URINARY TRACT INFECTIONS IN HOSPITALIZED PATIENTS

INFECCIONES URINARIAS EN PACIENTES HOSPITALIZADOS

INFECÇÕES URINÁRIAS EM PACIENTES HOSPITALIZADOS

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Las infecciones urinarias constituyen una de las principales causas de infecciones y representan uno de los motivos de internación más frecuentes a nivel mundial. El abordaje terapéutico adecuado de esta patología se basa en poder instaurar un tratamiento antibiótico adecuado lo más pronto posible. La dificultad que implica esto, es que con el paso de los años las bacterias responsables de las infecciones urinarias se están volviendo cada vez más resistentes a los principales antibióticos utilizados. Es por dicho motivo que el conocimiento de que bacterias son responsables de las infecciones urinarias y de cuales antibióticos serían efectivos para tratarlas en el medio local, serán de gran ayuda para mejorar los resultados en el tratamiento de dicha patología.

Key Concepts

A) ¿Qué se sabe sobre el tema?

- Las infecciones del tracto urinario son una causa importante de morbilidad en la comunidad, constituyendo además uno de los principales motivos de hospitalización.
- Las infecciones urinarias representan la 4° causa más frecuente de infecciones asociadas a la atención de la salud.
- Debido a los cambios constantes de perfiles de susceptibilidad antimicrobiana de los microorganismos responsables de dichas infecciones, es importante conocer su epidemiología local.

B) ¿Qué aporta este trabajo?

- Se trata de un estudio prospectivo de los episodios de infecciones urinarias en pacientes hospitalizados, incluyendo no sólo las infecciones urinarias intrahospitalarias, de las cuales existe mayor bibliografía, sino también las infecciones urinarias adquiridas en la comunidad que requirieron internación.
- Aporta un perfil actualizado de los principales agentes microbiológicos causales de las infecciones urinarias en pacientes hospitalizados en nuestro medio.
- Permite evidenciar los perfiles de resistencia cambiantes de los principales agentes causales de infecciones urinarias en pacientes hospitalizados en nuestro medio, donde existe escasa bibliografía.

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Resumen:

Introducción: Las infecciones del tracto urinario (ITU) constituyen una importante causa de morbilidad, representando uno de los principales motivos de hospitalización y la cuarta causa de infecciones asociadas a la atención sanitaria. Nuestros objetivos fueron determinar la frecuencia de ITU adquirida en la comunidad (ITU-AC) que requirieron hospitalización e ITU asociadas a la atención sanitaria (ITU-AAS), sus factores de riesgo, agentes etiológicos y espectros de susceptibilidad antimicrobiana.
Métodos: Estudio prospectivo y analítico donde se evaluaron todos los episodios de ITU-AC que requirieron internación e ITU-AAS durante el período de noviembre de 2016 a noviembre de 2017 en dos hospitales universitarios.
Resultados: Se identificaron 279 episodios de ITU en pacientes hospitalizados, de los cuales 178 correspondieron a ITU-AC. En ambos grupos, el promedio de edad fue de 60 años, existiendo una mayor proporción de mujeres. Las ITU-AC se asociaron más frecuentemente al antecedente de trasplante renal, ITU recurrente y enfermedad renal crónica, respecto a ITU-AAS. La instrumentación de la vía urinaria en el último mes fue más frecuente en las ITU-AAS (75,2% vs 32,6%, p<0,001). El microorganismo más frecuente fue *Escherichia coli* (62,9% de ITU-AC y 56,4% de ITU-AAS), seguido por *Klebsiella pneumoniae* y *Pseudomonas aeruginosa*. Se aislaron 101 gérmenes multirresistentes de los cuales el 53,5% eran ITU-AC, y se asociaron a hombres, uso de antimicrobianos en los tres meses previos, enfermedad renal crónica e ITU recurrente.
Conclusión: Es de gran importancia para las instituciones conocer el espectro de susceptibilidad antimicrobiana de las ITU para establecer tratamientos empíricos adecuados.

Palabra clave: infecciones urinarias; catéteres urinarios; infecciones comunitarias adquiridas; infección hospitalaria; antiinfecciosos.

