Antibiotic resistance: Microbiological profile of urinary tract infections in Mexico

Resistencia a antibióticos: Perfil microbiológico de las infecciones de vías urinarias en México

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Abstract

Objective: *The objective of this study was to describe the prevalence, microbiological profile, bacterial resistance, and the sensitivity to antibiotics of microorganisms causing urinary tract infection (UTI) at a single-site tertiary referral hospital in the western region of Mexico.* **Methods:** *A total of 5895 culture samples processed at the microbiology laboratory from August 1, 2014, to July 31, 2015, were analyzed.* **Results:** *A total of 5895 samples for urine cultures (UC) were collected, of which 3363 were taken in women (57.05%) and 2532 in men (42.95%). A prevalence of 24% was calculated. From 1444 positive UC, 1512 microorganisms were isolated; the major etiological agent was Escherichia coli, representing 67.28% followed by Pseudomonas with 7.12%. With respect to fungi, Candida glabrata was found as the most common agent. Susceptibility to daptomycin and linezolid was 100%, and meropenem, 91.4%. Highest antimicrobial resistance was found for ampicillin (77.47%) and moxifloxacin (72.89%). Nearly 49% of E. coli strains and 27% of Klebsiella pneumoniae strains showed extended-spectrum beta-lactamase (ESBL) production.* **Conclusions:** *Bacterial UTI persists as one of the most common infections affecting all age groups and both genders. As in other countries, E. coli ranks first in Mexico, with 67.28%, and nearly 50% of the strains produce ESBL.*

KEY WORDS: *Urinary tract infections. Antibiotic sensitivity and resistance. Extended-spectrum beta-lactamase-producing bacteria.*

Resumen

Objetivo: *Describir la prevalencia, el perfil microbiológico, la resistencia y la sensibilidad a los antibióticos de microorganismos causantes de infecciones de vías urinarias en un centro de referencia de tercer nivel en el occidente de México.* **Método:** *Se realizó un estudio transversal que incluyó 5895 urocultivos procesados en el laboratorio de microbiología del 1 de agosto de 2014 al 31 de julio de 2015.* **Resultados:** *De los 5895 urocultivos, 3363 correspondieron a mujeres (57.05%) y 2532 a varones (42.95%). De los 1444 resultados positivos, se aislaron 1512 microorganismos (prevalencia del 24%); el más común fue Escherichia coli, con un 67.28%, seguido por Pseudomonas con un 7.12%. Candida glabrata se reportó como el patógeno fúngico más frecuente. De manera general, la sensibilidad a la daptomicina y al linezolid fue del 100%, y al meropenem fue del 91.4%. La resistencia más alta se reportó para ampicilina y moxifloxacino (77.47 y 72.89%, respetivamente). Cerca del 49% y del 27% de las cepas de E. coli y Klebsiella pneumoniae mostraron producción de betalactamasas de espectro extendido.* **Conclusiones:** *Las infecciones de vías urinarias persisten como una de las formas más habituales de infección y afectan a todos los grupos de edad. En México, al igual que en otros países, E. coli se coloca en primer lugar de frecuencia, con el 67.28%.*

PALABRAS CLAVE: *Infección de vías urinarias. Sensibilidad y resistencia a antibióticos. Bacterias productoras de betalactamasas de espectro extendido.*

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Introduction

The increasing rate of antibiotic resistance in uropathogens, especially in *Escherichia coli* and *Klebsiella pneumoniae* as the most common etiologic agents of urinary tract infections (UTI), leads to difficulties in selecting adequate empirical therapy and achieving treatment success[1]. Since sulfonamide and penicillin were introduced into clinical use in the 1930s and 1940s, respectively, people was motivated by the illusion that infectious diseases were totally controlled by antibiotics. The widespread use of antibiotics, however, imposes strong selection pressure for the development of antibiotic resistance, a major, present-day public health problem[2]. In recent years, the problem has worsened due to the emergence of extended-spectrum beta-lactamases (ESBL), which mediate resistance to β-lactam antimicrobials, especially the third-generation cephalosporins among these organisms. Genes responsible for ESBL production arise by point mutation at the active site of the earlier β-lactamases and are usually plasmid mediated. In addition, ESBL-positive and Gram-negative bacteria often carry genes that confer high levels of resistance to many other antibiotics[3].

A summary of several international surveillance systems that have reported uropathogenic *E. coli* resistance to selected antibiotics in North and South America and Europe reports that there is considerable local variation in resistance. Resistance to ampicillin and trimethoprim ranges from 80% and 61% in Mexico to 33% and 9% in Quebec. In Mexico, resistance to ciprofloxacin has been reported at 72%[4].

