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Antimicrobial Resistance of Urinary Isolates from Non-Hospitalized Pregnant Women

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ABSTRACT

Background: Asymptomatic bacteriuria during pregnancy can lead to urinary tract infection (UTI) which if left untreated can progress to serious complications, such as acute pyelonephritis, bacteremia, and fetal loss. However, there is only a limited selection of oral antimicrobial agents that can be considered safe and effective for the treatment of UTIs during pregnancy. The objective of this study was to determine antimicrobial resistance (R) rates in uropathogens isolated from non-hospitalized pregnant women.

Methods: Pregnant women were identified from test requisitions submitted by clinicians and by use of an in-house software program, which identified additional pregnant cases. Non-duplicate isolates were identified by conventional methods from urine cultures processed from January 2015 to December 2016. Isolates were tested by disk diffusion or the Vitek-2 system (bioMérieux), in accordance with CLSI guidelines, against ampicillin (AM), amoxicillin-clavulanic acid (AMC), cefazolin (KZ), cefixime (CEF), nitrofurantoin (FM), and trimethoprim/ sulfamethoxazole (SXT). Screening was also performed for carbapenem-resistant *Enterobacteriaceae* (CRE), extended-spectrum beta-lactamases (ESBL) in *Escherichia coli* and *Klebsiella* spp, methicillin-resistant *Staphylococcus aureus* (MRSA), and vancomycin-resistant enterococci (VRE), in accordance with CLSI guidelines.

Results: Of 172,537 urine specimens processed, a total of 555 isolates were recovered from prenatal cultures that yielded ≥ 10^4 CFU/ml, including *E. coli* (*n* = 224), *Streptococcus agalactiae* (188), *Enterococcus* species (85), *K. pneumoniae* (28), *Proteus mirabilis* (12), *Enterobacter* spp (7), *Citrobacter* spp (5), *S. aureus* (5), and *Morganella morganii* (1). R rates for AM, AMC, KZ, CEF, FM, and SXT were 25.6%, 4.0%, 19.8%, 18.8%, 9.5%, and 40.1%, respectively. *E. coli* R rates were 42.8%, 5.8%, 5.4%, 4.5%, 0.9%, and 23.2% to AM, AMC, KZ, CEF, FM, and SXT, respectively. There were a total of 8 ESBL producing isolates (all *E. coli*), but no MRSA, VRE, or CRE strains were detected in this cohort.

Conclusions: Of the oral antimicrobial agents commonly used to treat UTI in pregnancy reported in this study, AMC and FM had the lowest resistance rates overall among community urinary isolates. These results provide support for AMC and FM as useful agents with low likelihood of resistance, for the empiric treatment of UTIs caused by various Gram-negative and Gram-positive organisms in non-hospitalized pregnant women.

INTRODUCTION

Asymptomatic bacteriuria during pregnancy can lead to symptomatic urinary tract infection (UTI) which can progress to serious complications, such as acute pyelonephritis and fetal loss.[1] Oral agents are the mainstay of UTI treatment in the community. However, there is only a limited selection of oral agents that can be considered safe and effective for UTI treatment during pregnancy.[2]

A few years ago, a study from our laboratory assessed antimicrobial resistance in urinary isolates recovered from pregnant women in the community, but was limited to only Gram-negative organisms.[3] The objective of the present work was to extend the examination of antimicrobial resistance to include all significant uropathogens, both Gram-negatives and Gram-positives that were identified in urine cultures obtained from non-hospitalized pregnant women over the past two years.

METHODS

From January 01, 2015 to December 31, 2016, all eligible isolates from positive urine cultures yielding ≥ 10^4 CFU/ml of one or two organisms, were identified by standard methods and were subsequently tested against appropriate antimicrobial agents by disk diffusion or the Vitek-2 system (bioMérieux) against ampicillin (AM), amoxicillin-clavulanic acid (AMC), cefazolin (KZ), cefixime (CEF), nitrofurantoin (FM), and trimethoprim/ sulfamethoxazole (SXT), in accordance with the Clinical and Laboratory Standards Institute (CLSI) guidelines.[4,5]

Screening was also performed for carbapenem-resistant *Enterobacteriaceae* (CRE), extended-spectrum beta-lactamases (ESBL) in *Escherichia coli* and *Klebsiella* spp, methicillin-resistant *Staphylococcus aureus* (MRSA), and vancomycin-resistant enterococci (VRE), in accordance with CLSI guidelines.[4,5]

Pregnant women were identified from test requisitions submitted by clinicians and by use of an in-house software program which identified additional pregnant cases, as previously described.[3]