Abstract:

Introduction: Urinary Tract Infections (UTI) are an important cause of morbidity in the community, constituting one of the main reasons for hospitalization, and the fourth cause of healthcare-associated infection. The objectives of this study were to determine the frequency of community-acquired UTI (CA-UTI) with need of hospitalization and healthcare-associated UTI (HA-UTI), their risk factors, etiologic agents and their antimicrobial susceptibility spectrum.
Methods: A prospective and analytic study was conducted, in which all admissions regarding CA-UTI with need of hospitalization and HA-UTI were evaluated during the period between 2016 and 2017 in two university hospitals.
Results: A total of 279 episodes of UTI in hospitalized patients were identified and, among those, 178 episodes corresponded to CA-UTI and 101 to HA-UTI. On average, patients were 60 years old in both groups. HA-UTI were more frequently associated with kidney transplant, recurrent UTI and chronic kidney disease compared with CA-UTI. The instrumentation of urinary tract within the previous month was more frequent in HA-UTI (75.2% vs 32.6%, p<0.001). *Escherichia coli* was the most frequent isolated microorganism (62.9% in CA-UTI and 56.4% in HA-UTI), followed by *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. A total of 101 multidrug resistant microorganisms were isolated, of which 53.5% were CA-UTI, and were associated with male patients, use of antimicrobials within the previous three months, chronic kidney disease and recurrent UTI.
Main conclusion: It is of great importance for the institutions to identify the local antimicrobial susceptibility spectrum of UTI in order to stablish adequate empiric treatments.

Keywords: urinary tract infections; urinary catheters; community-acquired infections; cross infection; anti-infective agents.

Resumo

Introdução: As infecções do trato urinário (ITUs) constituem um importante causa de morbidade, elas representam um dos principais motivos de hospitalização e são a quarta causa de infecções associadas à assistência à saúde. Nossos objetivos foram: determinar a frequência de ITUs adquiridas na comunidade (ITUs-AC) que requereram hospitalização e a frequência de ITUs associadas à assistência à saúde (ITUs-AAS), seus fatores de risco, seus agentes etiológicos e os espectros de susceptibilidade antimicrobiana.
Métodos: Trata-se de um estudo prospectivo e analítico no qual foram avaliados todos os episódios de ITU-AC que requereram hospitalização bem como os de ITUs-AAS no período compreendido entre os 2016 e 2017 em dois hospitais.
Resultados: Foram identificados 279 episódios de ITU em pacientes hospitalizados, dos quais 178 corresponderam a ITU-AC. Em ambos os grupos a média etária foi de 60 anos. As ITUs-AC estiveram associadas com maior frequência a transplante renal prévio, a ITU recorrente e a doença renal crônica, no que se refere às ITUs-AAS. A instrumentação das vias urinárias foi mais frequente no último mês no caso das ITUs-AAS (75,2% vs 32,6%, p<0,001). O microrganismo mais frequente foi Escherichia coli (62,9% das ITUs-AC e 56,4% das ITUs-AAS), seguido por Klebsiella pneumoniae y Pseudomonas aeruginosa. Foram isolados 101 germes multirresistentes, dos quais 53,5% eram ITUs-AC e associaram-se a pacientes masculinos, ao uso de antimicrobianos prévio, a doença renal crônica e a ITU recorrente.
Conclusão: Resulta de grande importância para as instituições conhecer o espectro de susceptibilidade antimicrobiana das ITUs para estabelecer tratamentos empíricos adequados.

Palavras chaves: infecções urinárias; cateteres urinários; infecções comunitárias adquiridas; infecção hospitalar; anti-infecciosos.

INTRODUCTION

Urinary tract infections (UTI) are one of the main causes of bacterial infections within the adult population, representing one of the most frequent reasons for consultation worldwide[1]. Even though most of them get ambulatory treatment, a growing percentage require hospitalization for their care. It has been proposed that this could be related to an increase in emergency department consultations of patients with sepsis criteria and a growth in antimicrobial resistance of the causative agents[2,3].

Moreover, UTI represent the fourth most common cause of healthcare associated infections, mainly related to urinary tract instrumentation[4]. This infections lead to an elevated risk of complications and health costs, mainly owing to prolonged hospital stay and need of intravenous antibiotics[5-7]. Other risk factors have been identified, besides urinary catheterization, that increase the risk of healthcare-associated urinary tract infection (HA-UTI). Among them, the most relevant are: length of hospital stay (particularly in intensive care units), diabetes mellitus, above 60 years of age, medical history of urinary tract structural abnormalities, immunosuppression status and prior antibiotic use[5,6].

Within the last decades, the rates of antimicrobial resistance from UTI causative agents has changed, both communities acquired and healthcare associated, particularly due to an increase of multidrug resistant microorganisms (MDR), extended spectrum beta-lactamase (ESBL) producing Enterobacteriaceae and carbapenemase-producing Enterobacteriaceae. This represents an important challenge at the moment of choosing effective empiric therapy[1,8,9]. Hence, it is relevant to understand the local UTI epidemiology and the antimicrobial susceptibility profiles of the causative agents, both in the community and in the hospital setting.