There are many reports in the literature describing the epidemiology of bacterial resistance; however, the microbiologic profile varies from place to place. At our institution, there are no reports on antibiotic resistance and susceptibility trends. The aim of this study was to examine the epidemiological data obtained from isolated bacteria in urine samples from patients at our hospital over a 1-year period. Data included the susceptibility, resistance, and prevalence of ESBL-producing bacteria and fungi.

Methods

A cross-sectional study was carried out with results from urine samples obtained from hospitalized and outpatients at the Western National Medical Center in Jalisco, Mexico, from August 2014 to July 2015.

Table 1. Etiologic agents

Microorganism	n (%)
Isolated bacteria	1461 (96.63)
Escherichia coli	983 (67.28)
Pseudomonas	104 (7.12)
Klebsiella	94 (6.43)
Enterococcus	88 (6.02)
Proteus	45 (3.08)
Staphylococcus	29 (1.98)
Acinetobacter baumanii	28 (1.92)
Enterobacter	25 (1.71)
Morganella morganii	19 (1.30)
Citrobacter freundii	18 (1.30)
Providentia	13 (0.89)
Streptococcus	7 (0.48)
Others	8(0.55)
Isolated fungi	51 (3.37)
Candida glabrata	18 (35.29)
Candida albicans	11 (21.57)
Candida krusei	9 (17.65)
Trichorosporon beigelli	8 (15.69)
Others	4 (7.84)

Samples were processed and analyzed in the Hospital's Microbiology Laboratory. The presence of $\geq 10^5$ colony-forming units/mL in urine culture (UC) media was considered significant for UTI. Isolated bacteria and antibiotic susceptibility were identified by standard laboratory techniques or an automated system (Vitek, Biomerieux®) as required.

Inadequate urine samples were excluded from the study: those not processed 1 h after collection, insufficient urine, or urine that was not well labeled. Results with more than 3 pathogens were also excluded.

The Microsoft Excel® program was utilized to analyze data to obtain demographic data from patients such as gender and age (averages and ranges). The prevalence and percentages of sensitivity and resistance were calculated with basic arithmetic operations. The study was approved by the Institutional Ethics Committee with registration number R-2015-1310-185.

Results

Demographic characteristics

A cross-sectional study was conducted with the objective of describing prevalence, microbiological profile, susceptibility, and resistance to antibiotics in UTI. A total of 5895 UC results were collected. Among the results analyzed, 3363 were of women (57.05%) and 2532 men (42.95%). Mean age was 53 years, with a range of 15-102 years. Of the UC performed, 24.5% (n = 1444) were positive. Based on the total number

Table 2. Susceptibility to antimicrobials

Antimicrobial	Total	Susceptible (%)	Antimicrobial	Total	Susceptible (%)
Daptomycin	124	124 (100.00)	Cefotaxime	1335	595 (44.57)
Linezolid	124	124 (100.00)	Cefazolin	1232	543 (44.07)
Meropenem	1364	1247 (91.42)	Ceftriaxone	1364	599 (43.91)
Imipenem	1336	1220 (91.32)	Cefuroxime	1307	556 (42.54)
Cefotetan	1203	1092 (90.77)	Trimethoprim/sulfamethoxazole	1260	467 (37.06)
Vancomycin	117	105 (89.74)	Synercid	117	43 (36.75)
Amikacin	1335	1163 (87.12)	Levofloxacine	1459	412 (28.24)
Piperacilin/tazobactam	1307	989 (75.67)	Amoxicillin/clavulanic acid	29	8 (27.59)
Gentamicin	1348	769 (57.05)	Moxifloxacin	1210	317 (26.20)
Ticarcilline/clavulanic acid	1335	744 (55.73)	Ampicillin/sulbactam	1260	330 (26.19)
Cefepime	1364	698 (51.17)	Ciprofloxacin	1452	374 (25.76)
Aztreonam	1307	582 (44.53)	Ampicillin	1327	276 (20.80)
Ceftazidime	1364	608 (44.57)			

