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

M.J. Saffar,[1] A.A. Enayti,[1] I.A. Abdolla,[1] M.S. Razai[1] and H. Saffar[1]

استجابة مسببات العدوى البولية للأدوية المضادة للجراثيم في ثلاثة مستشفيات في ساري، جمهورية إيران الإسلامية، 2002 – 2003

محمد جعفر صفار، أحمد علي عنايتي، عباس عبد اللهي، محمد صادق رضايي، هيوا صفار

الخلاصة: في سبيل التعرف على تكرار ونماذج استجابة مسببات العدوى البولية للأدوية المضادة للجراثيم في ثلاثة مستشفيات جامعية، أجريت دراسة استعادية استعرض الباحثون فيها مزارع البول والاستجابة للمضادات الحيوية لدى المرضى الخارجيين والداخليين الذين يشكون من أعراض خلال المدة 2002 – 2003. وقد شملت الدراسة 5600 عينة، منها 703 عينة (12.6٪) إيجابية بالزرع، وقد كان 38.7٪ منها لمرضى داخليين. ومثَّلت الإشريكية القولونية السببَ الرئيسي لالتهاب المجاري البولية في المرضى الداخليين والخارجيين. أما الجراثيم المسببة الأخرى فضمَّت أنواعاً من الزوائف (5.3٪ – 10.4٪)، وأنواعاً من المعويات (0٪ - 5.7٪)، وأنواعاً من العنقوديات (5.4٪ – 26.4٪)، وتختلف هذه الأنواع والمعدلات باختلاف المستشفيات. وقد لوحظت الاختلافات أيضاً في أنماط الاستجابة للأدوية المضادة للجراثيم، وكان الأكثر تواتراً بينها، ما كان منها مقاوماً للأمبيسلين (82٪ – 100٪) وللكوتريموكسازول (50٪ – 90٪). أما أنواع العنقوديات المقاومة للميثيسيلين فقد تراوحت بين 17٪ و60٪.

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 symptomatiques 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 antibactériens. La résistance à l'ampicilline (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 %.

[1]Department of Paediatrics, Mazandaran University of Medical Sciences, Sari, Islamic Republic of Iran (Correspondence to M.J. Saffar: saffar@softhome.net).
Received: 27/12/05; accepted: 14/03/06

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, Islamic Republic of Iran.

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. The study was conducted in 3 university hospitals in Sari, capital of Mazandaran province:

- Boali-Cina Hospital; a general hospital with ~300 active beds and various outpatient 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

Table 1 **Antibacterial policy for empirical treatment of urinary tract infection at 3 hospitals in Sari, 2003**

Hospital	Complicated, inpatients		Uncomplicated, outpatients	
	Children	Adults	Children	Adults
Boali-Cina & Imam				
1993–2000	Cephalosporin[a]	Ampicillin + gentamicin	Nalidixic acid	Co-trimoxazole
2000– ……	Cephalosporin[a]	Cephalosporin[a]	Cefixime	Co-trimoxazole/ ciprofloxacin
Zaree	No specific policy			

[a]3rd generation (mainly ceftriaxone).

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 cefazolin, cephalexin, 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

Table 2 **Distribution of positive cultures for urine samples at 3 hospitals in Sari, 2003**

Hospital	Total samples		Positive samples			
	No.	%	No.	%	Inpatient/ outpatient	Females/ males
Boali-Cina[a]	3363	60.0	404	57.5	166/238	2.3/1
Imam[b]	2036	36.4	261	37.1	68/193	2.4/1
Zaree[c]	201	3.6	38	5.4	38/0	3.0/1
Total	5600	100.0	703	12.6	272/431	2.7/1

[a]Age distribution: 80.0% < 20 years; 54.5% < 5 years; 35.9% < 12 months.
[b]Age distribution: 7.6% < 20 years; 27.4% > 70 years.
[c]All > 12 years.

