Etiology and Antibiotic Susceptibility Patterns of Community-Acquired Urinary Tract Infections in a Kuwait Hospital

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Abstract
Objective: The aim of this study was to determine the distribution and antibiotic susceptibility patterns of bacterial strains isolated from patients with community-acquired urinary tract infections (UTIs) at the Infectious Diseases Hospital, Kuwait. Materials and Methods: The study was conducted over a 7-year period. Patient information was obtained from medical record files. Antibiotic-sensitivity testing was performed by disk diffusion. E test and double disk diffusion methods were used to study the production of extended spectrum β-lactamases. Results: Of the 14,042 urine samples processed, significant bacteriuria (>10⁵ cfu/ml) was detected in 1,606 (11.4%). The majority (74.5%) of the isolates were from women while the remaining 25.5% were from men. The majority of infections (75%) were due to Enterobacteriaceae, coagulase-negative staphylococci (10.3%) and group B streptococci (8.7%). Among the gram-negative enteric bacilli high prevalence of resistance to ampicillin, amoxicillin/clavulanic acid, cephalothin, and trimethoprim/sulfamethoxazole was observed. Increasing resistance to ciprofloxacin and gentamicin was observed in E. coli isolates over the 7 years. Multiple resistance was detected in 53.8 and 41% of E. coli and Klebsiella spp. strains, respectively. No glycopeptide-resistant enterococci were isolated. Conclusion: This study revealed that Enterobacteriaceae were the predominant bacterial pathogen of community-acquired UTIs in Infectious Diseases Hospital, Kuwait. It also demonstrated an increasing resistance to ciprofloxacin, gentamicin and the production of extended spectrum β-lactamase among UTI pathogens in the community.

Introduction
Urinary tract infections (UTIs) represent one of the most common diseases encountered in medical practice today. However, its impact and frequency vary in different populations. It is estimated that about 20–30% of adult women experience UTI at least once during their life [1]. UTIs occur at a rate of 2–3 per 100 hospital admissions and constitute 35–40% of all hospital-acquired
infections [2–4]. Most episodes of UTI are caused by *Escherichia coli* (up to 85%) and *Staphylococcus saprophyticus* (up to 10%), while *Klebsiella pneumoniae* and *Proteus* spp. account for most of the remaining infections [4].

UTIs are often treated with different broad-spectrum antibiotics when one with a narrow spectrum of activity may be appropriate because of concerns about infection with resistant organisms. Consequently, the extensive uses of antimicrobial agents have invariably resulted in the development of antibiotic resistance, which, in recent years, has become a major problem worldwide [4, 5]. Several study groups have reported on the antibiotic susceptibility rates for Enterobacteriaceae or bacteria isolated from UTI. However, in most of these studies the bacterial isolates were recovered among inpatients [5–7].

The susceptibility pattern of community-acquired UTI pathogens has been documented in only a few studies [8–10]. The etiology of UTI and the antibiotic susceptibility of urinary pathogens have been changing over the past years, both in community- and hospital-acquired infections [11, 12]. However, there is no information on the etiology and susceptibility patterns of community-acquired UTIs in Kuwait. This retrospective study was conducted to compare the frequency and drug susceptibility patterns of urinary pathogens isolated from urine cultures received from outpatients at the Infectious Diseases Hospital (IDH), Kuwait during a period of 7 years, 1995–2001.

**Materials and Methods**

*Sample Collection and Analysis*

The study was conducted on patients attending outpatient clinics at the IDH, Kuwait between January 1995 and December 2001. Freshly voided midstream specimens of urine (n = 14,042) were submitted to the Clinical Microbiology Laboratory of IDH, Kuwait for processing. Semiquantitative urine culture using a calibrated loop was used to inoculate blood agar and MacConkey plates [13]. Following the recommendations of Kass [14] in distinguishing genuine infection from contamination, significant monomicrobial bacteria was defined as culture of a single bacterial species from the urine specimen at a concentration of \( >1 \times 10^5 \) cfu/ml. Only a single positive culture per patient was included in the analysis. Urine specimens containing \( >10^5 \) or \( <10^5 \) cfu/ml of nonpathogenic bacteria (lactobacilli, diphtheroids or non-group D *Streptococcus* spp.) or multiple (three or more) species of gram-negative enteric bacilli (GNEB), obtained from patients without clinical evidence of urinary infection, were considered as contaminants and were excluded from the study. The significant pathogens were identified by standard biochemical procedures [15]. Information about the patient’s age and sex were collected from medical records.