The primary endpoint of this study was to determine the frequency and the risk factors associated to community acquired UTI (CA-UTI) that required admission and HA-UTI, in two third-level hospitals. The secondary endpoints were to determine the frequency of microbiologic isolations and their resistance spectrum in both groups and analyze the risk factors associated with UTI due to MDR microorganisms and catheter associated UTI.

MATERIALS AND METHODS

A prospective analytic study was conducted in two third-level hospital centers, Hospital Privado Universitario de Córdoba and Hospital Raúl Angel Ferreyra, both located in the city of Cordoba, Argentina, in a period between November, 2016 and November, 2017. Both institutions share their electronic medical records, by which all urine cultures are ordered. All positives urine cultures from patients above 18 years of age were obtained through the database of the microbiology laboratory. Their healthcare records were reviewed, and only the patients that met criteria for HA-UTI and also for CA-UTI that required hospitalization were included. All cases of asymptomatic bacteriuria were excluded. Afterwards, epidemiological features from included patients were identified, together with UTI causative agents and their antimicrobial susceptibility profiles. The study was approved by the local ethical review board ("Comité Institucional de Etica de Investigación de Salud [CIEIS]").

Definitions:

- UTI: the patient had to meet the following 2 criteria: A) have at least one of the following signs or symptoms: temperature ≥38° Celsius in a patient below 66 years of age, suprapubic pain (without any other cause), costovertebral angle tenderness or discomfort (without any other cause), urinary urgency, dysuria and frequency of micturition; B) positive urine culture with no more than 2 microorganisms, and at least one of them with growth of more than 100,000 CFU/mL[10].
- CA-UTI: UTI that developed outside hospital setting (at least 48 hours after hospital discharge) or within the first 48 hours after hospital admission[10].
- HA-UTI: UTI not present at the time of admission and that developed after the second day[11].
- Catheter associated UTI: the patient had to meet the following 3 criteria: A) the patient needed to have a urinary catheter placed at least 2 days prior to date of event, and needed to be on site the day of the event or removed the day prior to the event; B) at least one of the following signs or symptoms: temperature ≥38° Celsius, suprapubic pain (without any other cause), costovertebral angle tenderness or discomfort (without any other cause), C) positive urine culture with no more than 2 microorganisms, and at least one of them with growth of more than 100,000 CFU/mL[10].
- Recurrent UTI: patient with at least 3 or more UTI during a period of 12 months, or at least 2 UTI within 6 months[12].
- Abnormalities of the urinary tract: organic, functional or structural anomalies, or placement of devices in the urinary tract [13].
- Urinary tract instrumentation within previous 30 days: insertion of indwelling or intermittent catheters, endourologic procedures (ureteroscopy, urethrocystoscopy, retrograde urethrography, percutaneous nephrostomy or any surgical procedure that changed urinary tract anatomy) performed between 30 days and 48 hours prior to urine culture sampling which defined the episode of HA-UTI.
- Multidrug resistant microorganisms (MDR): bacteria resistant to at least one drug of three or more relevant antimicrobial categories for each species[14]. In the case of Gram negative bacilli, a bacteria was considered to be multidrug resistant if it was resistant to 3 of the following categories: piperacillin tazobactam, cephalosporins, carbapenems, aminoglycosides or fluoroquinolones[15]. In the case of Gram positive microorganisms, it was considered to be MDR: methicillin resistant Staphylococcus sp. and vancomycin resistant Enterococcus sp[16].
- Antimicrobial susceptibility test: The Microbiology Laboratory used as a routine method the automated systems Vitek 2 Compact (bioMérieux, France) and Phoenix 100 (Becton Dickinson, USA) to determine the antimicrobial susceptibility, and mass spectrometry MALDI-TOF Microflex (Bruker, Germany) for species identification. The laboratory integrates with the external quality control program of antimicrobial susceptibility and identification of the "Instituto de Salud ANLIS 'Dr. Carlos Malbrán". The resistance spectrum to the most frequent antibiotics used within hospitalization were analyzed.

- Statistical Analysis: the continuous variables were reported as mean and standard deviation, and their comparison was analyzed with Student's t-test or Mann-Whitney, according to their homogeneity. The categorical variables were reported as numbers and percentages, and analyzed with chi square test or Fisher exact test, according to their expected frequencies. A probability value of <0.05 was considered statistically significant. SPSS 24 statistical software (SPSS, Inc., Chicago, IL) was used to perform the statistical analysis.