Table 3. Resistance to antimicrobials

Antimicrobial	Total	Resistant (%)	Antimicrobial	Total	Resistant (%)
Ampicillin	1327	1028 (77.47)	Gentamicin	1348	640 (47.48)
Moxifloxacin	1210	882 (72.89)	Cefepime	1364	649 (47.58)
Ciprofloxacin	1452	1058 (72.87)	Cefuroxime	1307	617 (47.21)
Amoxicilin/clavulanic acid	29	21 (72.41)	Ticarcilline/clavulanic acid	1335	203 (15.21)
Levofloxacin	1459	1012 (69.36)	Vancomycin	117	12 (10.26)
Trimethoprim/sulfamethoxazole	1260	792 (62.86)	Amikacin	1335	136 (10.19)
Cefazolin	1232	659 (53.49)	Imipenem	1336	113 (8.46)
Ampicillin/sulbactam	1260	643 (51.03)	Meropenem	1364	101 (7.40)
Cefotaxime	1335	674 (50.49)	Piperacilin/tazobactam	1307	75 (5.74)
Ceftriaxone	1364	672 (49.27)	Cefotetan	1203	37 (3.08)
Aztreonam	1307	623 (47.67)	Daptomycin	124	0 (0.00)
Ceftazidime	1364	649 (47.58)	Linezolid	124	0 (0.00)

of patients and the number of positive cases, a prevalence of 24% was calculated. From 3363 UC performed in women, 25.9% (n = 872) were positive; for the group of men, 22.5% (n = 572) were positive of a total of 2532 UC.

Microbiological profile

A total of 1512 bacteria and fungi were isolated; two microorganisms were isolated in 68 samples. The most common etiological agent was *E. coli* representing 67.2% (n = 983), and with regard to isolated fungi, *Candida glabrata* was reported as the most common agent. Table 1 reveals the distribution and percentages of isolated etiologic microorganisms.

Of 1512 isolated pathogens, 96.63% were bacterial agents (n = 1461) and 3.37% fungi (n = 51). Of 1461 isolated bacteria, *Escherichia coli* showed 67.28% (n = 983) followed by *Pseudomonas* and *Klebsiella*.

Table 4. Susceptibility of antimicrobials for *Escherichia coli*

Antimicrobial	S (%)	I (%)	R (%)	Antimicrobial	S (%)	I (%)	R (%)
Imipenem	99.69	0.00	0.31	Ceftriaxone	48.93	1.42	49.64
Meropenem	99.49	0.10	0.41	Cefazoline	45.37	1.63	53.00
Cefotetan	97.25	0.92	1.83	Tobramycin	47.30	10.17	42.52
Amikacin	95.02	2.85	2.14	Cefuroxime	43.64	3.15	53.20
Piperacilin/tazobactam	87.49	8.14	4.37	Trimethoprim/sulfamethoxazole	35.30	0.00	64.70
Ticarcilline/clavulanic acid	63.17	28.38	8.44	Ampicillin/sulbactam	23.70	24.52	51.78
Gentamicin	56.26	0.61	43.13	Levofloxacin	20.45	1.93	77.62
Cefepime	49.95	0.00	50.05	Moxifloxacin	20.45	0.71	78.84
Cefotaxime	49.64	0.71	49.64	Ciprofloxacin	19.94	0.51	79.55
Ceftazidime	49.44	0.10	50.46	Ampicillin	16.89	0.51	82.60
Aztreonam	49.24	0.92	49.85				

S: sensible, I: intermediate, R: resistant

Table 5. Susceptibility of antimicrobials for *Pseudomonas*

Antimicrobial	Susceptible (%)	Intermediate (%)	Resistant (%)
Cefepime	34.62	0.00	65.38
Meropenem	31.73	0.96	67.31
Imipenem	26.92	0.96	72.12
Gentamicin	25.96	1.92	72.12
Tobramycin	25.00	0.96	74.04
Amikacin	22.12	4.81	73.08
Ciprofloxacin	17.31	0.00	82.69
Levofloxacio	17.31	1.92	80.77
Piperacilin/tazobactam	2.88	88.46	8.65
Aztreonam	0.96	32.69	66.35
Ceftriaxone	0.00	18.27	81.73
Ceftazidime	0.00	31.73	68.27
Cefotaxime	0.00	18.27	81.73
Ticarcilline/clavulanic acid	0.00	32.69	67.31

Table 6. Bacteria producing β actamases of extended spectrum

Bacteria	*n* (%)	Global percentage
Escherichia coli	477/983 (48.52)	29.07
Klebsiella pneumonie	23/94 (27.38)	1.40
Klebsiella oxytoca	1/94 (10.00)	0.06
Proteus mirabilis	2/45 (4.44)	0.12

Of 51 fungi isolated, *C. glabrata* was the most common (35.29%), followed by *Candida albicans*, *Candida krusei*, and *Trichosporon beigelii*.

