain the evolution of the incidence of infections. In our opinion, the main reason is due to we are monitoring infections. Doctors, nurses and all personnel working with patients are aware of infections, and different measures are implemented to prevent infections [5]. Among them, a correct hand hygiene and avoid rings or watches. On the other hand, urinary catheter control has improved with prompt removal and reducing unnecessary placement. A program reviewing the appropriateness of urinary catheter has demonstrated that decrease the percentage of catheterization and the prevalence of infections [13]. Otherwise, we review our results periodically, so we are informed about our infection rates and we can design strategies to prevent them. Moreover, we identify some risk factors for infections that they are also related to specific microbiological patterns. The effect of our research monitoring HAIIs is demonstrated with the evolution of patients with suspicion of infection where cultures were not taken. The percentage of patients without culture decreased from 61% in 2012 to 0% and 35% in 2014 and 2015, respectively. Finally, antimicrobial prophylaxis is a key point as is used to prevent infections after diagnostic or therapeutics procedures. Perioperative prophylaxis must be chosen to take into account the type of surgery, the contamination burden, and some aspects related to specific risk factors of the patient, such as comorbidities, immunosuppression, indwelling catheters or a previous urinary infection [11].

Among the different types of HAIIs, SSIIs reported the greatest reduction in the number of infections. The total number of SSIs were 35 in 2012, 26 in 2013, 15 in 2014 and, 17 in 2015. Apart from monitoring and be aware of infections, others reason could explain the reduction in SSIs. First of all, a laparoscopic approach is performed more frequently. Several studies demonstrated that laparoscopic nephrectomy and cystectomy are associated with lower rates of SSIs [19]. Secondly, hand antisepsis using alcohol-based solutions may reduce the incidence of SSIs [20]. Radical cystectomy reported the highest incidence of HAIIs, up to 50% in our series, and SSI is the most common type of HAIIs. Kyoda et al. [21] demonstrated a reduction in the incidence of SSI from 32% to 18% with the standardization in suturing, drain removal and surgical dressing management. Finally, it should be pointed out that there is a higher incidence of infections after renal surgery in comparison with transurethral surgery. Although a laparoscopic approach is frequently performed, open surgery is required in some cases. HAIIs after renal surgery are more frequently after an open approach. Currently, open approach is indicated in patients with a complex surgery, and it is associated with risk factors for HAIIs such as higher amount of bleeding, longer operating time, longer hospitalization and in some cases, a contaminated surgical filed [22]. Moreover, although urinary catheter is removed earlier after renal surgery than in transurethral surgery, drainage is usually used. Therefore, it is necessary to remove all drainages as soon as possible, and the management of the wound must be optimized.

The microorganism most commonly isolated is Enterobacteriaceae, 59% in our series. Among them, E. coli is the most frequent, 40% according to Global Prevalence Study on Infections in Urology and 25% in our department [10,23]. Data from Study on the Prevalence of nosocomial infections in Spain study carried out in several hospitalization wards, showed that E. coli accounted 15%–17% of positive cultures
Healthcare-associated infections in urology

Enterococcus, Klebsiella, and Enterobacteria 33% [24]. Enterococcus is isolated in 17.5% and is the most common microorganism in patients with SSIs after abdominal surgery [18,25]. When Enterococcus is suspected antibiotics such as vancomycin are recommended as high susceptibility is achieved [26]. Furthermore, Klebsiella spp. and Pseudomonas are commonly isolated, 13.5% and 12.3% in our series, respectively. According to GPIU data, Klebsiella spp. and Pseudomonas accounted 11.1% and 10.8% [23]. The main awareness related to the isolation of non-E. coli bacteria are the high resistance rates. For instance, Klebsiella spp. resistant to carbapenems were found. Moreover, if previous urinary infection, diabetes mellitus, liver disease or immunosuppression; Klebsiella was the most frequently isolated pathogen.

The main point of worrisome regarding HAIIs is the high resistance rate. Both, our data, and GPIU reported resistance to quinolones and third generation cephalosporins up to 50% [11,23]. The highest resistance rate is found in South Europe, Asia, and South America [23,27]. The resistance rate is related to the prescription of antibiotics, and an appropriate selection of antibiotics may reduce resistances [28]. This point may be demonstrated with lower resistance to aminoglycosides in our department in comparison with GPIU. In our center, aminoglycosides are not usually prescribed as prophylaxis before surgery. Multiresistant pathogens are frequently isolated in a Urology ward; ESBL-producing bacteria were found in 34.3% of cultures where Enterobacteriaceae were isolated. The highest percentage was found among Klebsiella, 50%. Isolating of ESBL-producing bacteria is a key point in prevention of HAIIs as frequently cross-resistance is found. Risk factors described for ESBL-producing bacteria are older age, male sex, diabetes mellitus, urinary catheter and prior urinary infections [29,30]. Therefore, rationalization of antibiotic usage and select empirical antibiotics adequately is essential to achieve better outcomes. Observational studies are useful to improve outcomes and reduce the incidence of HAIIs. For instance, in our department, the incidence of HAIIs was 73% at the beginning of the research and 42% in 2015.

One of the strengths of the study is that we used a clinical definition of HAIIs, including patients with sterile cultures. Therefore, a more accurate estimation of the incidence of HAIIs is reached. Lower incidences are reported if only positive cultures are taking into account, and higher incidence is found in studies carried out evaluating HAIIs in one day due to patients with and infections have longer hospitalization period [5,10].

Our study also entails some limitations. First of all, it was carried out in one single center. However, it included patients during a period of 4 years, and the results may be extrapolated to similar hospitals in the area. On the other hand, patients who suffer HAIIs after discharge may be not included. However, HAIIs is developed after discharge and the patient required admission to our hospital; the HAIIs was associated with the previous hospitalization in the Urology ward.

**CONCLUSIONS**

Prospective monitoring of HAIIs and an adequate knowledge of the microbiological patterns may decrease the incidence of infections in patients hospitalized in a urology ward. Comorbidities, higher ASA physical status classification, previous urinary infections a urinary catheter are risk factors for HAIIs. The most common microorganism isolated is E. coli. However, Enterococcus, P. aeruginosa, and Klebsiella are commonly found. Klebsiella spp. were the most frequently isolated microorganism in patients with diabetes mellitus, liver disease, immunosuppression and prior urinary infection. Enterococcus is the most common pathogen in those with SSIs and after radical cystectomy.

**CONFLICTS OF INTEREST**

The authors have nothing to disclose.

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