**Antimicrobial Susceptibility Testing**

Antimicrobial susceptibility testing was performed using the disk diffusion method as described by the National Committee for Clinical Laboratory Standards [16]. Antimicrobial agents (disks) tested and reported were obtained from their respective manufacturers and included: penicillin G (10 U), ampicillin (10 µg), oxacillin (1 µg), ampicillin/clavulanic acid (30 µg), piperacillin/tazobactam (110/10 µg), cephalothin (30 µg), cefuroxime (30 µg), ceftoxitin (30 µg), ceftriaxone (30 µg), cefotaxime (30 µg), cefazidine (30 µg), imipenem (10 µg), ciprofloxacin (5 µg), nalidixic acid (30 µg), gentamicin (10 µg), gentamicin (200 µg), amikacin (30 µg), vancomycin (30 µg), teicoplanin (30 µg), trimethoprim/sulfamethoxazole (25/23.75 µg).

**Detection of ESBL Production**

Evaluation of isolates for ESBL production were done by double disk diffusion method, which revealed a synergistic effect between clavulanic acid and either cefotaxime or cefazidime and E-test ESBL strips (AB Biodisk, Solna, Sweden). Strains with reduced zones of inhibition below that of the normal susceptible population, but above the standard breakpoint for extended spectrum cephalosporins or aztreonam were screened for potential ESBL production. A reduction in \( \beta \)-lactam minimum inhibitory concentration (MIC) by greater than two log₂ dilutions indicated ESBL production [17–20]. The disk antagonism tests based on resistance to cefoxitin and cefotaxin/cefotaxime were used to determine the production of inducible chromosomal AmpC \( \beta \)-lactamases [19].

**Results**

Of the 14,042 urine samples processed 1,606 (11.4%) yielded significant growth of pathogens. The patients were between 10 and 80 years of age. More cases of UTIs were recorded among young and middle age patients (20–50 years, 63.4%). Pediatric patients (including teenagers) comprised 23.2% and adult and elderly (50–80 years) constituted 13.3% of the total number. More organisms were isolated from women (74.5%) than from men (25.5%).

Of the 1,606 significant isolates, gram-negative aerobic rods accounted for 74.7% while gram-positive cocci accounted for the remaining 22.3% of the pathogens. *Candida albicans* constituted 3% of the isolates. The frequency and distribution of the different microorganisms is summarized in table 1. *E. coli* (48.65%), *Klebsiella* spp. (12.2%), coagulase-negative staphylococci (10.3%), group B streptococci (8.7%) and *P. aeruginosa* (4.8%) were the most prevalent.
There was no significant shift in the types of organisms causing UTIs in outpatients over the 7-year period. Although the isolation of *E. coli* declined during 1998, 1999 and 2000 (46.2, 41.8, 43.5%) in comparison to 1995, 1996 and 1997 (51.4, 52.3, 52.3%), respectively, it remained the most common cause of community-acquired UTIs.

The antibiotic susceptibility rates for GNEB are presented in tables 2 and 3. Among the β-lactam antibiotics, imipenem had the widest coverage against gram-negative pathogens.
isolates (100%). This was followed by the third-generation cephalosporins, cefotaxime, ceftiraxone, ceftazidime, for which 96.0, 96.0 and 97.0% of the isolates, respectively, were susceptible. Cefuroxime was less active (89.8% susceptible). Whereas 91% of the GNEB were susceptible to ciprofloxacin, only 82.2% of them were susceptible to nalidixic acid. Among the aminoglycosides, amikacin (99.4% susceptibility) was more active than gentamicin (90% susceptibility). Trimethoprim/sulfamethoxazole was less active with only 54% of the isolates susceptible.

The analysis of the results of antibiotic sensitivity patterns of gram-negative urinary pathogens revealed high prevalence of resistance to ampicillin, amoxicillin/clavulanic acid, cephalexin and trimethoprim/sulfamethoxazole. Enterobacter spp. (96.6%) and Klebsiella spp. (98.3%) were more resistant to ampicillin than E. coli (74%) and Proteus spp. (43%). Multiresistance (resistance to more than two classes of antibiotics) was detected in 53.8 and 41% of E. coli and Klebsiella spp. isolates, respectively. Five isolates, 3 Klebsiella spp. and 2 E. coli, produced ESBL. Nine isolates, 6 Enterobacter spp. and 3 E. coli, produced inducible chromosomal AmpC ß-lactamase. All of the antipseudomonal agents examined demonstrated potent in vitro activity. However, 2 strains of P. aeruginosa were resistant to imipenem.

During the study period, we observed a gradual decrease in the susceptibility of E. coli to third-generation cephalosporins (1–3%), ciprofloxacin (3–5%), and gentamicin (1–3%).

Among the gram-positive cocci, all of the Enterococcus spp. and Streptococcus agalactiae isolates were susceptible to ampicillin and none of them was resistant to the glycopeptides. However, 8% of the coagulase-negative staphylococci was resistant to oxacillin.