Sensitivity and resistance to antibiotics

The sensitivity and resistance of isolated microorganisms were reviewed for 34 antibiotics, highlighting daptomycin and linezolid, both with 100% sensitivity. Carbapenems were tested in >1300 cases, reporting sensitivities of >90%. Table 2 details the number of tests conducted by antibiotic and sensitivity percentage for the microorganisms.

Similarly, antibiotic resistance was determined. Observed data demonstrated that ampicillin, moxifloxacin, and levofloxacin exhibited resistances in >70% in >1200 cases. Table 3 reports the details of antibiotic resistance.

As mentioned earlier, *E. coli* was the most prevalent pathogen. Table 4 lists antibiotic sensitivity and resistance to *E. coli.*

Pseudomonas aeruginosa was isolated as the second most common pathogen. It was also observed that the sensitivity index was <35% for the antibiotics tested. Table 5 records the sensitivity and resistance percentage of antibiotics tested for *P. aeruginosa*, while table 6 registers ESBL-producing bacteria.

Discussion

Escherichia coli is the most prevalent facultative Gram-negative bacillus among human fecal flora,

Table 7. Antibiotic resistance in Mexico

Antibiotics	Molina-Lopez et al.[7] (n = 119) (%)	Paniagua-Contreras et al.[8] (n =194) (%)	Miranda-Estrada et al.[9] (n =107) (%)	López-Banda et al.[10] (n =108) (%)	Sierra-Diaz (n =983) (%)
Ampicillin	83.70	97.4	92.5	55.7	82.6
Ciprofloxacin	56	-	45.8	62.3	79.5
Moxifloxacin	-	-	-	52.6	78.84
Levofloxacin	-	-	-	60.2	77.62
Trimethoprim/sulfamethoxazole	56.40	66	70.1	65.1	64.7
Cefuroxime	15	-	62.6	1.8	53.2
Ceftriaxone	10.20	48.9	18.7	0	49.64
Ceftazidime	9	-	57	0	50.46
Cefotaxime	-	72.7	57	0	49.64
Cefepime	7.60	-	15.9	0	50.05
Amikacin	1.70	14.4	14	6.5	2.14
Cefotetan	-	-	-	1.6	1.83
Meropenem	0.85	-	-	0	0.41
Imipenem	-	-	-	1.9	0.31

Table 8. Antibiotic resistance in North America

Antibiotic	Foxman[4] (%)			Sierra-Diaz (%)
	Canada	USA	Mexico	Mexico
Ampicillin	33	-	80	77.47
Trimethoprim/ sulfamethoxazol	9	-	61	62.86
Quinolones	0	5-10	72	71.7[a]

[a] Average: Moxifloxacin, 72.89%; Ciprofloxacin, 72.87%, and Levofloxacin, 69.36%.

usually inhabiting the colon as the innocuous commensal. UTI comprises the most common form of extraintestinal *E. coli* infection, and *E. coli is* the most common cause of UTI. At some point during their lives, at least 12% of men and 10-20% of women experience an acute symptomatic UTI, and an even greater number develop asymptomatic bacteriuria[5]. The susceptibility of uropathogens to various antibiotics or antibiogram profiling may aid in improving the treatment of UTI without any delay. However, there are many microorganisms responsible for UTI. Among these, some with a high rate of resistant ESBL species have gained much attention[6]. In 2011, Molina-López et al.[7] analyzed antimicrobial, serotypes, and phylogenetic groups among strains of *E. coli* isolated from outpatients with UTI in Mexico City. Among the 29 identified serotypes, the most frequent was 025:H4 (21.2%), which has been associated with multidrug resistance and a high virulence potential.

The uropathogenic strains expressed resistance rates as high as 83% for ampicillin and the lowest resistance rate was for meropenem, with 0.85%[7]. Our work does not identify the serotypes; however, we can add that 67.28% of isolated bacteria were *E. coli*, finding the highest index of resistance for ampicillin, with a percentage similar to the resistance reported by Molina-López et al. (83 vs. 82.6%)[7]. With regard to quinolones and trimethoprim/sulfamethoxazole, our study reported higher resistances.

In another study reported in 2015 by Paniagua-Contreras et al. in Mexico, nearly 48% of *E. coli* strains were resistant to cephalothin, 97.4% to ampicillin, and 72.7% for cefotaxime; of 188 isolated strains, 96.9% were resistant to at least 3-11 of the antimicrobials studied[8].

Miranda-Estrada et al. reported, in 2015, an analysis performed on 107 isolates of *E. coli* at two locations in Mexico. Resistance to ampicillin and trimethoprim/sulfamethoxazole was 92.5 and 70.1%, respectively[9].

