

Prevalence of Antimicrobial Resistance of Community Urinary Isolates against First-line Antimicrobial Agents Commonly Used in the Treatment of Uncomplicated Urinary Tract Infections, and Impact of Age on Resistance Rates

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ABSTRACT

Background: Monitoring trends of antimicrobial resistance is critical for guiding appropriate treatment of infection. The purposes of this study were (1) to investigate the prevalence of current antimicrobial resistance in community urinary isolates against first-line agents commonly used for the treatment of uncomplicated urinary tract infections (UTIs) in non-hospitalized patients, and (2) to determine whether rates of resistance varied by different age groups.

Methods: Isolates were identified from positive urine cultures processed from July 2009 to December 2009, and were tested against appropriate antimicrobials by disk diffusion susceptibility testing, in accordance with CLSI guidelines. Resistance rates were determined for ampicillin (AM), cephalothin (CF), ciprofloxacin (CIP), gentamicin (GM), nitrofurantoin (FM), norfloxacin (NOR), and trimethoprim/sulfamethoxazole (TMP/SMX), for all isolates and by patient age groups (<1 - 18; >18 - 30; >30 - 40; >40 - 50; >50 - 65; >65 - 75; and >75 years).

Results: A total of 4,290 isolates were tested including *Escherichia coli* (n = 2,805), *Enterococcus* (n = 531), *Klebsiella* (n = 332), *Proteus* (n = 218), coagulase-negative staphylococci (n = 106), *Citrobacter* (n = 86), *Enterobacter* (n = 67), *Pseudomonas* (n = 38), *Morganella* (n = 33), *Staphylococcus aureus* (n = 33), *Serratia* (n = 26), *Acinetobacter* (n = 5), *Edwardsiella* (n = 4), *Providencia* (n = 4), and *Hafnia* (n = 2) species. Resistance rates for AM, CF, CIP, FM, GM, NOR, and TMP/SMX were 44%, 31%, 12%, 9%, 17%, 12%, and 29%, respectively. Higher resistance rates were associated with increasing age. FM was the agent with the lowest resistance rate in each age group, except for the >30 - 40 year old age group, where CIP and NOR had the lowest resistance rate.

Conclusion: Current resistance patterns of community urinary isolates indicate that rates of antimicrobial resistance increase with age, and that FM is the most likely of the antimicrobials in this study to have a favorable antibacterial outcome in the empiric treatment of uncomplicated UTIs.

INTRODUCTION

Increasing resistance in clinical isolates, including an increase in the prevalence of multidrug-resistant extended-spectrum (ESBL) and ampC-type β-lactamase producers, and of methicillin-resistant *Staphylococcus aureus* (MRSA) has been previously described in both community and hospital settings.^{2,3,9} Knowledge of antimicrobial resistance may influence the empiric treatment of infection and the development and implementation of treatment guidelines. However, accurate and comprehensive data are scant on current resistance rates in organisms implicated in uncomplicated urinary tract infections (UTIs), and recent reports on resistance in urinary isolates have involved few and less diverse clinical isolates, or focused on *Escherichia coli* as the most frequently isolated uropathogen implicated in uncomplicated UTIs.^{4-6, 8, 10}

In order to provide a more comprehensive picture of the diverse uropathogens isolated and to monitor current trends of their antimicrobial resistance, we aimed to investigate the prevalence of resistance in community urinary isolates against first-line agents commonly used for the treatment of uncomplicated UTIs in non-hospitalized patients, and to determine whether rates of resistance varied by different age groups.

METHODS

Of 22,933 urine specimens submitted for culture from July 1st, 2009 to December 31, 2009, a total of 4,290 isolates (18.7%) from positive urine cultures yielding ≥ 10⁴ CFU/ml of one or two organisms were identified by standard methods and tested against appropriate antimicrobials by disk diffusion, in accordance with published guidelines of the Clinical and Laboratory Standards Institute (CLSI).¹ Organisms not recommended by CLSI for antimicrobial susceptibility testing were excluded from the study.

Resistance rates were determined for ampicillin (AM), cephalothin (CF), ciprofloxacin (CIP), gentamicin (GM), nitrofurantoin (FM), norfloxacin (NOR), and trimethoprim/sulfamethoxazole (TMP/SMX). Patient age groups were defined as follows: <1 - 18; >18 - 30; >30 - 40; >40 - 50; >50 - 65; >65 - 75; and >75 years.

RESULTS

The organisms and number of isolates tested in this study are listed in Table 1. Although *E. coli* was the most frequently isolated organism (65%), non-*E. coli* bacteria accounted for almost 35% of all isolates tested for antimicrobial susceptibility in this study. More isolates were tested from females (0-18 years, n = 252; >18-30 years, n = 487; >30-40 years, n = 464; >40-50 years, n = 586; >50-65 years, n = 735; >65-75 years, n = 509; >75 years, n = 593) than from males (0-18 years, n = 76; >18-30 years, n = 25; >30-40 years, n = 40; >40-50 years, n = 61; >50-65 years, n = 129; >65-75 years, n = 131; >75 years, n = 202). This high female to male ratio (5.5 : 1) is consistent with urinary isolation rates generally encountered in routine practice.

