Original Article

Antibiotic Susceptibility Patterns of Uropathogens in Obstetric Patients

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Abstract

Background: Urinary tract infections (UTI) are the most commonly encountered infections in obstetric patients. Although a variety of etiology is involved, *Escherichia coli* and other coliforms account for a large majority of these naturally acquired infections. The estimation of local etiology and susceptibility profile could support the most effective empirical treatment. **Aim:** The current study was undertaken to find the spectrum of micro-organisms responsible for causing UTI in obstetric patients and to find out the most appropriate antibiotic. **Materials and Methods:** Consecutive patients in different stages of pregnancy with or without symptoms of UTI attending the antenatal clinic during November 2011 to March 2012 were screened for significant bacteriuria. The bacterial uropathogens isolated were then subjected to antimicrobial susceptibility testing and screened for ESBL production and methicillin resistance. **Results:** During the 5-month study period, out of the 250 samples screened, a total of 60 (24%) samples of urine from pregnant females, in different stages of pregnancy were found to be positive on culture. The *Enterobacteriaceae* accounted for nearly two-thirds of the isolates and *E. coli* alone accounted for 63% of the urinary isolates followed by *Klebsiella pneumonia* 8%. Among the Gram-positive cocci, coagulase-negative *Staphylococcus* (15%) were more frequently isolated than *Staphylococcus aureus* (8.3%). A significantly high resistance was noted to the beta-lactam group of antimicrobials, fluoroquinolones and cotrimoxazole, both by the Gram-negative bacilli as well as Gram-positive cocci. Resistance was quite low against the aminoglycosides and nitrofurantoin and virtually absent against imipenem. **Conclusion:** The susceptibility patterns seen in our study seem to suggest that it is absolutely necessary to obtain sensitivity reports before initiation of antibiotic therapy in cases of suspected UTI.

Keywords: ESBL, Pregnancy, Urinary tract infection, Uropathogens

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Introduction

Urinary tract infections (UTI) are the most commonly encountered infections in obstetric patients. They can be classified as either asymptomatic or symptomatic. Asymptomatic bacteriuria (ASB) is defined as the presence of significant bacteriuria without the symptoms of an acute UTI and is reported to be seen in around 5-10% of the pregnancies. Symptomatic UTIs are divided into lower tract, acute cystitis, affecting 1-3% of patients, or upper tract, (acute pyelonephritis) which complicates 0.5-1.5% of the pregnancies. Most cases of pyelonephritis are sequelae of untreated, recurrent or inadequately treated lower UTI.[1,2]

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Pregnant women diagnosed with ASB or acute cystitis are often treated empirically before the results of culture and antibiotic sensitivity are available Although a variety of etiology is involved, *E. coli* and other coliforms account for a large majority of these naturally acquired infections.[2,3] These microorganisms vary in their susceptibility to antimicrobials from place to place and time to time.[4] Adequate treatment of these patients need a sound knowledge of the bacterial species involved and their antibiotic susceptibility patterns in a given geographical area. This information is also fundamental for care givers and health planners to guide the expected interventions.

Thus the present study was carried out to determine the spectrum of bacterial isolates causing UTI and their antibiotic susceptibility among pregnant women attending antenatal clinic.

Materials and Methods

This study was conducted prospectively in the Department of Microbiology, Jhalawar Medical College and Hospital, in the Antenatal Care Clinic from November 2011 to March 2012 after ethical clearance from the institution review board. Consecutive patients in different stages of pregnancy with or without symptoms of UTI attending the antenatal clinic were screened for significant bacteriuria. All the study subjects were first instructed to clean the area around the urethral meatus with soap and clean water and collect the urine with labia held apart. Fresh midstream urine was collected aseptically in sterile containers and submitted to the clinical microbiology laboratory. The samples which were received were inoculated onto Blood Agar and Mac Conkey agar. After an overnight aerobic incubation at 37°C, the plates showing significant growth as per the Kass count (single species count of more than 10^5 organisms per ml of urine) were processed further and the isolates were identified up to the species level by using standard biochemical tests. Antibiotic sensitivity testing was done by the Kirby Bauer disc diffusion method according to the CLSI guidelines.[5] The following antibiotic discs (drug concentrations in µg) were used: Ampicillin (10), Amoxicillin/clavulanic acid (Augmentin 20/10), Gentamicin (10), Ceftazidime (30), Cefoperazone (75), Ceftriaxone (30), Cotrimoxazole (25), Ciprofloxacin (5), Amikacin (30), Norfloxacin (10), Nitrofurantoin (300), Imipenem (10) and Cefoxitin (30).

