Pattern of Urinary Antibiograms in a Tertiary Care Hospital of Eastern India

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Abstract

Background: Indiscriminate use of antibiotics in urinary tract infections have led to emergence of ‘superbugs’ worldwide. Periodical review of antibiograms is of utmost importance for optimum patient benefit.

Objectives: To identify the spectrum of organisms responsible for urinary tract infection and evaluate the pattern of antibiotic sensitivity of the organisms.

Methods: Urine samples were collected from all consecutive patients getting admitted in the medicine indoor irrespective of symptomatology. The clean-catch technique of midstream urine was used for patients able to void spontaneously while specimens of catheterized patients were obtained prior to catheter change. All samples were sent for routine examination as well as culture sensitivity tests. Descriptive statistical methods were used with the help of SPSS-15th version.

Result: The total number of patients was 262, 160 (60.3%) were male and 102 (39.7%) female. The age of the subjects varied from 18 to 85 years. Significant bacteruria was found in 35.9% patients. The commonest organisms isolated overall were E coli (59.6%) followed by enterococcus spp (14.9%) and Klebsiella (10.6%). Among catheterized subjects apart from E coli (64%), Klebsiella was found to be commoner (12%) than Enterococcus 10%. Most Enterobactereacae showed good response to aminoglycosides, cephoperazone sulbactam and nitrofurantoin. However, organisms like Enterobacter, Citrobacter, Morganella and pseudomonas were poorly responsive to the above and required higher antibiotics like carbapenems, and polymixin B. Staph. aureus was responsive to linezolid and vancomycin only.

Conclusion

The progression of resistance of common urinary pathogens to higher antibiotics is an inexorable process. Our study reveals that new generation cephalosporins, quinolones and macrolides cannot keep up with the rapidity of emergence of multiresistant strains.

Editorial Viewpoint

• In this study involving midstream urine specimen cultures of indoor medical patients, 35.9% had significant bacteruria. E. coli was commonest followed by Enterococcus spp and Klebsiella.

• The prevalence of organisms in catheterised patients was similar.

• Organisms other than Enterobactereacae needed much higher antibiotics sounding a note of caution.

Introduction

Urinary tract infections (UTI) are a major cause of morbidity in our population leading to serious long term complications including hypertension and chronic kidney disease. Recurrent UTIs warrant the use of multiple courses of antibiotic therapy. Eventually, the risk of antibiotic-resistant organisms is increased. Therefore, choice of suitable antibiotics is a major determinant of appropriate therapy and prevention of chronic complications.

Studies concerning culture sensitivity profiles of urine have been performed over decades.¹-³ There have been changes in the sensitivity profiles over time and more so due to indiscriminate as well illogical use of antibiotics. We endeavoured to study the current trend of causative organisms and their antibiotic sensitivity and to compare it with previous work done in this field.
Objectives

1. To identify the spectrum of organisms responsible for urinary tract infections.
2. To evaluate the pattern of antibiotic sensitivity in the organisms.

Material and Methods

This is a prospective observational study conducted from January 2012 to July 2012. Samples were collected from all consecutive patients getting admitted in our unit in the Medicine indoor ward irrespective of symptomatology.

All patients underwent a clinical assessment with history regarding their symptoms, co-morbidities, and medications along with a complete physical examination.

The clean-catch technique of midstream urine was used for patients able to void spontaneously. Urine specimens of catheterized patients were obtained prior to catheter change or removal from each patient. Ten ml of urine was obtained from the distal edge of the catheter tube (after cleaning with an antiseptic) using a sterile needle and syringe into sterile universal container (Kunin and McCormack 1966; Kunin, 1979) and transported to the laboratory for testing. Those who were catheterized for less than three days were excluded in the study. The patients were not started on any antibiotics before urine samples were taken.

The samples were plated on Blood Agar and MacConkey Agar media by the semi-quantitative plating method using the calibrated loop technique (0.001 mL). Plates were incubated aerobically overnight at 37°C.

Plates showing growth suggestive of significant bacteruria, with colony counts exceeding 10^5 cfu/ml were subjected to standard biochemical tests for identification and antimicrobial sensitivity testing by Kirby-Bauer disc diffusion method. Interpretation as ‘Sensitive’ or ‘Resistant’ was done on the basis of the diameters of zones of inhibition of bacterial growth as recommended by the disc manufacturer.

