

Prevalence of Multidrug-Resistant Gram-Negative Bacilli (MDR-GNBs) among Community Urinary Isolates and Impact of Patient Age on MDR-GNB Prevalence and Resistance Rates

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ABSTRACT

Background: Monitoring trends of multidrug resistance is critical for guiding appropriate therapy and for antimicrobial resistance surveillance. The purposes of this study were (1) to investigate the prevalence of community urinary multidrug-resistant (MDR) Gram-negative bacilli (GNBs), and their resistance rates against four commonly used oral antimicrobial agents, and (2) to determine if these rates varied by different age groups.

Methods: GNBs identified from positive urine cultures over a 3 year period ending in December 2010, were tested by disk diffusion against appropriate antimicrobial agents, in accordance with CLSI guidelines. MDR-GNBs were defined as GNBs non-intrinsically resistant to ≥ 3 classes of antimicrobial agents, including ESBL, ampC-phenotype, and carbapenemase-producing organisms. MDR-GNB prevalence and resistance rates against ciprofloxacin (CIP), nitrofurantoin (FM), norfloxacin (NOR) and trimethoprim/sulfamethoxazole (TMP/SMX) were determined overall and by patient age group (< 1 – 18; >18 – 30; >30 – 50; >50 – 65; >65 years).

Results: Of 20,768 GNBs isolated from 136,747 urine cultures, 1,983 (9.5%) were identified as MDR. The MDR-GNB prevalence rate increased from 8.97% (2008), to 9.43% (2009), to 10.17% (2010). Of all MDR-GNBs, 66% and 40% were isolated from patients > 50 and > 65 years of age, respectively. Resistance rates for CIP, FM, NOR, and TMP/SMX were 69%, 8%, 69%, and 74%, respectively, with FM having the lowest resistance rate in all age groups. There was a trend for higher resistance rates against CIP and NOR with increasing age.

Conclusion: (1) Current resistance patterns indicate an increase over the past 3 years in MDR-GNB prevalence among community urinary isolates, with a trend towards higher prevalence in older patients. (2) FM is the most likely of the oral agents tested in this study to have a favourable antibacterial effect against community urinary MDR-GNBs.

INTRODUCTION

Increasing resistance in clinical isolates, including an increase in the prevalence of extended-spectrum (ESBL), ampC-type β -lactamase producers, and methicillin-resistant *Staphylococcus aureus* has been previously described in both community and hospital settings.^{2,3,7} Dissemination of infections caused by these and other multidrug-resistant (MDR) organisms is problematic, and has recently been described by a number of national and international health organizations as a significant threat of global crisis proportions.⁵ As a result, knowledge of antimicrobial resistance in MDR pathogens is critical for guiding appropriate treatment of infection and for developing public health strategies.

Monitoring trends of multidrug resistance requires testing and analysis of antimicrobial susceptibilities. Since a significant component of daily antimicrobial susceptibility testing involves urinary tract isolates, most of which are Gram negative bacilli (GNBs), we sought to investigate the prevalence of urinary MDR-GNBs in the community over the past three years, and to determine their resistance rates against four non-beta-lactam commonly used oral antimicrobial agents, and whether these rates varied by different age groups.

METHODS

Over a 3 year period, from January 1st, 2008 to December 31, 2010, all GNBs isolated from positive urine cultures yielding $\geq 10^4$ CFU/ml of one or two organisms, were identified by standard methods and were subsequently tested against appropriate antimicrobials by disk diffusion, in accordance with current guidelines of the Clinical and Laboratory Standards Institute (CLSI).¹

MDR-GNBs were defined as GNBs that were non-intrinsically resistant to ≥ 3 classes of antimicrobial agents, including ESBL, ampC-phenotype, and carbapenemase-producing organisms. MDR-GNB prevalence and resistance rates were determined for ciprofloxacin (CIP), nitrofurantoin (FM), norfloxacin (NOR), and trimethoprim/sulfamethoxazole (TMP/SMX). Patient age groups were defined as < 1 – 18; >18 – 30; >30 – 50; >50 – 65; and >65 years.

RESULTS & DISCUSSION

Of the 136,747 urine specimens submitted for culture over the study period, a total of 20,768 GNBs (15.2%) were isolated from positive urine cultures. Of all GNBs, 1,983 (9.5%) were identified as MDR. These included *Escherichia coli* (n = 1,882), *Klebsiella* (n = 51), *Proteus* (n = 30), *Citrobacter* (n = 6), *Morganella* (n = 5), *Enterobacter* (n = 4), *Serratia* (n = 3), *Edwardsiella* (n = 1), and *Providencia* (n = 1) species. Over the three year period, the MDR-GNB prevalence rate increased from 8.97% in 2008, to 9.43% in 2009, to 10.17% in 2010 (Figure 1). Of the 1,983 MDR-GNBs, 1,307 (66%) and 793 (40%) isolates were obtained from patients >50 and >65 years of age, respectively, suggesting a trend towards higher prevalence in older patients.