Screening of possible ESBL production was done using ceftriaxone (30 µg) and cefoperazone (75 µg). Those isolates with zone diameters less than 25 mm for ceftriaxone and less than 22 mm for cefoperazone were subsequently confirmed for ESBL production. Confirmation was done by Double Disk Synergy Test (DDST) as per CLSI guidelines.[6] Cefoperazone (75 µg) and Ceftazidime (30 µg) disks with and without Clavulanic acid (10 µg) were used. The organisms were phenotypically confirmed as ESBL producers only when they showed an increase in zone of inhibition greater than or equal to 5 mm when evaluated in combination with clavulanic acid. Quality control was performed testing *Escherichia coli* ATCC 25922.

Cefoxitin (30 µg) was used as a surrogate for oxacillin resistance. All strains of *Staphylococcus aureus* and coagulase-negative *Staphylococcus* resistant to cefoxitin were considered resistant to all the other beta-lactam antimicrobials including cephalosporins and carbapenems.[7]

Statistical Analysis

Statistical analysis was done using chi-square test and Student's *t* test.

Results

During the 5-months study period i.e., Nov'2011-Mar 2012, out of the 250 samples screened, a total of 60 (24%) samples of urine from pregnant females, in different stages of pregnancy were found to be positive on culture. Majority of the patients showing growth on culture had ASB (75%), while symptomatic UTI was present in only 25% of the pregnant females (*P*-value < 0.001). Most of the patients with symptomatic as well as asymptomatic UTI were in the first trimester of pregnancy (59%), followed by third trimester (38%), only 3% had bacteriuria in the second trimester of pregnancy.

The *Enterobacteriaceae* accounted for nearly two-thirds of the isolates and *E. coli* alone accounted for 63% of the urinary isolates followed by *Klebsiella pneumonia* 8%. Among the Gram-positive cocci, CONS 9 (15%) were more frequently isolated than *S. aureus* (8.3%) [Table 1].

Bacterial uropathogens isolated from pregnant women with UTI revealed the presence of high levels of single and multiple antimicrobial resistances against commonly prescribed drugs as shown in Table 2. A significantly high resistance was noted to the beta-lactam group of antimicrobials, fluoroquinolones and cotrimoxazole, both by the Gram-negative bacilli as well as Gram-positive cocci. Resistance was quite low against the aminoglycosides and nitrofurantoin and virtually absent against imipenem.

Discussion

Pregnancy is a unique state with anatomic and physiologic urinary tract changes. While ASB in non pregnant women is generally benign, pregnant women with bacteriuria have an increased susceptibility to pyelonephritis.[8] Screening for and treatment of ASB in pregnancy has become a standard of obstetric care and most antenatal guidelines include routine screening for ASB. The present study was conducted to evaluate the prevalence of UTI in pregnant females and to review the drugs that can be used for the treatment of the same. Moreover, the data would also help the authorities to formulate antibiotic prescription policies. Proper investigation and prompt treatment are needed to prevent serious life threatening condition and morbidity due to UTI that can occur in pregnant women.[1,2,8]

UTI may manifest as ASB or symptomatic bacteriuria. The prevalence of asymptomatic UTI has been previously reported to be 2- 13% in pregnant women compared with that of symptomatic UTI which occurs in 1-18% during pregnancy.[1,9-11] Our study findings also indicate that ASB was present in a fairly large percentage of pregnant females. We, therefore recommend screening of all

Table1: Distribution of bacterial uropathogens isolated from pregnant women

Organism isolated	No. of isolates	%
Escherichia coli	38	63.3
Klebsiella spp	5	8.3
Pseudomonas spp	1	1.7
Proteus spp	2	3.4
CONS	9	15
Staph aureus	5	8.3
Total positive urine culture	60	

Table 2: Resistance of bacterial uropathogens to antibiotics

Name of antibiotic	% of resistance
Ampicillin	90
Augmentin	78
Gentamicin	15
Amikacin	0
Cotrimoxazole	75
Ciprofloxacin	80
Norfloxacin	75
Nitrofurantoin	10
Ceftazidime	35
Ceftriaxone	35
Cefoperazone	35
Imipenem	0

pregnant women because timely intervention with the appropriate antibiotics can prevent drastic consequences. There is no consensus in literature as to the optimal timing and screening frequency for ASB. Few recent studies suggest that urine should be cultured in each trimester of pregnancy to improve the detection rate.[12] Screening for and treatment of ASB to prevent pyelonephritis has also been shown to be cost effective over a wide range of estimates according to earlier studies.[13]

