Antibacterial susceptibility of uropathogens in 3 hospitals, Sari, Islamic Republic of Iran, 2002–2003

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ABSTRACT To determine the frequency and pattern of antibiotic susceptibility of uropathogens in urinary tract infection (UTI) from 3 university hospitals we carried out a retrospective review of urine culture and antibiotic sensitivity testing from symptomatic outpatients and inpatients during 2002–2003. Of 5600 samples, 703 (12.6%) were culture positive, 38.7% of which were from hospitalized patients. Escherichia coli was the leading cause of UTI in both groups of patients. The rates and roles of other pathogens, including Pseudomonas spp. (5.3%–10.4%), Enterobacter spp. (0%–5.7%), Staphylococcus spp. (5.4%–26.4%), differed in each hospital. Differences in antibacterial susceptibility patterns were observed. Ampicillin (82%–100%) and co-trimoxazole (50%–90%) resistance were the most frequent. Methicillin resistance in Staphylococcus spp. ranged from 17% to 60%.

Sensibilité aux antibactériens des uropathogènes dans trois hôpitaux de Sari (République islamique d'Iran), 2002-2003

RÉSUMÉ Afin de déterminer la fréquence et les caractéristiques de la sensibilité aux antibiotiques des uropathogènes lors d'une infection urinaire dans trois hôpitaux universitaires, nous avons effectué un examen rétrospectif des urocultures et des tests de sensibilité aux antibiotiques pratiqués sur des malades asymptomatiques non hospitalisés et hospitalisés en 2002 et 2003. Sur 5600 échantillons, 703 (12.6 %) étaient positifs à la culture, et 38.7 % de ceux-ci provenaient des patients hospitalisés. Escherichia coli était la principale cause d'infection urinaire dans les deux groupes de patients. Les taux et le rôle des autres agents pathogènes, notamment Pseudomonas spp. (5.3 % à 10.4 %), Enterobacter spp. (0 % à 5.7 %) et Staphylococcus spp. (5.4 % à 26.4 %), n'étaient pas les mêmes dans chaque hôpital. Des différences ont été observées dans les profils de sensibilité aux antibiotiques. La résistance à l'amoxicilline (82 % à 100 %) et au cotrimoxazole (50 % à 90 %) était la plus fréquente. La résistance à la méthicilline de Staphylococcus spp. était comprise entre 17 % et 60 %.
Introduction

Urinary tract infection (UTI) remains a worldwide therapeutic problem, not only as a nosocomial disease but also as a community-acquired infection [1–5]. It poses a significant health risk because it can lead to urosepsis and/or renal scarring, progressive kidney damage with associated high mortality, morbidity, and economic loss [5,6]. Early diagnosis and prompt antimicrobial treatment are required to minimize these complications [7].

The etiology of UTI and the antibiotic susceptibility of urinary pathogens in both the community and hospitals have been changing, and in recent years antibiotic resistance has become a major problem worldwide [8–12]. Resistant organisms have emerged owing to several factors related to the genetic nature of the organisms and selective antimicrobial pressure in humans and animals [13]. To ensure appropriate treatment, knowledge of the organisms that cause UTI and their antibiotic susceptibility is mandatory. As both temporal and local variables can modify these data, they need to be constantly re-evaluated to achieve maximum clinical response before the antibacterial sensitivity profiles of the isolated uropathogen is known [8–12].

The aim of this study was to determine the relative role of each uropathogen and their antibacterial sensitivity patterns in nosocomial and community-acquired UTI in 3 university hospitals in Sari, capital of Mazandaran province:

- Boali-Cina Hospital; a general hospital with ~300 active beds and various out-patient clinics, the main medico-surgical centre serving neonatal and paediatric patients. Annual activity is 9300 admissions (4000 < 14 years), 3500 major surgeries and 315 000 outpatient visits;
- Imam Hospital; the main surgical hospital (general surgery; gynaecological; neurological; urological; orthopaedic) with ~400 active beds and yearly activity of 17 100 admissions, 7500 major surgeries and 200 000 outpatient visits;
- Zaree Hospital; the sole burn centre, with ~100 beds, yearly admissions ~800 patients and 8000 outpatients and emergency visits.

All the information recorded for each patient in the log books of each of the laboratories was reviewed. This included demographic data, urine culture results (type of bacterial growth and susceptibility patterns). The tests are routine procedures undertaken in a similar manner by professional laboratory technicians in the university hospital laboratories. The antibacterial policy for empirical treatment of UTI in each setting since 1992–93 is shown in Table 1.

