Hospital and community isolates of uropathogens at a tertiary hospital in South Africa

T M Habte, S Dube, N Ismail, A A Hoosen

Aim. To investigate the profile of common uropathogens isolated from urine specimens submitted to the diagnostic microbiology laboratory at a tertiary teaching hospital and assess their antimicrobial susceptibility patterns to commonly used antimicrobial agents.

Methods. We conducted a retrospective analysis of laboratory reports for all urine specimens submitted for investigations over a 1-year period. Isolates were tested by means of the Kirby-Bauer disc diffusion method for susceptibility to amoxicillin, ciprofloxacin, gentamicin, co-trimoxazole and nitrofurantoin, and for extended-spectrum beta-lactamase (ESBL) production.

Results. Out of the total specimens (*N*=2 203) received over the 1-year study period, 51.1% (1 126) of the urine samples were culture-positive, the majority (65.4%) having come from females. The most common isolate was *Escherichia coli* (39.0%) followed by *Klebsiella* species (20.8%) and *Enterococcus faecalis* (8.2%). The Gram-negative isolates displayed a very high level of resistance to amoxicillin (range 43 - 100%) and co-trimoxazole (range 29 - 90%), whereas resistance to gentamicin (range 0 - 50%) and ciprofloxacin (range 0 - 33%) was lower. *E. coli* isolates were susceptible to nitrofurantoin (94%), and ESBL production was significantly higher (p=0.01) in the hospital isolates, compared with those from the community referral sites.

Conclusions. The culture-positive rate for uropathogens was high, with a greater incidence among females. *E. coli* was the most common aetiological agent identified, and remained susceptible to nitrofurantoin. Resistance levels to amoxicillin and co-trimoxazole were very high for all Gram-negative isolates, and it is recommended that these antibiotics should not be used for the empiric treatment of urinary tract infections.

S Afr Med J 2009; 99: 584-587.

Urinary tract infections (UTIs) are a major public health problem in terms of morbidity and financial cost, and incur the highest total health care cost among urological diseases, exceeding that of chronic renal failure even when dialysis and renal transplantation are included.[1] The introduction of antimicrobial therapy has contributed significantly to the management of UTIs; however, the main problem with current antibiotic therapies is the rapid emergence of antimicrobial resistance in hospitals and the community.[2]

Routinely, urine culture and sensitivity is done to determine the cause of sepsis. Although the literature mostly profiles antimicrobial susceptibility in children, studies of uropathogens in adults show that in the last decade many urinary tract pathogens have become resistant to antimicrobial agents. This is of major public health importance, especially concerning *Escherichia coli*, a commonly isolated uropathogen, and other Enterobacteriaceae which have become less susceptible to widely used antibiotics such as ampicillin, amoxicillin, co-amoxiclav and co-trimoxazole.[3] All institutions should therefore continue surveillance of uropathogens, since antibiotic resistance varies over time, and their antimicrobial profile also varies depending on the locality from which they were isolated.[4]

This retrospective study investigated the common uropathogens isolated from patients attending Dr George Mukhari (DGM) Hospital in Ga-Rankuwa, Pretoria, and surrounding referral clinics and hospitals. DGM is a teaching tertiary hospital about 30 km north-west of Pretoria. The susceptibility pattern of the uropathogens to different antimicrobial agents was analysed, and we compared the resistance pattern of the uropathogens isolated at DGM with those from its referral sites.

Materials and methods

We reviewed laboratory records of urine specimens submitted for investigations from patients admitted to various specialties at DGM and its referral clinics over a 1-year period (1 November 2005 - 31 October 2006). Data collected included patients' age and sex, location (hospital or clinic), significant urinary isolates and their antimicrobial susceptibility profile.

Routine processing of urine specimens at the laboratory includes microscopic examination for cell count and culture

Department of Microbiological Pathology, University of Limpopo, Medunsa Campus, Pretoria
T M Habte, MB ChB
S Dube, MB ChB, DTM&H, MPH

Department of Medical Microbiology, Faculty of Health Sciences, University of Pretoria
N Ismail, MB ChB, MMed, FC Path Med Micro
A A Hoosen, MSc, MB ChB, MMed, FC Path Med Micro