Antimicrobial sensitivity tests were performed on bacteria considered significant. The antibiotics included in our study were co-amoxiclav (20/10 mcg), ampicillin (10 mcg), amikacin (30 mcg), trimethoprim/sulphamethoxazole (co-trimoxazole) (25/23.75 mcg), norfloxacin (5 mcg), ciprofloxacin (5 mcg), levofloxacin (5 mcg), ofloxacin, nitrofurantoin (300 mcg), gentamicin (10 mcg), amikacin (30 mcg) doxycycline, cefuroxime (30 mcg), ceftriaxone (30 mcg), ceftazidime (30 mcg), cefotaxime (30 mcg), netilmicin (30 mcg), polymixin B (2 mcg), piperacillin/tazobactam (100/10 mcg), cefoperazone/sulbactam (75/30 mcg), meropenem (10 mcg), imipenem (10 mcg), and vancomycin (30 mcg).

Descriptive and inferential statistical methods were used. Data were analyzed using SPSS-15th version. A probability of <0.05 was accepted as significant. For continuous variables having normal distribution, data were summarized using mean ± SD, range and median were used for all continuous variables having non-normal distribution (i.e. age).

Results

The study was undertaken in the medicine indoor of a tertiary care hospital from Jan 2012 to July 2012 in our unit. The total number of consecutive patients was 262 out of which 160 (60.3%) were male 102 (39.7%) were female. The age of the subjects varied from 18 to 85 years the mean age being fifty-two. Total number of catheterized patients was 96 (37%), the indications varying from unconscious patient, spinal cord disease to obstructive uropathy. The total number of patients documenting significant bacteruria was 96 (35.9%) out of which 50 (52%) were catheterized patients while the figure for non-catheterized patients was 44 (26.5%). Thirty six patients (14.5%) were culture negative but had greater than 5 WBCs/ml of urine. Of these about 74% patients presented with symptoms of flank pain, suprapubic discomfort, dysuria or cloudy urine rest were asymptomatic.

Comorbidities encountered most commonly in our medicine ward were diabetes mellitus, prostatomegaly, cerebrovascular accidents, spinal cord disease and encephalopathies often leading to catheterizations. There were 70 diabetic patients. The mean HbA1c value was 7.6 ± 0.82. Significant bacteruria was documented in 42.8% (30) cases. Severe infection and sepsis ensued in four such cases leading to acute kidney injury with mortality in two patients. The commonest organisms isolated overall were E. coli (59.6%) followed by Enterococcus spp (14.9%) and Klebsiella (10.6%) (Table 1). Among these isolates, there were 23.2% ESBLs in E. coli and 9.4% ESBLs in K. pneumoniae.

Among catheterized subjects some exotic organisms like Citrobacter, Acinetobacter, and Morganella were isolated apart from E. coli 64%, Klebsiella 12% and Enterococcus 10%. The scenario among diabetics was a 42.8% incidence of significant bacteruria, common organisms being E. coli, Klebsiella, Pseudomonas and Staph aureus.

The maximum sensitivity of E. coli was found to be following...
**Table 2: Antibiotics sensitivity pattern of urinary tract organisms**

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>E. coli Sensitivity (%)</th>
<th>Enteroococcus Sensitivity (%)</th>
<th>Klebsiella Sensitivity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>74</td>
<td>5</td>
<td>72</td>
</tr>
<tr>
<td>Gentamycin</td>
<td>72</td>
<td>10</td>
<td>75</td>
</tr>
<tr>
<td>Netilmicin</td>
<td>76</td>
<td>4</td>
<td>70</td>
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<td>Ciprofloxacin</td>
<td>25</td>
<td>10</td>
<td>50</td>
</tr>
<tr>
<td>Norfloxacin</td>
<td>5</td>
<td>10</td>
<td>25</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>52</td>
<td>33</td>
<td>50</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>25</td>
<td>5</td>
<td>30</td>
</tr>
<tr>
<td>Linezolid</td>
<td>2</td>
<td>67</td>
<td>5</td>
</tr>
<tr>
<td>Coamoxiclavanulate</td>
<td>20</td>
<td>50</td>
<td>10</td>
</tr>
<tr>
<td>Piperacillin tazobactam</td>
<td>35</td>
<td>10</td>
<td>50</td>
</tr>
<tr>
<td>Polimyxin B</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>0</td>
<td>30</td>
<td>5</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>0</td>
<td>ND</td>
<td>10</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>52</td>
<td>83.3</td>
<td>75</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>30</td>
<td>15</td>
<td>75</td>
</tr>
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<td>Co-trimoxazole</td>
<td>15</td>
<td>16</td>
<td>50</td>
</tr>
<tr>
<td>Imipenem</td>
<td>33</td>
<td>25</td>
<td>52</td>
</tr>
<tr>
<td>Meropenem</td>
<td>38</td>
<td>30</td>
<td>50</td>
</tr>
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<td>Cefipime</td>
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<td>20</td>
</tr>
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<td>Ceftriaxone</td>
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<td>Cefotaxime</td>
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<td>25</td>
</tr>
<tr>
<td>Cefixime</td>
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<td>10</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>10</td>
<td>5</td>
<td>15</td>
</tr>
<tr>
<td>Cefoperazone sulbactam</td>
<td>72</td>
<td>5</td>
<td>100</td>
</tr>
</tbody>
</table>

ND: Not done

 drugs – aminoglycosides (72-76%), cefoperazone-sulbactam (72%) nitrofurantoin (52%), carbapenems (33-38%) and piperacillin tazobactam (33%). They were mostly resistant to all quinolones except levofloxacin (52%) and all cephalosporins (except sulbactam combinations). Cotrimoxazole and doxycycline showed poor response (Table 2).