Quantitative urine culture was performed at the microbiology laboratories within each hospital with a 0.01 mL calibrated loop to inoculate a blood agar base plate (Merck, Germany) and eosin methylene blue agar plate (ATD-Antec Diagnostic, UK). The plates were incubated at 37 °C for 24 hours. Bacterial isolates were identified by conventional procedures [14]. A positive urine culture was defined as the growth of ≥ 10 000 colony forming units/mL of a single uropathogen for specimens obtained

Methods

Laboratory diagnosed UTIs in symptomatic patients were evaluated retrospectively over a period of 12 months (July 2002–July 2003) to document the common uropathogens and their antimicrobial susceptibility patterns.
by suprapubic or catheterization methods and > 100 000 colony forming units/mL for samples collected by the clean-catch midstream technique.

Antibiotic sensitivity testing was performed using the Kirby–Bauer disc diffusion method (Padtan–Teb, Tehran). Antibiotics tested for were: ceftriaxone, cefotaxime, ceftazidime (in Imam and Zaree hospitals), amikacin, gentamicin, nalidixic acid, ciprofloxacin, norfloxacin (in Imam and Zaree hospitals), ampicillin and co-trimoxazole and for Gram-positive bacteria ceftazolin, cephalaxin, methicillin, vancomycin and clindamycin.

The collected data were recorded and analysed using descriptive statistical methods: percentile for relative role of each uropathogen and antibacterial susceptibility pattern and chi-squared test to compare differences between relative roles of antibiotic susceptibility both within and between each hospital.

### Results

Of 5600 urine samples 703 (12.6%) were culture positive, 272 (38.7%) of which were from hospitalized patients. Distribution of samples collected from the 3 hospitals is shown in Table 2. Overall female/male ratio was 2.7.

*Escherichia coli* was the leading cause of UTI in this study but its relative role was lower in inpatients (54.8%) compared
to outpatients (70.0%), and the relative rates of other uropathogens were higher. As shown in Table 3, the rank order of isolated uropathogens and their relative roles in different settings (inpatients and outpatients) in the 3 hospitals was as follows: Boali-Cina Hospital: most patients were neonates/children with a first episode of UTI, even in hospitalized patients. In Imam Hospital, most patients were adults. In Zaree Hospital all cases were nosocomial. Urine cultures positive for fungi (*Candida* spp.) were reported from 3 (1.1%) hospitalized patients (2 neonates, 1 adult) who had urinary catheter.

Most of the nosocomial UTI cases were adults with burns or patients with medical or surgical problems having short duration urinary tract catheterization and/or antibacterial treatment, or children with febrile UTI.

Although there were no significant differences in antibacterial susceptibility patterns for samples from inpatients and outpatients for each uropathogen in each hospital, there were significant differences between hospitals. Most isolates were highly resistant to ampicillin (82%–100%) and cotrimoxazole (50%–90%). Conversely, most of the uropathogens isolated showed acceptable sensitivity to nitrofurantoin (57%–90%). *E. coli*, the leading pathogen, was highly sensitive to amikacin, gentamicin, ceftriaxone, and ciprofloxacin (Table 4). Other Gram-negative uropathogens except for *Pseudomonas* spp. showed moderate to high susceptibility to these drugs. *Pseudomonas* spp. were highly sensitive to amikacin and intermediate to gentamicin and quinolones. High levels of resistance to the third generation cephalosporins (ceftiraxone, cefotaxime, ceftazidime) were detected in *Pseudomonas* spp. isolates (100% in Zaree Hospital, even for ceftazidime).

The sensitivity testing profiles of *Staphylococcus* spp. (Table 5) showed high levels of sensitivity to clindamycin, vancomycin, and aminoglycosides, moderate to high susceptibility to methicillin and first generation cephalosporins (cephazolin and cephalaxin). The highest levels of resistance to methicillin, (60%) first generation cephalosporins (60%) and vancomycin (30%) were reported for *Staph. aureus* isolated from Zaree Hospital. However, complete resistance to ampicillin was noted (data not shown).

**Discussion**

In some previous studies, the relative role for *E. coli* varied between 32.4% [15] for nosocomial UTI and > 85–90% in patients with uncomplicated infections [10,11]. In 2 studies on children with nosocomial-complicated UTI, results indicated that *E. coli*, with 32.4% and 40.3% isolation rates, was the leading uropathogen followed by other Gram-negative bacilli, Gram-positive cocci and fungi [15,16]. Studies on adult patients with nosocomial UTI showed similar results: 26.6%–35.6% in catheterized patients [17] and 47% in hospitalized patients [12]. Studies on cases of uncomplicated community-acquired UTI in children and adults also indicated that *E. coli* with 47% [18], 63% [16] and more than 86% [10,11] isolation rates was the most common uropathogen, followed by other Gram-negative bacilli, Gram-positive cocci, and, rarely, fungi.