Corresponding author: *S Dube (samudan2001@yahoo.com)*

and antimicrobial susceptibility testing. Culture is done using a calibrated loop; 0.001 ml of urine is inoculated on 5% sheep blood agar and MacConkey agar plates. The presence of at least 10^5 colony-forming units (CFU) per ml of urine is considered as significant bacteriuria. The colonies are identified by means of standard biochemical tests. Susceptibility testing is done using the Kirby-Bauer disc diffusion method. McFarland 0.5 standardised suspension of bacteria (1.5×10^8 CFU/ml) is prepared and swabbed over the surface of a Mueller-Hinton agar plate. Paper discs containing single-concentration antimicrobial agent are placed onto the surface; these plates are then incubated at 35°C for 18 - 24 hours. Diameters and inhibition zones produced by the antimicrobial substance are measured, and a millimetre reading for each antimicrobial agent is compared with that specified in the interpretive tables provided in the Clinical and Laboratory Standards Institute (CLSI) documents.[5]

Isolates were tested for susceptibility to the following antibiotics: amoxicillin, ciprofloxacin, gentamicin, co-trimoxazole and nitrofurantoin, and for extended-spectrum beta-lactamase (ESBL) production.

Results

Uropathogens from DGM and the referral sites are listed in Table I. A positive culture for uropathogens was found in 1 125 (51.1%) of the 2 203 urine samples submitted for culture. Among the 1 125 culture-positive samples, a total of 1 235 isolates was obtained; of the samples, 1 015 (90.2%) had a single organism cultured, and 110 (9.8%) had more than one isolate.

The mean age of patients with culture-positive specimens was 35.2 years (SD 21.1 years); 736 (65.4%) were female, 360 (32%) male, and gender was not specified in 29 (2.6%).

The most common isolate at DGM was *E. coli* (38%), followed by *Klebsiella* species (22%), *Enterococcus faecalis* (8%) and *Proteus* species (7%). The trend was similar at the referral sites, the most common being *E. coli* (42%), followed by *Klebsiella* species (15%), *E. faecalis* (11%), and *Enterobacter* species (5%) (Figs 1 and 2).

Most of the common Gram-negative isolates displayed a very high level of resistance to amoxicillin (range 43 - 100%) and co-trimoxazole (range 29 - 90%) for isolates from both

Table I. Distribution of isolated uropathogens from Dr George Mukhari Hospital and referring sites

	N (%)	DGM *N* (%)	Non-DGM *N* (%)
Total No. of specimens	2 203 (100)	1 887/2 203 (85.7)	316/2 203 (14.3)
Total No. of specimens with uropathogens	1 125/2 203 (51.1)	953/1 887 (50.5)	172/316 (54)
Total isolates	1 235 (100)	1 040/1 235 (84.2)	195/1 235 (15.8)
1 organism isolated	1 015/1 235 (82.2)	866/1 040 (83.3)	149/195 (76.4)
2 organisms isolated	220/125 (17.8)	174/1 040 (16.7)	46/195 (23.6)
Total Gram-negatives	974/1 235 (78.9)	824/1 040 (79.2)	150/195 (76.9)
Isolates			
Escherichia coli	482/1 235 (39.0)	398/1 040 (38.3)	84/195 (43.1)
Klebsiella pneumoniae	209/1 235 (16.9)	188/1 040 (18.1)	21/195 (10.8)
Klebsiella oxytoca	30/1 235 (2.4)	21/1 040 (2.0)	9/195 (4.6)
Klebsiella ozaenae	19/1 235 (1.5)	19/1 040 (1.8)	0/195 (0)
Proteus mirabilis	69/1 235 (5.6)	65/1 040 (6.3)	4/195 (2.1)
Proteus vulgaris	16/1 235 (1.3)	12/1 040 (1.2)	4/195 (2.1)
Enterobacter spp.	47/1 235 (3.8)	37/1 040 (3.6)	10/195 (5.1)
Pseudomonas spp.	40/1 235 (3.2)	36/1 040 (3.5)	4/195 (2.1)
Acinetobacter spp.	26/1 235 (2.1)	22/1 040 (2.1)	4/195 (2.1)
Citrobacter spp.	24/1 235 (1.9)	17/1 040 (1.6)	7/195 (3.6)
Others	12/1 235 (1.0)	9/1 040 (0.9)	3/195 (1.5)
Total Gram-positives	186/1 235 (15.1)	152/1 040 (14.6)	34/195 (17.4)
Isolates			
Enterococcus faecalis	101/1 235 (8.2)	80/1 040 (7.7)	21/195 (10.8)
Group B streptococci	29/1 235 (2.3)	26/1 040 (2.5)	3/195 (1.5)
Staphylococcus spp.*	26/1 235 (2.1)	23/1 040 (2.2)	3/195 (1.5)
Other *Streptococus* spp.†	22/1 235 (1.8)	16/1 040 (1.5)	6/195 (3.1)
Staphylcoccus saprophyticus	4/1 235 (0.3)	3/1 040 (0.3)	1/195 (0.5)
Others	4/1 235 (0.3)	4/1 040 (0.4)	0/195 (0)
Yeast			
Candida albicans	52/1 235 (4.2)	43/1 040 (4.1)	9/195 (4.6)
Candida diversus	14/1 235 (1.1)	13/1 040 (1.3)	1/195 (0.5)
Non-*Candida* spp.	9/1 235 (0.7)	8/1 040 (0.8)	1/195 (0.5)

