Antimicrobial Resistance of Urinary Gram-Negative Bacilli Recovered from Pregnant Patients

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ABSTRACT

Background: There is only a limited selection of oral antimicrobial agents thought to be safe for the treatment of urinary tract infections during pregnancy. The purpose of this study was to determine the prevalence of antimicrobial resistance in community urinary Gram-negative bacilli (GNBs) isolated from pregnant patients.

Methods: Isolates were identified by conventional methods from urine cultures submitted from January 2012 to December 2013, and were tested against appropriate antimicrobial agents by disk diffusion or Vitek-2 antimicrobial susceptibility system, in accordance with CLSI guidelines. Pregnant patients were identified using an in-house software program. Prenatal GNB resistance rates were determined for ampicillin (AM), cephalothin (CF), cefixime (CEF), trimethoprim/sulfamethoxazole (TMP/SMX), and amoxicillin-clavulanic acid (AMC) for the 2 year period. Duplicate isolates with the same antibiogram from the same patient were excluded from the study.

Results: Of 105,314 urine specimens processed, 1,295 were from pregnant patients. A total of 131 non-duplicate GNBs were isolated from positive cultures, including *Escherichia coli* (n = 103), *Klebsiella pneumoniae* (n = 16), *Proteus mirabilis* (n = 6), *Enterobacter* species (n = 4), and *Morganella morganii* (n = 2). Resistance rates for AM, CF, CEF, TMP/SMX, and AMC were 49.6%, 31.3%, 4.2%, 19.8%, and 13.3%, respectively.

Conclusions: Of the five oral antimicrobial agents reported in this study, cefixime and amoxicillin-clavulanic acid had the lowest resistance rates, respectively, among urinary GNBs isolated from pregnant patients in the community.

INTRODUCTION

Most urinary tract infections (UTIs) are caused by Gram-negative bacilli (GNBs), with *Escherichia coli* described as the most frequently isolated etiologic agent.[1] In pregnant patients, asymptomatic bacteriuria can lead to UTI, which if left untreated can progress to serious complications, such as acute pyelonephritis and fetal loss.[2] Oral antimicrobial agents are usually used for treatment of UTIs in the community. However, there is only a limited selection of oral agents that can be considered safe and appropriate during pregnancy.

The purpose of this study was to determine the antimicrobial resistance rates of prenatal community urinary GNB isolates. We tested five oral antimicrobial agents commonly used during pregnancy against urinary GNBs isolated over the past two years from pregnant patients in the community setting.

METHODS

Over a 2 year period, from January 1st, 2012 to December 31, 2013, all GNBs isolated from positive urine cultures yielding ≥ 10⁴ CFU/ml of one or two organisms, were identified by standard methods and were subsequently tested against appropriate antimicrobials by disk diffusion or by the Vitek-2 antimicrobial susceptibility testing system, in accordance with current guidelines of the Clinical and Laboratory Standards Institute.[3]

Pregnant patients were identified using an in-house software program, which flagged all patients undergoing concurrent prenatal testing. Quality-assurance testing confirmed the accuracy of the software in identifying pregnant patients, including additional patients that were not initially indicated as pregnant by the test-ordering clinician.

The antimicrobial susceptibilities of prenatal urinary GNB isolates were determined for ampicillin (AM), cephalothin (CF), cefixime (CEF), trimethoprim/sulfamethoxazole (TMP/SMX), and amoxicillin-clavulanic acid (AMC) for the 2 year period. Duplicate isolates with the same antibiogram from the same patient were excluded from the study.

RESULTS & DISCUSSION

Prenatal GNBs: Of 105,314 urine specimens processed, 1,295 specimens were obtained from pregnant patients. A total of 131 GNBs were isolated from urine cultures obtained from these pregnant women. *E. coli* (n = 103) was the most frequently isolated organism. Other GNBs isolated included *Klebsiella pneumoniae* (n = 16), *Proteus mirabilis* (n = 6), *Enterobacter* species (n = 4), and *Morganella morganii* (n = 2).

Antimicrobial Resistance: Table 1 summarizes the rates of resistance of prenatal GNBs against the five agents tested in this study. AM had the highest resistance rate at almost 50%, providing further support for previous recommendations against its empiric use in pregnant patients.[2] Two of the other first-line antimicrobials, CF and TMP/SMX, had resistance rates of 31% and 20%, respectively, consistant with previous community urinary isolate resistance data.[4] Interestingly, CEF was the only antimicrobial with a single digit resistance rate, at only 4.2%, suggesting that this third-generation oral agent may be a useful alternative for pregnant patients with risk factors for first-line antimicrobial resistance, as previously recommended for a similar oral third-generation cephalosporin.[5]
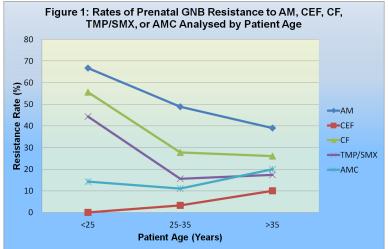
Effect of Age on Resistance: To determine if the rate of antimicrobial resistance varied by patient age, we stratified the prenatal resistance data by three age groups (<25, 25–35, and >35 years). CEF and AM had the lowest and highest resistance rate, respectively, in each patient age group. There was a trend for higher resistance rates observed with increasing age seen with CEF, but not with the other agents tested in this study. In contrast, a trend for lower resistance rates was seen with AM and CF (Figure 1).
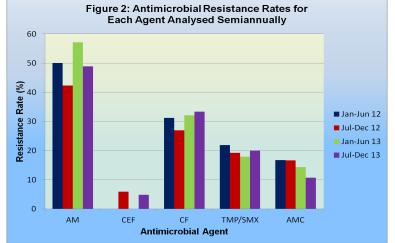
Semiannual Resistance Rates: Figure 2 shows the semiannual resistance rate for each antimicrobial agent tested during each interval. The resistance rate for each agent appears to have remained relatively stable over time.

Table 1: Number of Prenatal Resistant Isolates and Rates of Resistance by Age Group*

Age Group (yr)	AM		CEF		CF		TMP/SMX		AMC	
	R/T	%R	R/T	%R	R/T	%R	R/T	%R	R/T	%R
< 25	12/18	66.7	0/8	0	10/18	55.6	8/18	44.4	2/14	14.3
25 – 35	44/90	48.9	1/30	3.3	25/90	27.8	14/90	15.6	4/36	11.1
> 35	9/23	39.1	1/10	10.0	6/23	26.1	4/23	17.4	2/10	20.0
Cumulative Resistance	65/131	**49.6**	2/48	**4.2**	41/131	**31.3**	26/131	**19.8**	8/60	**13.3**

* %R, resistance rate (%); AM, ampicillin; AMC, amoxicillin-clavulanic acid; CEF, cefixime; CF, cephalothin; R/T, number of resistant isolates/number of total isolates; TMP/SMX, trimethoprim/sulfamethoxazole.

Figure 1: Rates of Prenatal GNB Resistance to AM, CEF, CF, TMP/SMX, or AMC Analysed by Patient Age

Figure 2: Antimicrobial Resistance Rates for Each Agent Analysed Semiannually

CONCLUSIONS

- Of the five oral antimicrobial agents reported in this study, cefixime and amoxicillin-clavulanic acid had the lowest resistance rates, respectively, among urinary GNBs isolated from pregnant patients in the community.

- Cefixime had the lowest resistance rate in *each* age group investigated (<25; 25-35; >35 years old).

- The prenatal GNB resistance rates for the antimicrobial agents in this study appear to have remained relatively stable over the past two years in the community.

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