Enterococcus had maximum sensitivity to nitrofurantoin (83%), linezolid (67%), coamoxiclav (50%) and levofloxacin (33%) They were to highly unresponsive to other quinolones, 3rd generation cephalosporins, cotrimoxazole and even aminoglycosides (Table 2).

The sensitivity profile of Klebsiella reflected good response to cefoperazone sulbactam, (100%) aminoglycosides (75%), nitrofurantoin (75%), quinolones (50%) and imipenem (Table 2).

The less common organisms isolated in our study were Citrobacter, Acinetobacter, Morganella, Pseudomonas and Staph aureus. Citrobacter showed 50% sensitivity was seen to carbapenems and to piperacillin tazobactam. It demonstrated 100% resistance to aminoglycosides, quinolones, 3rd generation cephalosporins and cotrimoxazole.

Acinetobacter manifested 100% sensitivity to levofloxacin, cefoperazone sulbactam and polymixin B. They were resistant to even carbapenems, other quinolones and 3rd generation cephalosporins.

Morganella, Pseudomonas and Staph aureus isolates proved to be multidrug-resistant with the first two responding only to carbapenems, colistin and polymixin B. Staph aureus showed 100% sensitivity to linezolid and vancomycin in our study, with 100% resistance to coamoxy clavulanate.

**Discussion**

There has been considerable variability in microbial etiology as well as antibiograms for urinary tract infections (UTI) over the decades. Moreover, different regional and socioeconomic milieus seem to have an effect on patterns of UTIs and their management protocol.

The prevalence of UTI was found to be 77.9% in South-Eastern Nigeria, 60% in North Central Nigeria; 7% in Turkey, and 24.5% in India. Our study documents a prevalence of 35.9%. This supports the suggestions of local and regional differences in UTI prevalence in various settings.

Regarding causative organisms E coli seems to be omnipotent over time, place and person. Other organisms documented were variable in different studies.

In a Western study conducted in 1999 Causative organisms included Escherichia coli (85%), Proteus mirabilis (6%), Klebsiella pneumonia (4%), Enterobacter species (2%), Citrobacter freundii (2%), Providencia species (<1%), and Morganella morganii (<1%).

In a Nigerian study Staphylococcus aureus was the most predominant pathogen isolated, followed closely by Escherichia coli, Klebsiella pneumoniae and Proteus mirabilis. Pseudomonas aeruginosa was the least common isolated pathogen.

In South East Asian territory, a study from Lahore in 2009 described the predominant species to be Escherichia coli, Klebsiella pneumoniae, Streptococcus faecalis, Staphylococcus aureus, Proteus vulgaris and Acinetobacter. A study from North-West India documented E coli followed by coagulase negative Staphylococcus and Klebsiella to be the commonest organisms isolated.

Our study conducted in 2012 showed though E coli was the commonest (59.6%), enterobacter (14.9%) to be a commoner finding then Klebsiella (10.6%), followed by Citrobacter, Pseudomonas, Acinetobacter and Staph aureus.

ESBL strains were detected in 23.2% ESBLs in E. coli and 9.4% ESBLs in K. pneumoniae. In a retrospective study from Jaipur, an increasing trend in the isolation of ESBL producing E. coli (from 9.52% to 30.08%) has been noticed over a period from 2007-2009.

In previous studies, the incidence of CAUTI ranged from 11.0–73.3%. In the present study, incidence was 52% since those who were catheterized for less than three
days were excluded in the study which might be the chief reason for a higher incidence of CAUTI in the present study. The corresponding figure in noncatheterized patients was 26.6% and the difference is statistically significant.

CAUTI increases the burden of the patient in terms of increased morbidity and mortality, prolonged hospital stay, and cost of the tests and medicines.16,17 Tambyah et al18 found that CAUTI had been responsible for an additional of USD 589 per CAUTI in diagnostic tests and in medications.