*Includes *S. aureus*, MRSA.

†Includes streptococcus groups D, F, G. *S. pnuemoniae.*

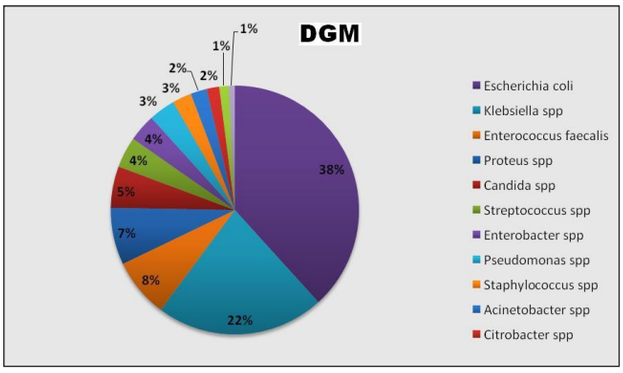

Fig. 1. The percentage distribution of uropathogens from Dr George Mukhari Hospital.

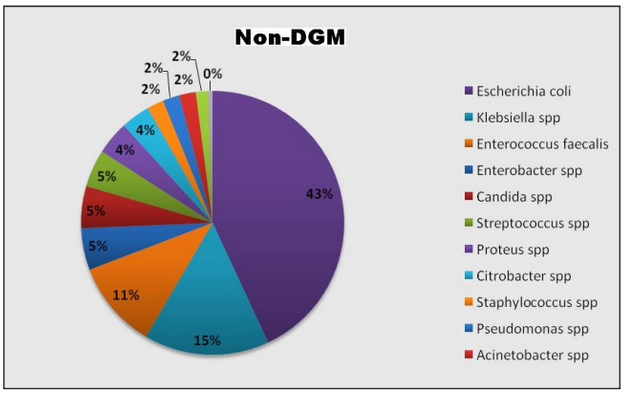

Fig. 2. The percentage distribution of uropathogens from the referral sites.

DGM and elsewhere. Resistance to gentamicin (range 0 - 50%) was lower, with similar results from the referral sites. Resistance to ciprofloxacin (range 0 - 33%) was also lower, with similar results from the referral sites (most notably to *Proteus* spp., which did not show any resistance (0%)) (Table II).

E. coli resistance to nitrofurantoin (6%) was very low; however, resistance to *K. pneumoniae* and *P. mirabilis* was high: 44% and 82% respectively (49 out of 60 isolates) for DGM. ESBL production was significantly higher (p=0.01) among DGM isolates than in those from the referral sites.

E. coli was highly resistant to amoxicillin and co-trimoxazole at DGM, with similar results for the referral sites; however, it remains susceptible to nitrofurantoin with no variation at the referral sites. ESBL production was significantly lower (p=0.01) among the non-DGM isolates (Fig. 3).

Discussion

E. coli (39.0%) was the most common uropathogen isolated at DGM and the referral sites, followed by *Klebsiella* species (20.8%) and *E. faecalis* (8.2%). This finding is in keeping with studies from other developing countries,[1,4,6-9] where *E. coli* was the predominant uropathogen, followed by *K. pneumoniae*. The distribution of the uropathogens at DGM was similar to that at the referral sites. The culture-positive rate (51%) for uropathogens was higher than found in Nicaragua[9] and India,[10]