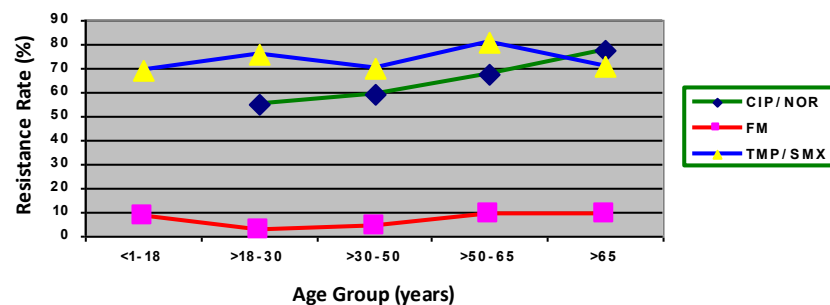
Table 1 summarizes the number and resistance rates (%) of MDR-GNB isolates by patient age group for the

Table 1: MDR-GNB Cumulative Resistance Rates (2008-2010) by Age Group*

Antimicrobial	CIP		FM		NOR		TMP/SMX	
	R/T	%R	R/T	%R	R/T	%R	R/T	%R
Age Group (yr)								
<1 - 18	NT	NT	8/97	8.2	NT	NT	67/97	69.1
>18 - 30	102/185	55.1	5/185	2.7	102/185	55.1	140/185	75.7
>30 - 50	234/394	59.4	17/394	4.3	234/394	59.4	276/394	70.1
>50 - 65	347/514	67.5	48/514	9.3	347/514	67.5	417/514	81.1
>65	614/793	77.4	75/793	9.5	614/793	77.4	564/793	71.1
Cumulative	1297/1886	68.8	153/1983	7.7	1297/1886	68.8	1464/1983	73.8

* %R, percent rate of resistance; CIP, ciprofloxacin; FM, nitrofurantoin; NT, not tested for patients ≤ 18 yr; NOR, norfloxacin; R/T, number of isolates resistant/number of isolates tested; TMP/SMX, trimethoprim/sulfamethoxazole.

Figure 2: Rates of MDR-GNB Resistance by Age (Cumulative 2008-2010)



three year period (Figure 2). Three of the four non-beta-lactams tested in this study, namely CIP, NOR, and TMP/SMX, were associated with high resistance rates of $\geq 50\%$ in every tested age group, and of $> 65\%$ in patients older than 50 years of age. Such high rates reflect the high resistance among a select group of organisms (MDR organisms) and may have been contributed to by the possible presence of repeat isolates from some patients in the course of the three years. The three-year trend for higher resistance rates observed with increasing age was consistently seen with CIP and NOR, but not with TMP/SMX.⁸ The identification of age groups with increasing fluoroquinolone resistance rates has been recommended for surveillance of resistance.⁶

The 2008, 2009, and 2010 MDR-GNB resistance rates were compared for each antimicrobial agent in the study. The yearly rate of resistance for each of the antimicrobials did not significantly change during the three year period (Figure 3). As recently observed with community urinary isolates that included MDR and non-MDR isolates,⁴ most MDR-GNB isolates in this study remained susceptible to FM.

Figure 1: MDR-GNB Prevalence Rate (2008-2010)

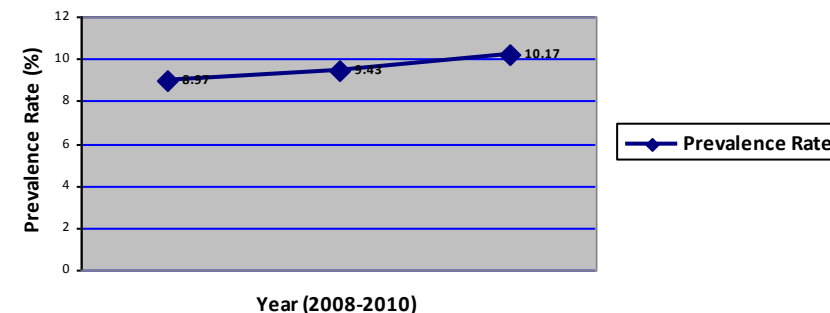
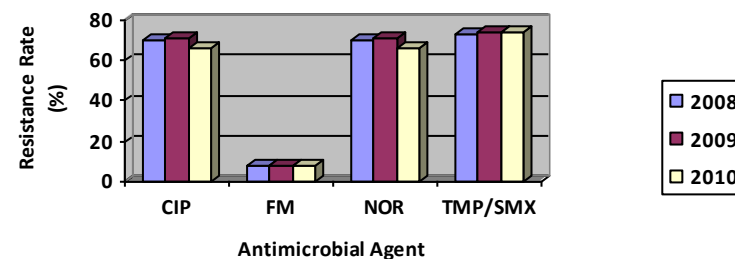


Figure 3: MDR-GNB Resistance Rates for Each Year in the Study (2008-2010)



CONCLUSIONS

- Current resistance patterns indicate an increase over the past 3 years in MDR-GNB prevalence among community urinary isolates, with a trend towards higher prevalence in older patients.
- FM is the most likely of the oral agents tested in this study to have a favourable antibacterial effect against community urinary MDR-GNBs.

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