Except for *Candida* spp. and enterococci in hospitalized patients, the results of this study are comparable with those of other studies. UTI caused by these microbes, usually occurred with long-term urinary tract catheterization and/or prolonged anti-
Table 3  Relative roles of isolated uropathogens in 3 hospitals in Sari, 2003

<table>
<thead>
<tr>
<th>Hospital</th>
<th>Escherichia coli</th>
<th>Pseudomonas spp.</th>
<th>Enterobacter</th>
<th>Proteus</th>
<th>Staphylococcus spp.</th>
<th>Othera</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Boali-Cina</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inpatients</td>
<td>105</td>
<td>63.3</td>
<td>21</td>
<td>12.7</td>
<td>13</td>
<td>7.8</td>
</tr>
<tr>
<td>Outpatients</td>
<td>185</td>
<td>77.7</td>
<td>21</td>
<td>8.8</td>
<td>10</td>
<td>4.2</td>
</tr>
<tr>
<td>Imam</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inpatients</td>
<td>25</td>
<td>36.8</td>
<td>4</td>
<td>5.9</td>
<td>3</td>
<td>4.4</td>
</tr>
<tr>
<td>Outpatients</td>
<td>117</td>
<td>60.6</td>
<td>8</td>
<td>4.1</td>
<td>10</td>
<td>5.2</td>
</tr>
<tr>
<td>Zaree</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inpatients</td>
<td>19</td>
<td>50.0</td>
<td>2</td>
<td>5.3</td>
<td>7b</td>
<td>18.4</td>
</tr>
<tr>
<td>Total (n=703)</td>
<td>451</td>
<td>64.2</td>
<td>56</td>
<td>8.0</td>
<td>43</td>
<td>6.1</td>
</tr>
</tbody>
</table>

E. coli role: Boali-Cina Hospital inpatients vs. Boali-Cina Hospital outpatients \( P = 0.001 \); Imam Hospital inpatients vs. Imam Hospital outpatients \( P = 0.0006 \).

*Boali-Cina Hospital inpatients: 2 cases Candida, 3 cases enterococci; Imam Hospital inpatients: 23 cases other Gram-negative bacilli, 1 case Candida, 1 case enterococci; Imam Hospital outpatients: 42 cases other Gram-negative bacilli, 1 case enterococci.

b*Citrobacter*.

The antibacterial sensitivity patterns showed some inter-hospital variation among isolated uropathogens. Activity of ampicillin and co-trimoxazole were the lowest. Studies in Trinidad and Israel obtained similar resistance levels to ours [21,22]. However, other studies have found lower levels [11,12,16]. Based on these empirical therapy with these drugs for UTI is not satisfactory and is not recommended.

In contrast to ampicillin and co-trimoxazole, the antibacterial activity of nitrofurantoin against isolated uropathogens was acceptable, so as cephalosporins, aminoglycosides, and quinolones. Accordingly, until the results of sensitivity testing are available, empirical therapy with one of these drugs is recommended.

The majority of nosocomial UTI cases were adult patients with burns or patients with medical or surgical problems with shorter duration of urinary tract catheterization and antibacterial therapy, especially in patients in neonatal or paediatric intensive care units or in elderly patients [19,20]. In our study, the majority of nosocomial UTI cases were adult patients with burns or patients with medical or surgical problems with shorter duration of urinary tract catheterization and antibacterial therapy. This may explain the rarity of fungal or enterococcal UTI cases in our study.

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in Zaree Hospital. There was little variation among centres in prevalence of resistance to tested antibiotics except for methicillin and cephazolin. More than 60% of isolates at Zaree Hospital were resistant to methicillin and cephazolin. The rates of resistance to methicillin and first generation cephalosporins, especially at Zaree Hospital, are among the highest figures reported \cite{18,23,24}. The highest anti-staphylococcal activity was seen for clindamycin and vancomycin.