Table 2 shows the number (%) of resistant isolates for each antimicrobial agent tested in accordance with CLSI guidelines.¹

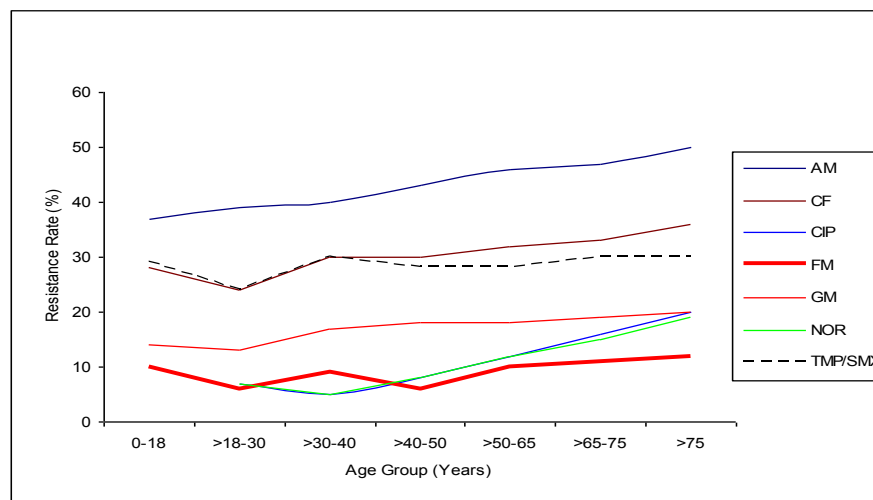
Of the 5 antimicrobial classes tested in this study, 1,526 isolates (36%) were resistant to 2 or more antimicrobial classes and 885 isolates (21%) were resistant to 3 or more classes. Of the 33 *S. aureus* isolates, one was identified as MRSA, and of the combined 3,137 *E. coli* and *Klebsiella* isolates, 106 (3.4%) and 26 (0.8%) ESBL and AmpC-phenotype expressing isolates were identified, respectively.

As seen in Table 2, the overall resistance rates for AM, CF, CIP, FM, GM, NOR, and TMP/SMX were 44%, 31%, 12%, 9%, 17%, 12%, and 29%, respectively. There was a trend towards higher resistance rates with increasing age (Table 2; Figure 1). FM was the agent with the lowest resistance rate in each age group, except for the >30 - 40 year old age group, where CIP and NOR had the lowest resistance rate. However, both fluoroquinolones showed a trend for increasing resistance rates of ≥ 12% in isolates from patients over the age of 50 and reached about 20% in isolates from those older than 75 years of age. Identification of age groups with fluoroquinolone resistance rates surpassing 10% has been recommended for surveillance of resistance.⁵

Table 1: Organisms Tested in this Study

Organism	Number of isolates (%)
<i>Escherichia coli</i>	2,805 (65)
<i>Enterococcus</i> spp.	531 (12)
<i>Klebsiella</i> spp.	332 (8)
<i>Proteus</i> spp.	218 (5)
Coagulase-negative staphylococci	106 (2.5)
<i>Citrobacter</i> spp.	86 (2)
<i>Enterobacter</i> spp.	67 (<2)
<i>Pseudomonas aeruginosa</i>	38 (<1)
<i>Morganella morganii</i>	33 (<1)
<i>Staphylococcus aureus</i>	33 (<1)
<i>Serratia</i> spp.	26 (<1)
<i>Acinetobacter</i> spp.	5 (<1)
<i>Edwardsiella</i> spp.	4 (<1)
<i>Providencia</i> spp.	4 (<1)
<i>Hafnia alvei</i>	2 (<1)
Total	4,290 (100)

Figure 1: Trends in Antimicrobial Resistance by Age*



*AM, ampicillin; CF, cephalothin; CIP, ciprofloxacin; FM, nitrofurantoin; GM, gentamicin; NOR, norfloxacin; TMP/SMX, trimethoprim/sulfamethoxazole.

Table 2: Number of Resistant Isolates and Rates of Resistance by Age Group*

Antimicrobial	AM		CF		CIP		FM		GM		NOR		TMP/SMX	
	R/T	%R	R/T	%R	R/T	%R	R/T	%R	R/T	%R	R/T	%R	R/T	%R
0 - 18	120/328	37	92/328	28	NA	NA	32/328	10	44/308	14	NA	NA	96/328	29
>18 - 30	199/512	39	125/512	24	34/471	7	32/510	6	66/500	13	33/470	7	125/512	24
>30 - 40	200/504	40	152/504	30	22/417	5	44/502	9	84/482	17	21/416	5	150/504	30
>40 - 50	278/647	43	196/647	30	45/556	8	36/646	6	110/625	18	45/556	8	182/647	28
>50 - 65	398/864	46	275/864	32	93/750	12	89/856	10	149/842	18	87/744	12	240/864	28
>65 - 75	303/640	47	214/640	33	90/554	16	70/630	11	116/620	19	82/546	15	189/640	30
>75	394/795	50	284/795	36	140/686	20	90/775	12	152/774	20	129/675	19	241/795	30
Total	1892/4290	44	1338/4290	31	424/3434	12	393/4247	9	721/4151	17	397/3407	12	1223/4290	29

* %R, percent rate of resistance; AM, ampicillin; CF, cephalothin; CIP, ciprofloxacin; FM, nitrofurantoin; GM, gentamicin; NA, not applicable; NOR, norfloxacin; R/T, number of isolates resistant/number of isolates tested; TMP/SMX, trimethoprim/sulfamethoxazole.

CONCLUSIONS

1. Current resistance patterns of community urinary isolates show a trend towards higher resistance rates with increasing age.
2. Nitrofurantoin exhibited excellent in vitro activity against the common uropathogens identified in this nonhospitalized patient population and was the agent with the lowest resistance rate compared to those of the other antimicrobials tested in this study.

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