**Discussion**

This study investigated the distribution and antibiotic susceptibility patterns of bacterial pathogens isolated from patients with uncomplicated community-acquired UTI. The results showed that 11% of urine samples from patients attending outpatient clinics at IDH, Kuwait yielded significant pathogens and more than 95% of UTIs were caused by a single bacterial pathogen. Uropathogenic E. coli was the most common pathogen in acute UTI in previous studies [4]. In this study, it accounted for approximately 49% of all clinically significant urinary isolates and 65% of all Enterobacteriaceae (table 1). This is consistent with the findings of previous studies in which E. coli was the predominant pathogen isolated from patients with community-acquired UTIs [21].

The rate of susceptibility of GNEB to third-generation cephalosporins and amikacin in this study was over 95%. Ciprofloxacin, frequently used in the community, was ac-

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**Table 3. Antimicrobial potency and spectrum for seven selected antimicrobial agents against most frequently occurring UTI pathogens (GNEB) 1995–2001**

<table>
<thead>
<tr>
<th>Microorganisms</th>
<th>Years (tested strains, n)</th>
<th>Antimicrobial agent/% sensitive strains</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Tzp</td>
</tr>
<tr>
<td>E. coli</td>
<td>1995–2001 (780)</td>
<td>97.8</td>
</tr>
<tr>
<td></td>
<td>1995 (90)</td>
<td>100.0</td>
</tr>
<tr>
<td></td>
<td>2001 (83)</td>
<td>98.8</td>
</tr>
<tr>
<td>Klebsiella spp.</td>
<td>1995–2001 (196)</td>
<td>85.7</td>
</tr>
<tr>
<td></td>
<td>1995 (15)</td>
<td>100.0</td>
</tr>
<tr>
<td></td>
<td>2001 (13)</td>
<td>100.0</td>
</tr>
<tr>
<td>Proteus spp.</td>
<td>1995–2001 (48)</td>
<td>100.0</td>
</tr>
<tr>
<td></td>
<td>1995 (8)</td>
<td>100.0</td>
</tr>
<tr>
<td></td>
<td>2001 (10)</td>
<td>100.0</td>
</tr>
<tr>
<td>Other GNEB</td>
<td>1995–2001 (70)</td>
<td>94.9</td>
</tr>
<tr>
<td>All GNEB</td>
<td>1995–2001 (1094)</td>
<td>94.8</td>
</tr>
</tbody>
</table>

GNEB = Gram–negative enteric bacilli; Tzp = piperacillin/tazobactam; Ipm = imipenem; Gm = gentamicin; An = amikacin; Cip = ciprofloxacin; Na = nalidixic acid; Sxt = trimethoprim/sulfamethoxazole.
tive on average against 91% of Enterobacteriaceae urinary isolates. These results are consistent with those of other community-based studies [8, 22, 23]. Our data also showed a substantial reduction in susceptibility to antibiotics frequently used in the community such as ampicillin, cephalexin and trimethoprim/sulfamethoxazole among E. coli isolates (from 31 to 19%, 77.8 to 56%, 53 to 45.5%, respectively). The percentage of multiple resistant strains among E. coli urinary isolates was 53.8%. The slow, but persistent decrease in sensitivity of E. coli to ciprofloxacin and gentamicin is worrying because these antibiotics have proven very effective for the treatment of UTI in both outpatients and hospitalized patients [9, 20]. Other Enterobacteriaceae, such as Klebsiella spp., Enterobacter spp. and Proteus spp., are also common uropathogens. However, Klebsiella spp. is rarely encountered among urinary isolates (from 31 to 19%, 77.8 to 56%, 53 to 45.5%, respectively). The finding suggests that ESBL-producing strains are present within the community; therefore monitoring of antibiotic susceptibility of bacteria isolates in the community should be mandatory.

In addition, 9 isolates, consisting of 6 Enterobacter spp. and 3 E. coli produced chromosomally meditated, inducible AmpC class β-lactamase. This is an important finding, since it indicates that infection with these strains that are usually found in hospitals are now being acquired in the community.

Gram-positive bacteria, such as S. saprophyticus and Enterococcus, can produce UTIs in certain patient populations [24, 25]. For example, S. saprophyticus is a common pathogen in young, sexually active women and causes approximately 10% of UTIs among this group of patients [24–26]. Enterococcus often is a problem in complicated UTI, in patients with indwelling urethral catheters, or in patients receiving broad-spectrum antibiotics for another infection. The low prevalence of enterococci (2.5%) in this study is consistent with the fact that the patients in this study were outpatients with no indwelling catheters.

Conclusion

This study revealed that Enterobacteriaceae were the predominant bacterial pathogens of community-acquired UTIs detected in IDH, Kuwait. It has also demonstrated an increasing resistance to ciprofloxacin, gentamicin and the production of ESBL. The finding suggests that ESBL-producing strains are present within the community; therefore monitoring of antibiotic susceptibility of bacteria isolates in the community should be mandatory.

References


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