RESULTS

A total of 300 hospitalized patients with positive urine cultures were identified during the study period. Among them, 21 patients were excluded due to clinical presentation compatible with asymptomatic bacteriuria; hence, 279 episodes of UTI in hospitalized patients were included. 63.8% of the episodes corresponded to CA-UTI. Both in HA-UTI and CA-UTI, the majority of episodes took place in women, with low pregnancy rate, similar in age, and only one fourth of patients showed urinary tract abnormalities and diabetes mellitus as comorbidities. Patients with CA-UTI had higher frequency of chronic kidney disease, kidney transplant, immunosuppressive therapy within previous 3 months and recurrent UTI. Patients with HA-UTI had higher frequency of chronic obstructive pulmonary disease, urinary tract instrumentation

d admission to intensive care unit within previous 30 days. (Tables 1 and 2).

History of recurrent UTI was more frequent between patients with CA-UTI (32.6% vs 18.8%, p=0.001). Furthermore, patients with HA-UTI had been admitted to intensive care unit in the previous 30 days (43.6% vs 13.5%, p<0.001). As regards the history of urinary tract instrumentation, 75.2% of patients with HA-UTI had a catheterization within previous 30 days, compared to 31.5% with CA-UTI (p<0.001). Moreover, 63.4% of patients in the latter group had a catheterization performed within 72 hours prior to UTI episode, mainly due to intermittent catheter placement (73.43%). All-cause mortality associated with UTI was 8.24%, showing no difference between the groups. (Table 2) The main isolated microorganisms in all UTI episodes were: Escherichia coli (60.57%), Klebsiella pneumoniae (15%) and Pseudomonas aeruginosa (7%), showing no difference between both groups. (Table 3) The antimicrobial resistance from the main Gram negative bacilli are detailed in Table 4. More than 20% of Escherichia coli isolation were resistant to ciprofloxacin and non-carbapenem beta-lactams, except piperacillin tazobactam. The majority of Klebsiella pneumoniae isolations were resistant to all tested antimicrobials, except imipenem, meropenem and amikacin. Similar scenario to what happened with Pseudomonas aeruginosa, observing more antimicrobial susceptibility against amikacin.

Altogether, 101 MDR microorganisms (36.2%) were identified, and 59.4% were in patients with CA-UTI. These patients had more frequency of antimicrobial use within previous 3 months, chronic kidney disease, recurrent UTI, and an admission at least for 48 hours within the previous year. (Table 5) As regards multi-resistant microorganisms, 78 ESBL-producing Enterobacteriaceae (62.8% in patients with CA-UTI), and 9 carbapenemase-producing Enterobacteriaceae (66.7% in HA-UTI).

A total of 98 episodes of catheter associated UTI (35.1%) were identified, most frequently in patients with HA-UTI (59.2% vs 23.8%, p<0.001). Furthermore, catheter associated UTI episodes were mainly related to males, patients with urinary tract abnormalities, active neoplasia and those with intensive care unit admission within the previous 30 days. Moreover, as regards non-catheter associated UTI, a major proportion of transplanted patients and with immunosuppressive therapy were observed. There was no significant difference in the number of MDR microorganisms isolated between both groups (36.7% vs 35.9%, p=0.891). (Table 6).

Table 1. Demographic features and comorbidities of hospitalized UTI patients

	CA-UTI (n=178)	HA-UTI (n=101)	p
Age in years, (mean ± SD)	58.65±20.7	62.78±16.58	0.121
Female sex, n (%)	98 (55.1)	57 (56.4)	0.82
Pregnancy, n (%)	6 (3.4)	1 (0.4)	0.42
Chronic kidney disease, n (%)	63 (35.4)	23 (22.8)	0.028
Kidney transplant, n (%)	44 (24.7)	11 (10.9)	0.005
Immunosuppressive therapy within previous 3 months, n (%)	58 (32.6)	21 (20.8)	0.036
Diabetes, n (%)	44 (24.7)	31 (30.7)	0.27
HIV patients, n (%)	3 (1.7)	0 (0)	0.55
Urinary tract abnormalities, n (%)	51 (28.7)	21 (20.8)	0.14
Kidney stones, n (%)	12 (6.7)	7 (6.9)	0.95
Neoplasia, n (%)	35 (19.7)	29 (28.7)	0.08
Chronic obstructive pulmonary disease, n (%)	10 (5.6)	13 (12.9)	0.034
Liver disease, n (%)	12 (6.7)	6 (5.9)	0.79

UTI: urinary tract infection. CA-UTI: community acquired urinary tract infection. HA-UTI: healthcare-associated urinary tract infection. SD: standard deviation. HIV: human immunodeficiency virus.

Table 2. Associated features in UTI hospitalized patients.

