



Urinary tract infection etiology and antimicrobial sensitivity in a Mexican hospital from 2010 to 2015

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Abstract

BACKGROUND: urinary tract infections are common in both community-based and hospitalized patients. The complexity of their management is increasing, as a result of antimicrobial resistance.

OBJECTIVE: to assess the prevalence and antimicrobial susceptibility profile of uropathogens present in urine cultures analyzed at the *Hospital Regional ISSSTE*, Monterrey, Nuevo León, Mexico.

MATERIALS AND METHODS: a retrospective cohort study was conducted, based on urine sample analyses performed at the hospital laboratory between January 2010 and September 2015.

RESULTS: data on 4,394 urine cultures were obtained. *Escherichia coli* was identified in 47.1% of the isolates. A total of 59.4% of the *Escherichia coli* and 59.6% of the *Klebsiella pneumoniae* isolates showed production of extended-spectrum beta-lactamases. *Candida albicans* was found in 3.6% of the isolates. Most of the *Escherichia coli* and *Klebsiella pneumoniae* isolates showed sensitivity to carbapenems.

CONCLUSIONS: these study results provide valuable insight for improving urinary tract infection management at the *Hospital Regional ISSSTE* of Monterrey. Institutions elsewhere should carry out these investigations, to understand antimicrobial resistance trends in their area of activity and improve their antimicrobial prescription practices.

KEY WORDS: urinary tract infection, UTI, uropathogens, antimicrobial sensitivity

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Etiología de las infecciones urinarias y sensibilidad antimicrobiana en un hospital mexicano (2010-2015)

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Resumen

ANTECEDENTES: la infección urinaria es frecuente en pacientes ambulatorios y hospitalizados. La complejidad de su tratamiento está aumentando como consecuencia de la resistencia antimicrobiana.

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OBJETIVO: evaluar en cultivos de orina la prevalencia y perfil de sensibilidad antimicrobiana de los uropatógenos analizados en el Hospital Regional del ISSSTE, Monterrey, Nuevo León, México.

MATERIAL Y MÉTODOS: estudio de cohorte, retrospectivo, de muestras de orina analizadas entre enero de 2010 y septiembre de 2015.

RESULTADOS: se obtuvieron datos de 4394 urocultivos en los que se identificó *Escherichia coli* en 47.1% de los aislamientos. El 59.4% de los aislados de *E. coli* y 59.6% de los aislados de *Klebsiella pneumoniae* (*K. pneumoniae*) mostraron producción de betalactamasas de amplio espectro. *Candida albicans* se encontró en 3.6% de los aislamientos. La mayor parte de los aislados de *E. coli* y de *K. pneumoniae* mostraron sensibilidad a carbapenémicos.

CONCLUSIONES: estos resultados proporcionan valiosa información para el mejor tratamiento de pacientes con infección de vías urinarias en el Hospital Regional del ISSSTE de Monterrey. Las demás instituciones deberían efectuar estas investigaciones para comprender las tendencias de resistencia antimicrobiana en su área de actividad y, de esta manera, mejorar las prácticas de prescripción de antimicrobianos.

PALABRAS CLAVE: infecciones urinarias, ITU, uropatógenos, sensibilidad antimicrobiana.

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INTRODUCTION

Urinary tract infections (UTIs) are one of the most commonly diagnosed infections, both in community-based and hospitalized patients.¹ In the United States, UTIs accounted for 10.5 million outpatient visits in 2007, of which about 21% corresponded to the emergency department.² In Mexico, UTIs were the third leading cause of morbidity in 2014, with a total of 4,244,053 notified cases.³

The financial burden imposed by UTIs is remarkable, especially in Latin American countries, where antimicrobial prescription is less strictly controlled.⁴ A cross-sectional study carried out at a pediatric hospital in the Mexican state of Sonora, found that the average cost of medical care per episode of nosocomial UTI was \$2062.00 USD.⁵

In general, women are more affected by UTIs than men. It is estimated that, by the age of 24, 33% of women will require antimicrobial treatment for at least one episode of UTI and more than 50% will experience at least one UTI during their lifetime.⁶ In fact, 75.6% of the cases of UTI reported in 2008 in Mexico were diagnosed in female patients.⁷