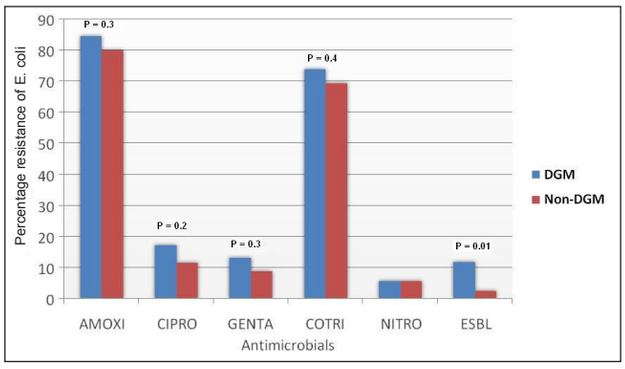

Fig. 3. Percentage resistance of E. coli *to various antimicrobials at DGM v. non-DGM.*

Table II. Antimicrobial susceptibilities among common Gram-negative uropathogens from DGM and non-DGM

Pathogen	Site	Amoxi r (%)	Cipro r (%)	Genta r (%)	Cotri r (%)	Nitro r (%)	ESBL production (%)
Escherichia coli	DGM	327/387 (84.5)	63/366 (17.2)	49/370 (13.2)	265/359 (73.8)	21/372 (5.6)	42/354 (11.9)
	Non-DGM	72/90 (80)	10/87 (11.5)	8/90 (8.9)	59/85 (69.4)	5/88 (5.7)	2/77 (2.6)
Klebsiella pneumoniae	DGM	190/193 (98.4)	58/182 (31.9)	94/189 (49.7)	115/177 (65)	81/183 (44.3)	76/187 (40.6)
	Non-DGM	18/19 (94.7)	2/17 (11.8)	6/17 (35.3)	8/16 (50)	5/16 (31.3)	5/16 (31.3)
Klebsiella oxytoca	DGM	17/18 (94.4)	5/18 (27.8)	6/17 (35.3)	12/17 (70.6)	2/18 (11.1)	3/14 (21.4)
	Non-DGM	9/9 (100)	3/9 (33.3)	2/9 (22.2)	5/9 (55.6)	1/9 (11.1)	1/7 (14.3)
Proteus mirabilis	DGM	28/58 (48.3)	0/58 (0)	8/59 (13.6)	27/53 (50.9)	49/60 (81.7)	4/54 (7.4)
	Non-DGM	3/7 (42.9)	0/7 (0)	0/7 (0)	2/7 (28.6)	6/7 (85.7)	0/7 (0)
Proteus vulgaris	DGM	10/11 (90.9)	0/11 (0)	3/11 (27.3)	9/10 (90)	8/10 (80)	1/10 (10)
	Non-DGM	3/4 (75)	0/4 (0)	0/4 (0)	2/4 (50)	1/4 (25)	0/3 (0)

R = resistance.

with culture rates of 30% and 39% respectively. For the culture-positive specimens, 65% were from females and 32% from males, which is a finding similar to those reported from India[10] (63% females and 37% males) and Palestine[11] (75% females and 25% males). These findings are to be expected as women are more prone to UTIs than men.

The common Gram-negative isolates had a very high-level resistance to amoxicillin and co-trimoxazole, as in reports from the Central African Republic[6] and India[4,10] and from a previous local study on urinary *E. coli*.[12] This high level of resistance may be attributed to the frequent use of these antibiotics for therapy and prophylaxis. Although these common Gram-negative bacteria displayed much lower resistance to ciprofloxacin and gentamicin compared with other antimicrobial agents, the levels of resistance were higher than found in studies from the Central African Republic,[6] Kuwait,[2] and even than the urinary *E. coli* isolates finding in the previous local study.[12]

E. coli isolates are susceptible to nitrofurantoin at DGM and the referral sites. However, *K. pneumoniae* and *P. mirabilis* are less susceptible to nitrofurantoin; similar findings were reported in several other countries.[1,2,7,13,14] ESBL production was significantly higher (p=0.01) in DGM than non-DGM isolates, reflecting greater use of broad-spectrum antibiotics for the hospitalised patient population.

Conclusion

In our study, the culture-positive rate for uropathogens was high, with the majority coming from female patients. As expected, *E. coli* was the most common aetiological agent identified, and remains susceptible to nitrofurantoin. It would therefore be the ideal antibiotic to use for uncomplicated lower UTIs. Resistance levels to amoxicillin and co-trimoxazole are extremely high, and we recommend that these antibiotics should not be used for the empiric treatment of UTIs. However, it was beyond the scope of this study to determine whether co-amoxiclav instead would be a suitable antibiotic. Although most of the isolates remain sensitive to ciprofloxacin, of interest is its use in managing multidrug-resistant tuberculosis in South Africa. A policy decision must be made on whether this drug should be restricted from use in other conditions such as UTI so that it may be used more specifically – if not exclusively – in tuberculosis.