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 were 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 (ceftriaxone, 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 cephalexin). 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**

Hospital	***Escherichia coli***		***Pseudomonas***		***Enterobacter***		***Proteus***		***Staphylococcus* spp.**		**Other[a]**	
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
Boali-Cina												
Inpatients (***n*** = 166)	105	63.3	21	12.7	13	7.8	9	5.4	10	6.0	8	4.8
Outpatients (***n*** = 238)	185	77.7	21	8.8	10	4.2	6	2.5	12	5.0	4	1.7
Imam												
Inpatients (***n*** = 68)	25	36.8	4	5.9	3	4.4	2	2.9	7	10.3	27	39.7
Outpatients (***n*** = 193)	117	60.6	8	4.1	10	5.2	3	1.6	11	5.7	44	22.8
Zaree												
Inpatients (***n*** = 38)	19	50.0	2	5.3	7[b]	18.4	0	0.0	10	26.3	0	0.0
Total (***n*** = 703)	451	64.2	56	8.0	43	6.1	20	2.8	50	7.1	83	11.8

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.***

[a]***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.

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

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 this, 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 noted in a previous study [*9*], it can be recommended in cases of simple afebrile UTI and/or for completion of therapy.

In this study, *E. coli* and other Gram-negative bacilli (except *Pseudomonas* spp.) showed high levels of sensitivity to most tested third generation cephalosporins, aminoglycosides, and quinolones. Accordingly, until the results of sensitivity testing are available, empirical therapy of UTI with one of these drugs is recommended.

The results showed that 7.1% of uropathogen isolates were *Staphylococcus* spp. *Staph. aureus* was the second commonest cause of nosocomial UTI

Table 4 **Antibacterial sensitivity patterns of uropathogens isolated at 3 hospitals in Sari, 2003**

Pathogen & antibiotic	Boali-Cina Hospital		Imam Hospital		Zaree Hospital
	Inpatients %	Outpatients %	Inpatients %	Outpatients %	Inpatients %
Escherichia coli					
Ceftriaxone	96	97	75	82	73
Amikacin[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
Pseudomonas spp.					
Ceftriaxone[b]	38	48	25	50	0
Ceftazidime	NT	NT	67	67	0
Amikacin[a]	80	86	50	75	100
Gentamicin	71	67	50	50	50
Ciprofloxacin	76	76	50	75	50
Enterobacter spp.[c]					
Ceftriaxone	85	90	67	90	28
Amikacin[a]	85	90	66	90	86
Gentamycin	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
Proteus spp.[d]					
Ceftriaxone	89	100	50	72	–
Amikacin[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	–

[a]***Boali-Cina Hospital, Imam Hospital:*** P ***= 0.02.***
[b]***Boali-Cina Hospital, Imam Hospital: P = 0.005.***
[c]Citrobacter ***in Zaree Hospital.***
[d]***Other Gram-negative bacilli in Imam Hospital.***
NT = not tested.

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 [*18,23,24*]. The highest anti-staphylococcal activity was seen for clindamycin and vancomycin.

Table 5 **Antibacterial susceptibility patterns for *Staphylococcus* spp. in 3 hospitals in Sari, 2003**

Antibiotic	Boali-Cina Hospital		Imam Hospital		Zaree Hospital
	Inpatients % (*n* = 10)	Outpatients % (*n* = 12)	Inpatients % (*n* = 7)	Outpatients % (*n* = 11)	Inpatients % (*n* = 10)
Methicillin	80	83	72	82	40
Cefazolin	80	75	72	73	40
Vancomycin	90	95	86	91	70
Clindamycin	100	92	86	91	90
Amikacin	90	83	86	82	90
Gentamicin	90	72	56	73	80

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.

Acknowledgement

We would like to thank L. Barati MD and F. Qasalsoflu MD for their critical help in data collection for this project.