Escherichia coli (*E. coli*) is the most frequent causative agent of UTIs, accounting for 75%-95% of infections.⁸ The remaining episodes are mostly caused by other Enterobacteriaceae, namely *Proteus mirabilis* (*P. mirabilis*) and *Klebsiella pneumoniae* (*K. pneumoniae*), followed by Gram positive cocci, such as *Staphylococcus saprophyticus* (*S. saprophyticus*).⁸ Fungal microorganisms are relatively common uropathogens in nosocomial UTIs.⁹



Treatment selection for UTI management is becoming increasingly challenging. Antimicrobial resistance, mostly due to antimicrobial misuse, is on the rise, thus limiting therapeutic options.¹⁰ The emergence of *E. coli*, as well as of other Enterobacteriaceae that produce extended-spectrum β -lactamases (ESBLs) is of particular concern, since these enzymes confer resistance to a number of antimicrobials.¹¹

The aim of this study was to assess the prevalence of uropathogens identified in urine cultures analyzed at the laboratory of the *Hospital Regional ISSSTE* of Monterrey, as well as their antimicrobial susceptibility profiles, to help guide therapy selection at the local level.

MATERIALS AND METHODS

Study design

This was a non-interventional, retrospective cohort study based on urine sample analysis performed at the laboratory of the *Hospital Regional ISSSTE* of Monterrey (Nuevo León, Mexico) between January 2010 and September 2015. Information on microbial species and antimicrobial susceptibility was obtained from the laboratory's electronic system.

The urine samples were obtained through sterile urine collection techniques (suprapubic aspiration or collection from catheters). Using a calibrated loop, these samples were inoculated on CLED and MacConkey agar media and incubated at 37° C.

Only urine cultures considered positive (microbial growth $> 10^5$ CFU/mL) and exhibiting growth of a single microbial strain were included in this analysis. Each urine culture corresponded to a single patient.

Uropathogen identification and antimicrobial sensitivity testing were performed using the Vi-

tek® 2 system (bioMérieux, Inc., Durham, NC, USA) according to the manufacturer's instructions. The Gram-negative (GN), Gram-positive (GP), and Yeast (YST) identification cards and the GP67, GN70, and XL05 antimicrobial susceptibility testing cards were used. Production of ESBLs was also assessed by the Vitek® 2 system. Quality control was performed using American Type Culture Collection strains.

The Ethics Committee of the *Hospital Regional ISSSTE* of Monterrey approved the study, and due to its retrospective design and in compliance with the provisions of Mexican law, written informed consent from the individuals whose urine samples were analyzed was not required.

Statistical analysis

Descriptive statistics (absolute and relative frequencies, as applicable) were used to summarize the data on uropathogen identification and the antimicrobial sensitivity of the isolates.

RESULTS

Data on 4,394 positive urine cultures were obtained for analysis. The most frequently isolated uropathogen was *E. coli*, which was identified in 47.1% of the cultures (Table 1).

The most common uropathogens after *E. coli* were *Enterococcus faecalis* (*E. faecalis*) and *Pseudomonas aeruginosa* (*P. aeruginosa*), which were isolated in 13.2% and 10.2% of the cultures, respectively. *K. pneumoniae*, the second most frequently identified Gram-negative bacterium, was found in 410 (9.33%) urine cultures. Among the fungal species, *Candida albicans* (*C. albicans*) was the most common, identified in 3.6% of the urine cultures.

E. coli and *K. pneumoniae* were the ESBL-producing uropathogens found in the urine cultures

Table 1. Frequency of uropathogens in urine cultures of patients at the Hospital Regional ISSSTE of Monterrey (Nuevo León, Mexico) between January 2010 and September 2015

Microorganism	No. of isolates (%) (n = 4394)
Gram-negative bacteria	
<i>Escherichia coli</i>	2070 (47.1)
<i>Klebsiella pneumoniae</i>	410 (9.3)
<i>Pseudomonas aeruginosa</i>	450 (10.2)
<i>Enterobacter cloacae</i>	115 (2.6)
<i>Proteus mirabilis</i>	113 (2.6)
<i>Acinetobacter baumannii</i>	42 (1.0)
Gram-positive bacteria	
<i>Enterococcus faecalis</i>	582 (13.2)
<i>Enterococcus faecium</i>	155 (3.5)
<i>Staphylococcus haemolyticus</i>	52 (1.2)
<i>Staphylococcus aureus</i>	44 (1.0)
<i>Staphylococcus epidermidis</i>	40 (0.9)
Fungi	
<i>Candida albicans</i>	158 (3.6)
<i>Candida glabrata</i>	82 (1.9)
<i>Candida tropicalis</i>	81 (1.8)

and they presented similar prevalences: 59.4% and 59.6%, respectively (Table 2).