The Gram-negative bacteria predominated, with *E. coli* being the most common pathogen (63.3%) isolated in the study. Other studies had also reported a similar frequency of UTI caused by *E. coli*.[14,15] Among the Gram-positive cocci, CONS was isolated most frequently (15%), followed by *S. aureus* (8.3%), a view also corroborated by Rizvi *et al*.[16]

There has been no systematic review of which antibiotic is best for the treatment of ASB. The antibiotic chosen should not only have a good maternal and fetal safety profile, but also excellent efficacy and low resistance rates in a given population.[17,18] Although many review articles suggest antibiotic regimens for both symptomatic and ASB in pregnancy, increasing antibiotic resistance complicates empirical regimens. On antimicrobial susceptibility testing, it was noted that both the Gram-negative as well as Gram-positive isolates showed a significantly high resistance to the beta-lactam group of antimicrobials which are considered the traditional drugs safe in pregnancy. Along with this the presence of ESBLs in 45% of the *E. coli* and 40% of the *Klebsiella* spp. isolates is a further cause of worry. In a study from PGI Chandigarh on complicated UTIs, ESBL production was noted in a similar frequency.[19] Among the Gram-positive cocci more than one third of the isolates were found to be methicillin resistant. This is especially unfortunate because these isolates are then considered resistant to all the other currently available beta-lactam antimicrobials including cephalosporins and carbapenems. Although the usage of beta-lactam antimicrobials is considered safe in pregnancy, but the resistance to these drugs, by the common pathogens is alarmingly high as seen in our study which restricts their use to only the sensitive strains. There are similar reports of high-level resistance in the general population to these drugs by the urinary pathogens.[15]

Fluoroquinolones have been shown to impair cartilage development in animal studies. Although this adverse effect has not been described in humans, quinolones should rather be avoided in pregnancy. As it is a high level of resistance to the tune of 75-80% resistance was noted in the current study. Other studies have also reported high resistance to the fluoroquinolones, to even the newer ones such as ofloxacin and pefloxacin.[15,20,21]

Aminoglycosides were found to have a better profile than other group of drugs but unfortunately these cannot be used in pregnant women. Similarly the carbapenems to which all the isolates were found to be uniformly sensitive cannot be given in pregnancy. Regarding cotrimoxazole, concerns have been raised over the use in the first trimester due to association with neural tube and other birth defects. However, its use near term may lead to displacement of bilirubin causing jaundice and kernicterus in the infant.[13,20] For this reason its use in pregnant women nearing term is also discouraged. Overall a high rate of resistance (75%) was seen among the urinary isolates in the current study. Similar discouraging results are also seen in another contemporary study.[13,15,21] To conclude, we demonstrated a high level of resistance to the commonly used first line agents like beta-lactams, fluoroquinolones and cotrimoxazole. As these oral agents usually achieve high urinary concentrations, it was initially thought that *in vitro* resistance may not result in treatment failure. However, recent studies have demonstrated otherwise.[17,22]

Nitrofurantoin has been used for more than five decades for the treatment of uncomplicated cystitis and it was found to remain active against most of the uropathogens. Recent data suggests that nitrofurantoin has retained a

good amount of sensitivity (90.98%), both against ESBL producers and non-ESBL producers.[23,24] The absorption of oral nitrofurantoin is 40-50% and hence, it is enhanced when taken with food. The drug has minimal side effects and can be safely used for the treatment of uncomplicated cystitis even during pregnancy.[13,23]

The susceptibility patterns seen in our study seem to suggest that it is absolutely necessary to obtain sensitivity reports before initiation of antibiotic therapy in cases of suspected UTIs. High resistance rates to oral antibiotics in our study may be due to the uncontrolled consumption of these antibiotics in the community in the past decade.[25] On the other hand, resistance to amikacin, gentamicin and imipenem are low, likely reflecting lower usage of these drugs. Their safety in pregnancy is, however, questionable.[13] Various studies corroborate our findings suggesting lower resistance rates among uropathogens to nitrofurantoin.[13,23] This along with the fact that it is considered safe in all trimesters of pregnancy suggests that nitrofurantoin may be considered as a first line agent for treatment of UTIs among the pregnant females.

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