Our study provides useful information for the proper treatment of UTIs and discourages the indiscriminate use of antibiotics, so helping to prevent further development of drug-resistant bacteria – a major public health problem in both hospital- and community-acquired UTIs. We therefore suggest a continual audit of antimicrobial susceptibility patterns among uropathogens as a cause of morbidity, especially in children, for the purpose of gathering more data.

We thank the DGM laboratory personnel for their assistance in the collection of specimens.

References

1. Gales AC, Sader HS, Jones RN, The SENTRY Participants Group (Latin America). Urinary tract infection trends in Latin American hospitals: report from the SENTRY antimicrobial surveillance program (1997-2000). *Diagn Microbiol Infect Dis* 2002; 44: 289-299.
2. Al-Sweih N, Jamal W, Rotimi VO. Spectrum and antibiotic resistance of uropathogens isolated from hospital and community patients with urinary tract infections in two large hospitals in Kuwait. *Med Princ Pract* 2005; 14: 401-407.
3. Kahlmeter G. The ECO•SENS Project: A prospective, multinational, multicentre epidemiological survey of the prevalence and antimicrobial susceptibility of urinary tract pathogens – interim report. *J Antimicrob Chemother* 2000; 46: 15-22.
4. Gupta V, Yadav A, Joshi RM. Antibiotic resistance pattern in uropathogens. *Indian J Med Microbiol* 2002; 20: 96-98.
5. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing; Fifteenth Informational Supplement. CLSI document M100-S16 (ISBN 1-56238-588-7). Wayne, PA, USA: 2005.
6. Hima-Lerible H, Menard D, Talarmin A. Antimicrobial resistance among uropathogens that cause community-acquired urinary tract infections in Bangui, Central African Republic. *J Antimicrob Chemother* 2003; 51: 192-194.
7. Dromigny JA, Ndoye B, Macondo EA, Nabeth P, Siby T, Perrier-Gros-Claude JD. Increasing prevalence of antimicrobial resistance among *Enterobacteriaceae* uropathogens in Dakar, Senegal: a multicenter study. *Diagn Microbiol Infect Dis* 2003; 47: 595-600.
8. Stratchounski LS, Rafalski VV. Antimicrobial susceptibility of pathogens isolated from adult patients with uncomplicated community-acquired urinary tract infections in the Russian Federation: two multicentre studies, UTIAP-1 and UTIAP-2. *Int J Antimicrob Agents* 2006; 28S: S4-S9.
9. Matute AJ, Hak E, Schurink CAM, *et al*. Resistance of uropathogens in symptomatic urinary tract infections in León, Nicaragua. *Int J Antimicrob Agents* 2004; 23: 506-509.
10. Tambekar DH, Dhanorkar DV, Gulhane DR, Khanadelwal VK, Dudhane MN. Antibacterial susceptibility of some urinary tract pathogens to commonly used antibiotics. *Afr J Biotechnol* 2006; 5: 1562-1565.
11. Astal ZY, Sharif FA. Relationship between demographic characteristics and community-acquired urinary tract infection. *East Mediterr Health J* 2002; 8: 164-171.
12. Sein PP, Mogoregi TE, Hoosen AA. Antimicrobial susceptibility profile of *Escherichia coli* strains isolated from mid stream urine specimens at Ga-Rankuwa hospital. *Geneeskunde* 1998; 40: 12-15.
13. Zhanel GG, Karlowsky JA, Harding GKM, *et al*. A Canadian National Surveillance Study of urinary tract isolates from outpatients: comparison of the activities of trimethoprim-sulfamethoxazole, ampicillin, mecillinam, nitrofurantoin, and ciprofloxacin. *Antimicrob Agents Chemother* 2000; 44: 1089-1092.
14. Farrell DJ, Morrissey I, De Rubeis D, Robbins M, Felmingham D. A UK multicentre study of the antimicrobial susceptibility of bacterial pathogens causing urinary tract infection. *J Infect* 2003; 46: 94-100.

Accepted 3 March 2009.