The sensitivity of the isolated Gram-negative bacteria varied widely across antimicrobial classes (Table 3).

Table 2. Frequency of ESBL-producing uropathogens in urine cultures of patients at the Hospital Regional ISSSTE of Monterrey (Nuevo León, Mexico) between January 2010 and September 2015

Microorganism	No. of ESBL-producing isolates (%)
<i>Escherichia coli</i>	1229 (59.4)
<i>Klebsiella pneumoniae</i>	244 (59.6)

ESBL: Extended spectrum beta-lactamase

Carbapenems were the most active antimicrobial agents against *E. coli*, with 100% of the isolates showing sensitivity to both imipenem and meropenem and 99.6% displaying sensitivity to ertapenem. The majority of *E. coli* isolates were also very sensitive to tigecycline (99.8%) and amikacin (98.5%).

K. pneumoniae presented a similar sensitivity pattern, also in its range of sensitivity to the various cephalosporins. However, more isolates of *K. pneumoniae* than *E. coli* were sensitive to ampicillin/sulbactam (51.8% vs. 28.2%, respectively).

As did *E. coli* and *K. pneumoniae*, *P. mirabilis* isolates showed a degree of sensitivity to all antimicrobials, with the exception of colistin.

A generally low proportion of *P. aeruginosa* isolates presented with sensitivity to the antimicrobials studied herein. Nevertheless, 71.9% of the isolates were sensitive to piperacillin/tazobactam.

Gentamicin, ciprofloxacin, moxifloxacin, and vancomycin were the only antimicrobials to which a proportion of all species of Gram-positive bacteria were sensitive (Table 4). One hundred percent of the isolates of all the species, except *Staphylococcus epidermidis* (*S. epidermidis*), were sensitive to tigecycline. Nitrofurantoin also showed good action against these bacteria, excluding *Enterococcus faecium* (*E. faecium*).

In general, the isolated fungal species presented good sensitivity to the antifungals analyzed (Table 5). *Candida tropicalis* (*C. tropicalis*) isolates, in particular, were all sensitive to the four antifungals. One hundred percent of *C. albicans* isolates were sensitive to fluconazole and voriconazole. The majority of *Candida glabrata* (*C. glabrata*) isolates were sensitive to flucytosine (96.3%).

Table 3. Proportion of Gram-negative bacteria isolates with sensitivity to the selected antimicrobials

Antimicrobial classes	Gram-negative bacteria					
	<i>Escherichia coli</i> , % (n = 2070)	<i>Pseudomonas aeruginosa</i> , % (n = 450)	<i>Klebsiella pneumoniae</i> , % (n = 410)	<i>Enterobacter cloacae</i> , % (n = 115)	<i>Proteus mirabilis</i> , % (n = 113)	<i>Acinetobacter baumannii</i> , % (n = 42)
<i>Penicillins</i>						
Ampicillin	21.1	0.0	4.3	14.7	52.3	0.0
<i>Penicillins/β-lactamase inhibitor</i>						
Ampicillin/Sulbactam	28.2	0.0	51.8	0.0	82.2	33.5
Piperacillin/Tazobactam	83.9	71.9	81.8	25.7	92.3	17.4
<i>Cephalosporins</i>						
Cefazolin	54.2	0.0	58.0	0.0	67.3	0.0
Cefepime	46.7	25.6	60.8	42.8	68.3	18.9
Ceftriaxone	57.3	0.2	59.4	25.3	69.1	7.1
<i>Aminoglycosides</i>						
Amikacin	98.5	33.0	91.7	57.9	97.3	76.1
Gentamicin	68.4	30.3	75.1	56.0	85.5	32.4
Tobramycin	55.3	30.9	65.0	47.2	85.8	24.6
<i>Streptomycin</i>						
<i>Fluoroquinolones</i>						
Ciprofloxacin	34.3	19.5	68.5	35.2	92.8	21.3
Moxifloxacin	33.4	15.6	69.6	37.5	88.4	11.8
<i>Carbapenems</i>						
Ertapenem	99.6	0.0	96.8	76.6	94.5	0.0
Imipenem	100.0	22.6	97.3	94.1	NA	22.8
Meropenem	100.0	28.9	98.1	93.1	95.4	23.8
<i>Other antimicrobials</i>						
Nitrofurantoin	82.9	0.0	8.8	13.9	7.3	0.0
Tigecycline	99.8	0.4	86.3	58.6	31.1	31.0
TMP/SMX	42.5	0.8	62.3	28.8	56.8	11.0
Colistin	0.0	30.0	0.0	0.0	0.0	40.6
Aztreonam	57.7	14.6	45.9	32.8	63.0	2.3