RESULTS & DISCUSSION

Antimicrobial Resistance: Of the 172,537 urine specimens tested from January 2015 to December 2016, a total of 555 isolates were recovered from prenatal cultures. Table 1 lists the organisms and corresponding number of isolates. Not surprisingly, *E. coli* was the most common pathogen identified. Resistance rates of the organisms combined versus those of *E. coli* and those of non-*E. coli* tested against the antimicrobial agents included in this study are summarized in Table 2. While AMC had the lowest resistance rate overall, FM had the lowest resistance rate for *E. coli* and the second-lowest resistance rate for all organisms combined; thus FM may be a useful option in pregnant patients with severe penicillin allergy or history of anaphylaxis.[6]

Resistance by Age: Resistance data were plotted by patient age (<25, 25-35, >35 years). Interestingly, among all the drugs tested, both AMC and FM had the lowest rate of resistance in each age group (Figure 1).

MDR Isolates: There were a total of 8 ESBL-producing isolates (all *E. coli*), but no MRSA, VRE, or CRE strains were detected in this cohort.

Comparative Resistance per Organism: For most organisms, AMC retained a low resistance rate per organism, ranging from 0% to 5.8% (Figure 3). Taken together, the vast majority of tested isolates belonged to organisms that had a low AMC and FM resistance rate, an observation that supports the usefulness of both agents for the empirical treatment of prenatal UTIs in the community.

Table 1: Organisms Isolated from Prenatal Urine Cultures

Organism	Number of isolates (%)
Escherichia coli	224 (40)
Streptococcus agalactiae	188 (34)
Enterococcus species	85 (15)
Klebsiella pneumoniae	28 (5)
Proteus mirabilis	12 (2)
Enterobacter spp.	7 (<2)
Citrobacter spp.	5 (<1)
Staphylococcus aureus	5 (<1)
Morganella morganii	1 (<0.5)
Total	555 (100)

Table 2: Number of Prenatal Resistant Urinary Isolates and Rates of Resistance

Antimicrobial Agent	AM		AMC		CEF		FM		KZ		SXT	
	R/T	%R	R/T	%R	R/T	%R	R/T	%R	R/T	%R	R/T	%R
All Organisms	142/ 555	**25.6**	22/ 555	**4.0**	104/ 554	**18.8**	35/ 367	**9.5**	110/ 555	**19.8**	147/ 367	**40.1**
E. coli	96/ 224	**42.8**	13/ 224	**5.8**	10/ 224	**4.5**	2/ 224	**0.9**	12/ 224	**5.4**	52/ 224	**23.2**
All Organisms excluding *E. coli*	46/ 331	**13.9**	9/ 331	**2.7**	94/ 330	**28.5**	33/ 143	**23.1**	98/ 331	**29.6**	95/ 143	**66.4**

* %R, percent rate of resistance; AM, ampicillin; AMC, amoxicillin-clavulanic acid; CEF, cefixime; FM, nitrofurantoin; KZ, cefazolin; R/T, number of resistant isolates/number of isolates tested; SXT, trimethoprim/sulfamethoxazole

Figure 1: Antimicrobial Resistance Plotted by Patient Age

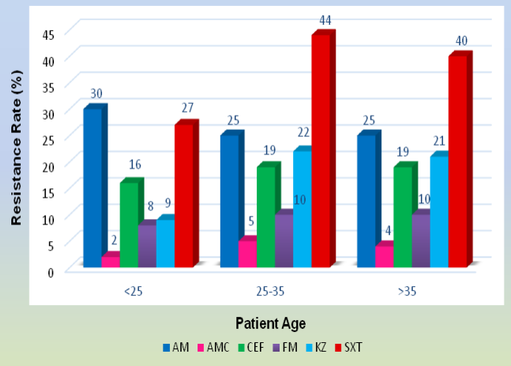
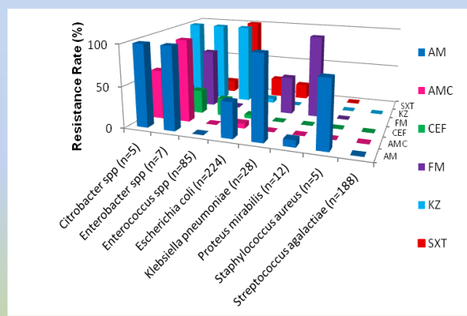


Figure 2: Antimicrobial Resistance per Organism



*Organisms with <5 isolates are not shown.

CONCLUSIONS

- Of the oral antimicrobial agents commonly used to treat UTI in pregnancy reported in this study, AMC and FM had the lowest resistance rates overall among community urinary isolates.
- These results provide support for AMC and FM as useful agents with low likelihood of resistance, for the empiric treatment of UTIs caused by various Gram-negative and Gram-positive organisms in non-hospitalized pregnant women.

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