	CA-UTI (n=178)	HA-UTI (n=101)	p
Previous UTI, n (%)			
UTI within previous year	82 (46.1)	32 (31.7)	0.019
Recurrent UTI	59 (32.6)	19 (18.8)	0.001
Antibiotics within previous 3 months, n (%)	**91 (51.1)**	**46 (45.5)**	**0.37**
Hospitalization, n (%)			
During at least 48 h, within the last year, prior to the episode	111 (62.4)	60 (59.4)	0.62
ICU admission within previous 30 days	24 (13.5)	44 (43.6)	<0.001
Urinary tract instrumentation, n (%)			
Urologic procedure within previous 6 months	31 (17.4)	14 (13.9)	0.43
Instrumentation within previous 30 days	58 (32.6)	76 (75.2)	<0.001
Urologic procedure within previous 30 days	3 (1.7)	1 (1.0)	1.00
Urinary catheterization within previous 30 days	56 (31.5)	76 (75.2)	<0.001
Catheterization 72 hours prior to UTI episode	40 (22.5)	64 (63.4)	<0.001
a)Intermittent catheterization within previous 72 h	32 (18.0)	47 (46.5)	<0.001
b) Indwelling catheterization within previous 72 h	8 (4.5)	17 (16.8)	<0.001
Suprapubic catheterization	1 (0.6)	4 (4.0)	0.05
Nephrostomy	5 (2.8)	3 (3.0)	1.0
Blood cultures, n (%)			
Concomitant blood culture	117 (65.73)	65 (64.35)	0.91
Isolation of same microorganism in blood and urine culture in patients with blood culture (n=182)	25 (21.4)	8 (12.3)	0.12
UTI related death	13 (7.3)	11 (10.9)	0.30

CA-UTI: community acquired urinary tract infection. **HA-UTI:** healthcare-associated urinary tract infection. **UTI:** urinary tract infection. **ICU:** intensive care unite.

Table 3. Microbiologic isolations

	CA-UTI (n=178)	HA-UTI (n=101)	p
Escherichia coli , n (%)	112 (62.9)	57 (56.4)	0.28
Klebsiella pneumoniae , n (%)	23 (12.9)	19 (18.8)	0.18
Pseudomonas aeruginosa , n (%)	11 (6.2)	10 (9.9)	0.25
Enterococcus faecalis , n (%)	7 (3.9)	0 (0)	0.05
Staphylococcus aureus , n (%)	5 (2.8)	0 (0)	0.16
Enterobacter spp. , n (%)	4 (2.2)	5 (5.0)	0.29
Negative coagulase Staphylococcus , n (%)	4 (2.2)	1 (1.0)	0.65
Enterococcus faecium , n (%)	1 (0.6)	0 (0)	1.0
Enterococcus spp. , n (%)	0 (0)	1 (1.0)	0.36
Other isolations, n (%)	11 (6.2)	8 (7.9)	0.57

CA-UTI: community acquired urinary tract infection. **HA-UTI:** healthcare-associated urinary tract infection.