NA: Not available

TMP/SMX: Trimethoprim/Sulfamethoxazole

DISCUSSION

The most commonly isolated uropathogen in this sample of urine cultures was *E. coli*, accounting for 47.1% of all isolated microorganisms. This finding is consistent with numerous studies that

have shown this bacterium to be the most important etiologic agent of UTI worldwide.^{8,12-14} In Mexico, this trend has been observed in both adult and pediatric populations, with local studies reporting frequencies of *E. coli* isolates ranging from 41% to 79%.¹⁵⁻¹⁸

Table 4. Proportion of Gram-positive bacteria isolates with sensitivity to selected antimicrobials

Antimicrobial classes	Gram-positive bacteria				
	<i>Enterococcus faecalis</i> , % (n = 582)	<i>Enterococcus faecium</i> , % (n = 155)	<i>Staphylococcus haemolyticus</i> , % (n = 52)	<i>Staphylococcus aureus</i> , % (n = 44)	<i>Staphylococcus epidermidis</i> , % (n = 40)
<i>Penicillins</i>					
Ampicillin	62.1	13.3	0.0	0.0	0.0
Benzylpenicillin	62.1	0.0	0.0	2.3	0.0
<i>Aminoglycosides</i>					
Gentamicin	33.4	22.6	47.9	82.6	44.9
Streptomycin	47.0	43.5	0.0	0.0	0.0
<i>Fluoroquinolones</i>					
Ciprofloxacin	43.9	8.4	32.6	52.3	47.7
Moxifloxacin	43.4	11.2	50.1	56.8	72.4
Levofloxacin	44.8	0.0	5.8	54.5	47.7
<i>Other antimicrobials</i>					
Nitrofurantoin	96.3	0.0	100.0	100.0	100.0
Tigecycline	100.0	100.0	100.0	100.0	0.0
TMP/SMX	0.0	0.0	28.7	86.4	41.7
Vancomycin	98.8	65.9	98.0	97.8	80.0
Linezolid	96.8	88.2	100.0	0.0	100.0
Tetracycline	35.1	71.7	0.0	95.5	87.6
Colistin	0.0	0.0	9.6	0.0	0.0
Clindamycin	0.0	0.0	51.9	54.7	72.5
Rifampicin	0.0	0.0	94.1	95.5	100.0
Erythromycin	15.5	0.0	23.2	50.2	67.7

Table 5. Proportion of fungi isolates with sensitivity to the selected antimicrobials

Antimicrobial classes	Fungi		
	<i>Candida albicans</i> %	<i>Candida glabrata</i> %	<i>Candida tropicalis</i> %
<i>Antifungals</i>			
Amphotericin B	96.0	89.8	100.0
Flucytosine	99.3	96.3	100.0
Fluconazole	100.0	79.4	100.0
Voriconazole	100.0	87.6	100.0

After *E. coli*, the most frequently isolated microorganisms were *E. faecalis* (13.2%), *P. aeruginosa* (10.2%), and *K. pneumoniae* (9.3%), with preva-

lences similar to those reported elsewhere in Latin America.^{12,15,18}

More than half of the *E. coli* isolates (59.4%), as well as of the *K. pneumoniae* isolates (59.6%), showed ESBL production. A similar prevalence of ESBL-producing *K. pneumoniae* (53.3%) was found by Flam et al. across 16 Latin American medical centers. However, the prevalence of ESBL-producing *E. coli* reported by those authors (37.6%) was lower than ours.¹⁹

The high rates of ESBL-producing bacteria identified in our sample are cause for concern. In the past, the majority of ESBL-producing



bacteria were isolated from hospitalized patients, but recent data have shown that ESBL production by common, community-acquired uropathogens, such as *E. coli*, has markedly increased.²⁰⁻²¹ This has also been reported in Latin America.^{4,14} ESBL-producing bacteria often show co-resistance to various antimicrobial drug classes (e.g. penicillins, cephalosporins, trimethoprim/sulfamethoxazole [TMP/SMX], among others).²²⁻²³ This issue is further complicated by the fact that these agents frequently cause serious invasive infections and are associated with a worse prognosis.²⁴

In the present study, fungi were isolated in 321 urine cultures. Isolation frequency, specifically of *C. albicans* (3.6%), was lower than that reported in other studies,²⁵⁻²⁸ which could be explained by differences between study populations.