References

1. Bacheller CD, Bernstein JM. Urinary tract infection. ***Medical clinics of North America***, 1997, 81(3):719–30.
2. Kalsi J et al. Hospital-acquired urinary tract infection. ***International journal of clinical practice***, 2003, 57(5):388–91.
3. Hoberman A, Wald ER. Urinary tract infection in young febrile children. ***Pediatric infectious disease journal***, 1997, 16(1):11–7.
4. Orrett FA et al. Paediatric nosocomial urinary tract infection at a regional hospital. ***International urology and nephrology***, 1999, 31(2):173–9.
5. Gupta K et al. Antimicrobial resistance among uropathogens that cause community-acquired urinary tract infections in women: a nationwide analysis. ***Clinical infectious diseases***, 2001, 33(1):89–94.
6. Foxman B. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. ***Disease-a-month***, 2003, 49(2):53–70.
7. Committee on Quality Improvement. Subcommittee on Urinary Tract Infection. The diagnosis, treatment, and evaluation of the initial UTI in febrile infants and young children. ***Pediatrics***, 1999, 103:843–52.
8. Sefton AM. The impact of resistance on the management of urinary tract infection. ***International journal of antimicrobial agents***, 2000, 16:489–91.
9. Gupta K. Emerging antibiotic resistance in urinary tract infections. ***Infectious disease***

clinics of North America, 2003, 17(2):243–59.

10. Chomarat M. Resistance of bacterial in urinary tract infections. ***International journal of antimicrobial agents***, 2000, 16:483–7.

11. Prais D et al. Bacterial susceptibility to oral antibiotics in community acquired urinary tract infections. ***Archives of disease in childhood***, 2003, 88(2):215–8.

12. Gordon KA, Jones RA, SENTRY Participant Groups Europe, LA. Susceptibility patterns of orally administered antimicrobials among urinary tract infection pathogens from hospitalized patients in North America: comparison report to Europe and Latin America. Results from the SENTRY Antimicrobial Surveillance Program (2000). ***Diagnostic microbiology and infectious disease***, 2003, 45:295–301.

13. Opal SM, Mayer KH, Medioras AA. Mechanisms of bacterial resistance. In: Mandell GL, Bennet JE, Dolin R, eds. ***Principles and practice of infectious diseases***, 5th ed. New York, Churchill Livingstone, 2000:239–53.

14. Reisner BS et al. Specimen processing. In: Murray PR et al. ***Manual of clinical microbiology***, 7th ed. Washington DC, American Society for Microbiology Press. 1999:75–6.

15. Leblebicioglu H, Esen S, Turkish Nosocomial Urinary Tract Infection Study Group. Hospital-acquired urinary tract infection in Turkey: a nationwide multicenter point prevalence study. ***Journal of hospital infection***, 2003, 53(3):207–10.

16. Landhani S, Grandsen W. Increasing antibiotic resistance among urinary tract isolates. ***Archives of disease in childhood***, 2003, 88(5):444–5.

17. Wazait HD et al. Catheter-associated urinary tract infections: prevalence of uropathogens and pattern of antimicrobial resistance in a UK hospital (1996–2001). ***BJU international***, 2003, 91(9):806–9.

18. Daza R, Gutierrez J, Piedrola G. Antibiotic susceptibility of bacterial strains isolated from patients with community-acquired urinary tract infections. ***International journal of antimicrobial agents***, 2001, 18:11–5.

19. Sobel JD, Vazquez JA. Fungal bacterial susceptibility to oral antibiotics in community infections of the urinary tract. ***World journal of urology***, 1999, 17(6):410–4.

20. Fegin RD et al., eds. ***Textbook of pediatric infectious diseases***, 5th ed. Philadelphia, WB Saunders, 2004:1175–92, 2573.

21. Orrett FA, Shurland SM. The changing patterns of antimicrobial susceptibility of urinary pathogens in Trinidad. ***Singapore medical journal***, 1998, 39:256–9.

22. Raz R et al. Demographic characteristics of patients with community-acquired bacteriuria and susceptibility of urinary pathogens to antimicrobials in Northern Israel. ***Israel medical association journal***, 2000, 2(6):426–9.

23. Gur D, Unal S. Resistance to antimicrobial agents in Mediterranean countries. ***International journal of antimicrobial agents***, 2001, 17:21–6.

24. Dietrich DW, Auld BB, Mermel LA. Community-acquired methicillin-resistant ***Staphylococcus aureus*** in southern New England children. ***Pediatrics***, 2004, 113:347e.