Table 4. Antimicrobial resistances

	CA-UTI	HA-UTI	p
***Escherichia coli* (n=169), n (%)**	**112 (62.9)**	**57 (56.4)**	**0.28**
Amikacin, n/N (%)	2/109 (1.8)	3/55 (5.5)	0.33
Ampicillin, n/N (%)	95/111(85.6)	43/57 (75.4)	0.10
Ampicillin - Sulbactam, n/N (%)	64/110 (58.2)	30/57 (52.6)	0.49
Cefazoline, n/N (%)	45/108 (41.7)	30/56 (53.6)	0.14
Ceftriaxone, n/N (%)	33/109 (30.3)	20/56 (35.7)	0.47
Ceftazidime, n/N (%)	32/104 (30.8)	19/55 (34.5)	0.62
Cefepime, n/N (%)	33/110 (30.0)	20/56 (35.7)	0.45
Ciprofloxacin, n/N (%)	55/111 (49.5)	22/56 (39.3)	0.20
Gentamycin n/N (%)	14/108 (13.0)	11/55 (20)	0.23
Imipenem/Meropenem, n/N (%)	4/104 (3.8)	1/55 (1.8)	0.47
Piperacillin - Tazobactam, n/N (%)	4/106 (3.8)	9/56 (16.1)	0.001
Trimethoprim - Sulfamethoxazole, n/N (%)	58/109 (53.2)	28/56 (50.0)	0.69
Extended spectrum beta-lactamase, n/N(%)	31/112(28.7)	17/57(33.3)	0.76
Carbapenemase producers, n/N(%)	1/112(0.89)	1/57(1.75)	0.79
Multidrug resistant microorganism, n/N(%)	35/112(31.3)	20/57(35.1)	0.61
***Klebsiella pneumoniae* (n=42), n (%)**	**23 (12.9)**	**19 (18.8)**	**0.18**
Amikacin, n/N (%)	2/23 (8.7)	8/19 (42.1)	0.02
Ampicilllin - Sulbactam, n/N (%)	15/19 (78.9)	15/19 (78.9)	1.0
Cefazoline, n/N (%)	18/22 (81.8)	14/19 (73.7)	0.70
Ceftriaxone, n/N (%)	16/22 (72.7)	13/19 (68.4)	0.76
Cefepime, n/N (%)	15/23 (65.2)	13/19 (68.4)	0.82
Trimethoprim - Sulfamethoxazole, n/N (%)	16/23 (69.6)	12/19 (63.2)	0.66
Ciprofloxacin, n/N (%)	17/23 (73.9)	12/19 (63.2)	0.45
Gentamycin, n/N (%)	11/21 (52.4)	10/19 (52.6)	0.98
Imipenem/meropenem, n/N (%)	2/22 (9.1)	5/18 (27.8)	0.12
Piperacillin - Tazobactam, n/N (%)	13/22 (59.1)	11/19 (57.9)	0.93
Extended spectrum beta-lactamase, n/N(%)	13/23(56.5)	8/19(42.1)	0.352
Carbapenemase producers, n/N (%)	2/23(8.7)	5/19(26.3)	0.214
Multidrug resistant microorganism, n/N (%)	16/23(69.6)	13/19(68.4)	0.93
***Pseudomonas aeruginosa* (n=21), n (%)**	**11 (6.2)**	**10 (9.9)**	**0.25**
Amikacin, n/N (%)	1/11 (9.1)	1/10 (10.0)	1.0
Cefepime, n/N (%)	3/11 (27.3)	3/10 (30.0)	1.0
Ceftazidime, n/N (%)	4/10 (40.0)	2/9 (22.2)	0.40
Ciprofloxacin, n/N (%)	5/11 (45.5)	4/9 (44.4)	1.0
Colistin, n/N (%)	1/9 (11.1)	0/7 (0)	1.0
Gentamycin, n/N (%)	3/10 (30.0)	3/10 (30.0)	1.0
Imipenem, n/N (%)	2/11 (18.2)	3/10 (30.0)	0.63
Meropenem, n/N (%)	2/10 (20)	2/10 (20)	1
Piperacillin - Tazobactam, n/N (%)	3/10 (30.0)	3/9 (33.3)	1.0
Multidrug resistant microorganism, n/N (%)	3/11(27.3)	3/10(30)	0.89

CA-UTI: community acquired urinary tract infection. HA-UTI: healthcare-associated urinary tract infection. n/N (%): antimicrobial resistant bacteria / total of isolations with performed tests (%)

Table 5. Comparis on between MDR and non-MDR microorganisms

	MDR (n=101)	Non-MDR (n=178)	p
Male sex, n (%)	54 (53.5)	70 (39.3)	0.02
CA-UTI, n (%)	60 (59.4)	118 (66.3)	0.25
Pregnancy, n (%)	2 (2.0)	5 (2.8)	1.0
Kidney transplant, n (%)	25 (24.8)	30 (16.9)	0.11
Immunosuppressive therapy within previous 3 months, n (%)	33 (32.7)	46 (25.8)	0.22
Diabetes, n (%)	34 (33.7)	41 (23.0)	0.05
Urinary tract abnormalities, n (%)	31 (30.7)	41 (23.0)	0.16
Kidney stones, n (%)	7 (8.9)	10 (5.6)	0.29
Antibiotic use within previous 3 months, n (%)	66 (65.3)	71 (39.9)	<0.001
Chronic kidney disease, n (%)	39 (38.6)	47 (26.4)	0.03
Neoplasia, n (%)	23 (22.8)	41 (23.0)	0.96
Chronic obstructive pulmonary disease, n (%)	7 (6.9)	16 (9.0)	0.96
Liver disease, n (%)	6 (5.9)	12 (6.7)	0.79
UTI within previous year, n (%)	52 (51.5)	62 (34.8)	0.007
Recurrent UTI, n (%)	39 (38.6)	38 (21.3)	0.002
Admission at least for 48 h within previous year, n (%)	73 (72.3)	98 (55.1)	0.005
catheter associated urinary tract infection, n (%)	36 (35.6)	62 (34.8)	0.89
Instrumentation within previous 30 days, n (%)	43 (42.6)	65 (36.5)	0.31
Catheterization within previous 72 h, n (%)	42 (41.6)	62 (34.8)	0.26
Death, n (%)	8 (7.9)	16 (9.0)	0.76

MDR: multidrug resistant. Non-MDR: non-multidrug resistant microorganism.

CA-UTI: community acquired urinary tract infection. UTI: urinary tract infection.