In our sample, almost half (42.5%) of the *E. coli* isolates were sensitive to TMP/SMX. The number of isolates sensitive to fluoroquinolones was lower (ciprofloxacin: 34.3%; moxifloxacin: 33.4%). Fluoroquinolones have been prescribed empirically when there is clinical suspicion of UTI, due to the known, widespread resistance to TMP/SMX. It appears, however, that such frequent use has compromised their efficacy.²⁹

Overall, the number of *E. coli* and *K. pneumoniae* isolates sensitive to the antimicrobials tested was low. This could be explained by the high prevalence of ESBL-producing isolates of both species. Nevertheless, the sensitivity of these Enterobacteriaceae to carbapenems was high, with over 95% of the isolates of each species showing sensitivity to all the tested antimicrobials of this class. This is in accordance with the findings of the SENTRY and SMART surveillance programs.^{12,14} Indeed, carbapenems have been identified as the antimicrobials of choice for infections caused by ESBL-producing microorganisms.³⁰ However, caution should be used,

given that carbapenem resistance is reportedly increasing.²⁴

Isolates of *P. aeruginosa*, which is a frequent etiologic agent of nosocomial infections,³¹ showed overall low sensitivity to the antimicrobials listed. Concerns over infections caused by drug-resistant *P. aeruginosa* are not new. A 5-year analysis of *P. aeruginosa* susceptibility rates in Latin American centers participating in the SENTRY surveillance program showed rapidly increasing resistance to common antipseudomonal agents, especially meropenem (from 83.0% in 1997 to 64.4% in 2001, $p < 0.001$).³²

The antimicrobials that exerted the most action on Gram-positive bacteria were nitrofurantoin and tigecycline, with 100%, or nearly 100%, of the isolates showing sensitivity to them (except those of *E. faecium* and *S. epidermidis*, respectively). Nitrofurantoin is still rarely used for the empirical treatment of UTIs. Its spectrum of susceptible organisms has remained virtually unchanged, with little evidence of resistance emergence, despite its being on the market for over 60 years.³³ Nitrofurantoin might therefore be considered an interesting alternative for the treatment of UTIs caused by multi-drug resistant microorganisms.³⁴

Tigecycline also presents strong antimicrobial activity against both Gram-positive and Gram-negative bacteria. Data on antimicrobial susceptibility of microorganisms collected in Mexico between 2005 and 2012 show 100% tigecycline susceptibility reported among isolates of *Enterococcus* sp. and *S. aureus*,³⁵ which was similar to what we found. Jones et al. reported identical susceptibility rates in their 2011 analysis of Latin American isolates.³⁶

Nearly 100% of the isolates of every fungal species identified in the present sample were sensitive to the antifungals tested. Nonetheless, it is worth

noting that fungi in urine cultures are often asymptomatic and may not require pharmacologic treatment. Eliminating the elements that facilitate colonization, such as indwelling catheters, may suffice.³⁷ Fluconazole has been the recommended treatment option, when applicable.³⁸⁻³⁹

Antimicrobial sensitivities show great geographic variability. Therefore, the present study is limited by the fact that our sample came from a single institution. Each institution should be aware of the relevance of collecting this type of information to better guide therapy selection for UTIs and implement control strategies for any antimicrobial resistance patterns identified.

Moreover, because the hospital laboratory system did not contain such information, it was not possible to assess relationships between uropathogen frequencies and the antimicrobial sensitivity of the isolates to factors such as sex, infection origin, type of UTI, or presence of risk factors, among others.

CONCLUSIONS

The results presented herein provide additional evidence in relation to the role of different microorganism species as etiologic agents of UTIs. Furthermore, they provide valuable antimicrobial sensitivity information that will help guide antimicrobial selection for the treatment of UTIs diagnosed at the *Hospital Regional ISSSTE* of Monterrey, in Mexico.

Implementation of the appropriate public health actions (e.g. antimicrobial susceptibility surveillance) is necessary to better understand the patterns of antimicrobial sensitivity in Mexico and thus aid in the appropriate decision-making regarding their prescription in clinical practice. This, in turn, is essential for preventing the spread of resistance mechanisms and for reducing direct healthcare costs associated with UTIs.

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