\begin{table}[h]
\centering
\caption{Antibacterial sensitivity patterns of uropathogens isolated at 3 hospitals in Sari, 2003}
\begin{tabular}{|l|c|c|c|c|c|}
\hline
\textbf{Pathogen} & \textbf{Boali-Cina Hospital} & \textbf{Imam Hospital} & \textbf{Zaree Hospital} \\
& \textbf{Inpatients} & \textbf{Outpatients} & \textbf{Inpatients} & \textbf{Outpatients} & \textbf{Inpatients} \\
\hline
\textit{Escherichia coli} & & & & & \\
Ceftriaxone & 96 & 97 & 75 & 82 & 73 \\
Amikacin\textsuperscript{a} & 98 & 98 & 80 & 91 & 95 \\
Gentamicin & 95 & 97 & 85 & 92 & 90 \\
Ciprofloxacin & 98 & 99 & 97 & 97 & 79 \\
Nitrofurantoin & 90 & 90 & 57 & 57 & 73 \\
Ampicillin & 7 & 6 & 16 & 17 & 16 \\
Co-trimoxazole & 30 & 20 & 44 & 47 & 10 \\
\hline
\textit{Pseudomonas} spp. & & & & & \\
Ceftriaxone\textsuperscript{b} & 38 & 48 & 25 & 50 & 0 \\
Ceftazidime & NT & NT & 67 & 67 & 0 \\
Amikacin\textsuperscript{a} & 80 & 86 & 50 & 75 & 100 \\
Gentamicin & 71 & 67 & 50 & 50 & 50 \\
Ciprofloxacin & 76 & 76 & 50 & 75 & 50 \\
\hline
\textit{Enterobacter} spp.\textsuperscript{c} & & & & & \\
Ceftriaxone & 85 & 90 & 67 & 90 & 28 \\
Amikacin\textsuperscript{a} & 85 & 90 & 66 & 90 & 86 \\
Gentamicin & 85 & 100 & 100 & 100 & 86 \\
Ciprofloxacin & 92 & 100 & 100 & 100 & 59 \\
Nitrofurantoin & 69 & 80 & 67 & 70 & 71 \\
Ampicillin & 8 & 10 & 0 & 10 & 0 \\
Co-trimoxazole & 23 & 30 & 0 & 10 & 14 \\
\hline
\textit{Proteus} spp.\textsuperscript{d} & & & & & \\
Ceftriaxone & 89 & 100 & 50 & 72 & – \\
Amikacin\textsuperscript{a} & 100 & 100 & 72 & 69 & – \\
Gentamicin & 100 & 100 & 54 & 67 & – \\
Ciprofloxacin & 100 & 100 & 50 & 72 & – \\
Nitrofurantoin & 66 & 67 & 50 & 67 & – \\
Ampicillin & 22 & 17 & 0 & 33 & – \\
Co-trimoxazole & 33 & 33 & 50 & 33 & – \\
\hline
\end{tabular}
\end{table}

\textsuperscript{a}Boali-Cina Hospital, Imam Hospital: $P = 0.02$.
\textsuperscript{b}Boali-Cina Hospital, Imam Hospital: $P = 0.005$.
\textsuperscript{c}Citrobacter in Zaree Hospital.
\textsuperscript{d}Other Gram-negative bacilli in Imam Hospital.
NT = not tested.
Table 5 Antibacterial susceptibility patterns for Staphylococcus spp. in 3 hospitals in Sari, 2003

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Boali-Cina Hospital Inpatients</th>
<th>Imam Hospital Inpatients</th>
<th>Zaree Hospital Inpatients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (n = 10)</td>
<td>% (n = 12)</td>
<td>% (n = 7)</td>
</tr>
<tr>
<td>Methicillin</td>
<td>80</td>
<td>83</td>
<td>72</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>80</td>
<td>75</td>
<td>72</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>90</td>
<td>95</td>
<td>86</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>100</td>
<td>92</td>
<td>86</td>
</tr>
<tr>
<td>Amikacin</td>
<td>90</td>
<td>83</td>
<td>86</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>90</td>
<td>72</td>
<td>56</td>
</tr>
</tbody>
</table>

Boali-Cina Hospital vs. Zaree Hospital: \( P = 0.38 \).
Boali-Cina Hospital inpatients vs. Zaree Hospital inpatients: \( P = 0.04 \).
Boali-Cina Hospital outpatients vs. Imam Hospital outpatients: \( P = 0.45 \).

Conclusion

The results of this study emphasize the necessity of monitoring the relative roles of each uropathogen in community- and nosocomial-UTI, and the antibiotic resistance level varies between centres. Initiation of optimal empirical antibiotic therapy should be based on local knowledge of the most likely infecting microorganisms and their sensitivity to antimicrobial drugs.

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References