Table 6. Comparis on between CAUTI vs Non-CAUTI

	Catheter associated urinary tract infection (n=98)	Non- Catheter associated urinary tract infection (n=181)	p
Male sex, n (%)	55 (56.1)	69 (38.1)	0.004
HA-UTI, n (%)	58 (59.2)	43 (23.8)	<0.001
Pregnancy, n (%)	0 (0)	7 (3.9)	0.10
Kidney transplant, n (%)	13 (13.3)	42 (23.2)	0.04
Immunosuppressive therapy within previous 3 months, n (%)	20 (20.4)	59 (32.6)	0.03
Diabetes, n (%)	27 (27.6)	48 (26.5)	0.85
Urinary tract abnormalities, n (%)	33 (33.7)	39 (21.5)	0.02
Kidney stones, n (%)	4 (4.1)	15 (8.3)	0.18
Antibiotic use within previous 3 months, n (%)	41 (41.8)	96 (53.0)	0.07
Chronic kidney disease, n (%)	28 (28.6)	58 (32.0)	0.54
Neoplasia, n (%)	32 (32.7)	32 (17.7)	0.005
Chronic obstructive pulmonary disease, n (%)	10 (10.2)	13 (7.2)	0.38
Liver disease, n (%)	7 (7.1)	11 (6.1)	0.72
Recurrent UTI, n (%)	28 (28.6)	49 (27.1)	0.78
ICU admission within previous 30 days	38 (38.8)	30 (16.6)	<0.001
Death, n (%)	10 (10.2)	14 (7.7)	0.48

HA-UTI: healthcare-associated urinary tract infection. UTI: urinary tract infection. ICU: intensive care unit.

DISCUSSION

The recognition of UTI epidemiological features in hospitalized patients, both in HA-UTI and CA-UTI, is of great relevance due to its prevalence and associated morbidity, particularly if no effective treatment is provided timely. There are few studies that compared the episodes of CA-UTI and HA-UTI in the same population of hospitalized patients. In our study, it was noted that the majority of UTI episodes in hospitalized patients were acquired in the community, an observation similar to other publications[17, 18]. Even though multiple programs of infections control have been developed during the last decades, HA-UTI continue being a significant healthcare issue. This could be because its development is influenced by different aspects of urinary catheterization, history of prolonged length of stay, previous antimicrobial use, among others[9, 17]. Although the majority of CA-UTI and HA-UTI occurred more frequently in female patients, the proportion of males was just slightly lower, as reported in the literature[1,19,20]. It is important to highlight that UTI episodes in male are associated to an increased risk of complications, mainly due to abnormalities of male anatomy[1].

It should be emphasized that patients with CA-UTI and HA-UTI from this study frequently showed significant risk factors for UTI, as described in the literature. Moreover, it was noted that patients with CA-UTI had higher frequency of chronic kidney disease, kidney transplant, immunosuppressive therapy within previous 3 months and urinary tract abnormalities. Of note, almost half of the patients had history of antimicrobial use within previous 3 months, although no significant differences were found between both groups. This data is relevant as it could determine not only the development of UTI, but also an increase in multidrug resistant microorganisms[1,9,20,21]. Furthermore, there was an important number of patients with medical history of diabetes and urinary tract abnormalities in both groups, which are recognized risk factors for development of UTI[9,21]. On the other hand, chronic obstructive pulmonary disease (COPD) was the only analyzed comorbidity found to be frequently associated with HA-UTI. This could be explained as COPD patients have higher risk of hospitalization, together with immune system abnormalities associated to the disease, which predispose to nosocomial infections[22], although this causes were not found in our study. There is also a description of an association between anticholinergic bronchodilators use in COPD patients and an increased risk of UTI[23]. In the studied population, there was a great proportion of patients with an episode of UTI within the previous year, being even more frequent in patients with CA-UTI. This would stand for, not only a risk factor to develop an infection, but also for MDR occurrence. Some authors have found an association between recurrent UTI and CA-UTI, although it has been on a lesser percentage, among 11 to 21%[1,18]. Similarly, it should be highlighted that an elevated proportion of patients with UTI had a history of hospitalization within one year prior to the infection, including patients with CA-UTI. This fact takes on great epidemiological relevance, owing to patient exposure to instrumentation (mainly in the urinary tract), nosocomial microorganisms and antimicrobials, promoting an increase, not only of the infection risk, but also of the antimicrobial resistance[9]. Certainly, it could be observed in our study that this was one of the main risk factors associated to the development of UTI secondary to MDR. Other studies reported lesser frequency of history of prior hospitalization[24, 25].

We should consider two important aspects related to previous urinary tract catheterization in patients of our study. First, almost one third of patients with CA-UTI had a history of urinary catheterization within previous month, an observation also reported in other studies[1]. Second, although there is vast association between HA-UTI episodes and urinary catheterization, a quarter of those did not have one placed during the previous month. Therefore, other important risk factors arise for the development of UTI, such as history of hospital stay, previous antibiotics, among others, which has been already described in the literature.