Pathogenic organisms responsible for CAUTI and their antibiotic sensitivity pattern also vary with time and place.19,20 The commonest pathogen isolated in an African study CAUTI was Klebsiella spp followed by Pseudomonas spp, Escherichia coli, Staphylococcus aureus, Candida albicans.21 In an Ethiopian study Klebsiella spp. (33.3%) and E. coli (27.7%) were the most common bacteria pathogens isolated in both groups and followed by Enterobacter spp. (6%). Proteus spp., Pseudomonas spp. and coagulase-negative staphylococci were isolated only from catheterized patients.22

In a study, Jha et al23 found that most common organisms responsible for CAUTI were E. coli (49%), S. aureus (23%), Proteus spp. (3.6%), Klebsiella (9.71%), Pseudomonas (0.8%), and Citrobacter (2.8%). Another Indian study documented Candida species to be most frequently isolated followed by E. coli.24 In the present study, E. coli 64%, Klebsiella 12%, enterobacter 10%, Staph aureus 6% Citrobacter 4%, Pseudomonas 2.1% and Acinetobacter 1.9% were isolated. Urinary calculi, vesicoureteral reflux, interval of catheter change, and previous antibiotic treatment were not investigated in our study. If these factors were additionally investigated, the relationship between voiding methods and our results could be clarified further.25

Asymptomatic bacteriuria (ABU) occurs when bacteria colonize the urinary tract without causing clinical symptoms and can affect both cathetered patients (catheter-associated ABU [CA-ABU]) and noncathetered patients.26 Our study revealed 36% patients to be having asymptomatic bacteriuria. Absence of symptoms breeds complications and delay in diagnosis. Hence routine urine examination in case of admitted patients may have some importance in reducing morbidity.

Risk factors for urosepsis are previous incidence of UTI, diabetes mellitus, dementia prostatomegaly, renal calculi, reflux disease, prior urological or gynaecological surgery, catheterization or urethral instrumentation along with other structural abnormalities like posterior urethral valve, CAKUT (congenital anomalies of kidney and urinary tract) and ADPKD (autosomal dominant polycystic kidney disease). An Indian study had demonstrated high prevalence of emphysematous pyelonephritis in uncontrolled diabetics with a mortality of 8.3%.27 However, demonstration and detailed evaluation of the comorbidities and underlying predisposing factors for urosepsis, was not in the purview of our present study.

The antibiotic sensitivity shows a trend towards resistance to higher antibiotics over time. Cotrimoxazole resistance had been declared in the eighties while norfloxacin was hailed as a very good option.28 In an Indian study in 1993 early quinolones like norfloxacin and ciprofloxacin were found to be promising drugs against E coli and Klebsiella.29 Then came drugs like cefotaxime and other 3rd generation cephalosporins. This era was short-lived as the late nineties saw the addition of sulbactam to the drugs like ceftoperazone or ceftriaxone to increase effectiveness.30 Newer drugs like carbapenems emerged later to which multiresistant organisms responded. New studies are documenting organims elaborating carbapenemases making even these drugs ineffective in certain cases of catheter-associated UTI (CAUTI) or structural urogenital abnormalities. An Indian study from Kanpur documented carbapenem resistance maximally in Staph aureus isolates followed by E coli and Pseudomonas.31

However strangely enough a recent study from Bareily showed 75% of E. coli isolates were sensitive to minocycline, showing a good utility of this drug for the treatment of outdoor patients with urinary tract infections.32

In our study, the highest sensitivity against Gram negatives was produced by aminoglycosides, third generation cephalosporins + sulbactam, carbapenems and nitrofurantoin. Nitrofurantoin being the earliest drug effective against uropathogens seems to have regained its glory. Among the fluoroquinolones, levofloxacin showed some promise. For Gram positive organisms drugs like, vancomycin and linezolid showed reliable sensitivity. It is to be noted that there was a paucity of orally effective drugs in a high percentage of cases.

Small study population and limited duration was a pitfall of our study. Moreover detailed investigations regarding the predisposing factors and comorbidities could not be undertaken because of various constraints. Further studies are warranted to elucidate these correlations.

Conclusion

The prevalence of UTI among admitted patients was found to be 35.9%, the commonest culprits being E coli, Enterobacter and Klebsiella. Management of UTI is often empirical without recourse to urine culture or susceptibility testing to guide therapy. A continuous review of antibiograms is also necessary to
track changes in aetiological agents and antimicrobial patterns to help in empirical treatment.

Overuse of antibiotics and improper use of higher groups seems to be the main factor in the expansion of drug resistance and emergence of ‘superbugs’. The current status of sensitivity of common organisms rests mainly on nitrofurantoin, levofloxacin, cefoperazone-sulbactam and aminoglycosides. Multiresistant organisms still show some responsiveness to polymixin B, colistin and linezolid. In this miserable scenario it seems awareness and prevention of UTI would be a better policy than finding newer drugs for cure.

References