López-Banda et al. analyzed antibiotic resistance in 108 isolated *E. coli* obtained from 2008 to 2010 in Mexico City. Approximately 20% of the isolates registered the presence of β-lactamases. The authors did not report a statistical relationship between multiresistance and phylogenetic group[10].

Table 9. *E. Coli* resistance reported in other countries

Antibiotics	Abujnah et al.[3] (Libya) (n = 208) (%)	ARESC et al.[11] (Europe and Brazil) (n =2315) (%)	Can et al.[12] (Turkey) (n = 294) (%)	Sohail et al.[13] (Pakistan) (n = 244) (%)	Mamuye et al.[14] (Ethiopia) (n = 85) (%)	Yilmaz et al.[15] (Turkey) (n = 8975) (%)	Sierra-Diaz (Mexico) (n = 983) (%)
Ampicillin	69.2	48.3	-	-	79.2	66.9	82.6
Ciprofloxacin	23.1	8.1	39	82	54.7	49.9	79.5
Levofloxacin	19.2	-	-	82	-		77.62
Trimethoprim/sulfamethoxazole	37	29.4	44	78	22.6	20	64.7
Cefuroxime	-	2.4	25	80	-	30.9	53.2
Ceftriaxone	6.7	-	-	71	45.3	28	49.64
Ceftazidime	6.7	-	-	71	-	14.9	50.46
Cefepime	6.3	-	-	71	-	12	50.05
Amikacin	0	-	-	91	-	0.3	2.14
Meropenem	0.5	-	0	3	-	0	0.41
Imipenem	0.5	-	0	3	-	0	0.31

Table 10. Uropathogens susceptibility comparison between Mexico and other countries

Antibiotics	Mubanga et al.[16] (Lesotho) (n = 200) (%)	Stefaniuk et al.[17] (Poland) (n = 381) (%)	Osthoff et al.[18] (Australia) (n = 200) (%)	Hernandez & Sierra (Mexico) (n = 983) (%)
Ampicillin	-	38.6	-	20.8
Ciprofloxacin	95.1	60.8	70	25.76
Trimethoprim/sulfamethoxazole	32.5	60.2	53	37.06
Cefuroxime	-	82.1	-	42.54
Ceftazidime	-	88.2	-	44.57
Cefotaxime	-	86.5	-	44.57
Cefepime	-	91.1	-	51.17
Amikacin	-	96	-	87.12
Meropenem	-	100	100	91.42

Table 7 presents the comparison of our work with the aforementioned studies conducted in Mexico.

With regard to data on resistance to antibiotics in North America, Foxman[4] presented a review in 2010. Table 8 demonstrated the comparison of our study with that reported by Foxman.

The Antimicrobial Resistance Epidemiological Survey on Cystitis study was conducted in nine countries in Europe, as well as in Brazil, to determine the susceptibility of the major uropathogens circulating in the communities of these geographic areas[11]. The authors reported that not all sites exhibited the same susceptibility profile, with some countries less affected by resistance problems than others. In Germany, Hungary, Poland, and the Netherlands, > 90% of strains were susceptible to fosfomycin, mecillinam, nitrofurantoin, and ciprofloxacin. Susceptibility rates varied widely among countries for ampicillin (32.7-65.5%), amoxicillin/clavulanic acid (51.9-93.5%), cefuroxime (73-93%), and trimethoprim/sulfamethoxazole (54.5-87.8%)[12].

In terms of *E. coli* bacterial resistance specifically, there are reports from other countries[13-15]. Table 9 shows the analysis and the comparison with our results.

Table 10 compares susceptibility profiles between our results and those of other countries[16-18] regarding general uropathogens.

Our study sheds light on useful data including those antibiotics such as daptomycin and linezolid may be effective in the treatment of multidrug-resistant cases

because they exhibited no bacteria resistance. Other medications with a low index of resistance comprised cefotetan, piperacillin/tazobactam, and carbapenems with resistance percentages <10. However, it is prudent to analyze the tables of the results obtained in this study at the time of the empirical treatment indicated, due to that the majority of antimicrobial drugs available for oral administration presented resistance percentages of >50 for the majority of the pathogens isolated.

Conclusions

With the described results, it is possible to define an overall panorama of resistance and susceptibility to antibiotics in our working area. This study may also be submitted as a national projection due to the results reported, and it can be concluded that the spectrum of sensitivity and resistance of uropathogenic bacteria to antibiotics coincides partially with those reported by other sources of information at national and international levels. In addition, it is clear that there is more resistance to antibiotics, in general, in our study population, as in other national studies, compared with other countries. Data tables can be useful for the judicious use of antibiotics in our unit.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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