The mortality associated with UTI was related to the severity of the infection, patient's comorbidities and time in which appropriate antibiotic treatment was initiated. In our study, the reported mortality was almost 8%, similar percentage outlined in the literature and not showing difference between both UTI groups[26].

As reported in other publications, Escherichia coli was the most frequent microorganism isolated in both UTI groups, although with a slightly lower proportion of HA-UTI, in which other nosocomial pathogens has arised, such as Klebsiella sp. or Pseudomonas sp., but with a considerably lesser proportion compared to the first one[1,17,18]. Understanding the local antimicrobial susceptibility profiles becomes highly relevant because international recommendations suggest that antibiotics with local resistance of more than 20% should not be used for empiric treatment[27]. This is of great interest because during the last years, an important increase in antimicrobial resistance has been observed worldwide, together with an increase in MDR, which is worrisome. Descriptions of risk factors for the development of UTI include previous antibiotic use, recurrent UTI and male sex, which have been observed more frequently in our study. Other risk factors are urinary tract abnormalities and its instrumentation[1,25].

Several studies have shown resistances against fluoroquinolones above 20% within Escherichia Coli isolations[1], similar to our findings. Although there was no significant difference between CA-UTI and HA-UTI episodes, there was evidence of resistance in almost half of the isolations, which is alarming. There is such a worldwide concern as regards this issue that, in 2017, the World Health Organization (WHO) included ciprofloxacin in the list of essential medicines, with the objective of decreasing its indiscriminate use and guaranteeing its availability when needed[28].

Furthermore, it was distinctive in our analysis the elevated resistance of E. coli against almost all antimicrobial groups, except piperacillin tazobactam, carbapenem beta-lactams, amikacin and gentamycin, both in CA-UTI and HA-UTI. This numbers are similar to the ones shown in other studies, although their results included lower resistance against third and fourth generation cephalosporins[17,29]. Moreover, when comparing the antimicrobial resistance spectrum of patients with HA-UTI from our study with another previously done in the same population, an important increase in bacteria's resistance was observed against ciprofloxacin, cefepime and ceftriaxone[9].

As regards CA-UTI episodes secondary to Klebsiella pneumoniae, amikacin and carbapenem beta-lactams were the only antibiotics with less than 20% resistance isolations. On the contrary, in the case of what was observed in HA-UTI, more than 20% of the isolations were resistant to each tested antimicrobial. This data was similar to what had been presented in the literature, denoting the increase in antimicrobial resistance of this microorganism[1,9,17].

As described in other studies, we also observed a large amount of resistant Pseudomonas aeruginosa strains, particularly within HA-UTI, and found that only colistin and amikacin were the antibiotics with less than 20% isolations resistance[29]. In comparison to our previous study, we observed an important increase in Pseudomonas resistant to piperacillin tazobactam[9].

Nowadays, there is great worldwide concern about the growing development of ESBL-producing Enterobacteriaceae. This has become of great relevance, not only in the hospital but also in the community setting, where almost 30% of colonization in the population has been reported in a Latin-American study[30]. In our analysis, it should be highlighted that most of the isolations were from the community. In our previous study of patients with HA-UTI, the percentage of ESBL-producing microorganisms was slightly lower (around 19%)[9]. Furthermore, some carbapenemase producers strains were identified, mainly within HA-UTI episodes.

When comparing UTI episodes related and not-related to urinary tract catheterization, it should be highlighted that the first ones were more frequent in male patients, with urinary tract abnormalities and neoplasia, and also more associated to hospital setting. Nevertheless, there was an important number of patients with catheter associated UTI associated with CA-UTI, denoting an increase of urinary tract catheterization in the community setting. In our previous study, 60.9% of HA-UTI were related to catheter associated UTI, similarly to what was observed in the new analysis, same as their associated risk factors[9].

Although this is a one year prospective study in two hospital centers at the city of Cordoba, one of its main limitations is that both are third-level hospitals and the prevalence of comorbidities could be larger compared to the rest of the population.

CONCLUSION

It is essential to become acquainted with the local epidemiology of the most frequent infections so as to choose more effective empiric treatments. To conclude, we observed that the majority of UTI episodes in hospitalized patients were related to CA-UTI. Furthermore, several associated risk factors were frequently identified, of note: history of recurrent UTI, hospitalization or previous treatment with antibiotics.

Escherichia coli was the most frequent isolated microorganism, with a concerning number of MDR microorganisms isolated in both groups.

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Este artículo es original y no ha sido enviado para su publicación a otro medio de difusión científica en forma completa ni parcialmente.

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