ANTIMICROBIAL RESISTANCE PATTERNS OF GRAM-NEGATIVE BACTERIA ISOLATED FROM URINE CULTURES IN ALMANA GENERAL HOSPITAL

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Urinary tract infections are common both in the community and hospitalized patients. Widespread use of antimicrobial agents often leads to the selection of multi-drug resistant micro-organisms. Acquired or emerging bacterial resistance to one or several antimicrobial agents is a global problem.[1,2] Many micro-organisms have become resistant to antimicrobial agents.[3] Some bacteria, especially *Klebsiella pneumoniae*, are showing increasing resistance to cephalosporins. These organisms produce extended-spectrum β-lactamases, which are coded by genes located on transferable plasmids.[4] Resistance to the quinolones in strains of *E. coli* isolated from urine specimens of outpatients is also increasing.[5]

As the pattern of bacterial resistance is constantly changing, monitoring of antimicrobial susceptibilities is important. It provides information on the pathogenic organisms isolated from patients, and assists in choosing the most appropriate empirical antimicrobial therapy. In addition, continuous surveys of antimicrobial resistance are crucial for monitoring changes in this resistance. In this report, we analyze the antimicrobial resistance patterns of bacteria isolated from urine specimens examined at Almana General Hospital, Al-Khobar, Saudi Arabia.

Materials and Methods

Organisms isolated from urine specimens of hospitalized and outpatients over a two-year period (January 1998 to December 1999) were identified and tested for antimicrobial susceptibilities. In this report, only samples with significant growth were studied (significant growth was defined as the presence of $>10^5$ colony-forming units per milliliter [cfu/mL] of urine). In symptomatic patients, however, fewer organisms (10^4-10^5 cfu/mL) may also indicate infection. Isolated micro-organisms were identified by standard methods[6] and API (BioMerieux, France). Antimicrobial susceptibility of the isolates was performed by the Stokes' method of disc sensitivity testing,[7] supported when required by testing for minimum inhibitory concentration (MIC), using E strip test (AB Biodisk, Solna, Sweden). All gram-negative isolates, except *Pseudomonas* species, were tested for susceptibility with a control strain of *E. coli* NCTC 10418. Strains of *Pseudomonas* species were tested with a control strain of *P. aeruginosa* NCTC 10662. A β-lactamase-producing control strain of *E. coli* was used to test organisms against a disc containing amoxycillin + clavulanic acid. Control and the test organisms were inoculated on the same sensitivity plate.

Results

The microbiology laboratory of Almana General Hospital at Al-Khobar, in the Eastern Province of Saudi Arabia, received and examined 12,938 urine specimens between January 1998 and December 1999. The total number of urine samples showing significant growth was 2394 (18.5%), of which 1434 (59.9%) were from outpatients and 960 (40.1%) were from inpatients. Gram-negative organisms totalled 1864 (77.9%), and gram-positive organisms constituted 530 (22.1%) of all the isolates. The species distribution was as follows: *E. coli* 1145 (47.8%), *Klebsiella* spp. 270 (11.3%), *P. aeruginosa* 165 (6.9%), *Proteus* spp. 92 (3.8%), *Enterobacter* spp. 75 (3.1%), *Acinetobacter* spp. 54 (2.3%), *Citrobacter* spp. 33 (1.4%), other gram-negative bacteria 30 (1.3%), *Streptococcus* group B 241 (10.1%), *Streptococcus* group D 196 (8.2%), and other gram-positive bacteria 93 (3.9%).

Among the gram-negative, *E. coli* was the most frequently isolated organism (61.4%), followed by *K. pneumoniae* (14.5%), and *P. aeruginosa* (8.9%). More than 42% of *E. coli* and *Proteus* species isolates were resistant to trimethoprim and amoxycillin (Table 1). Tables 1 and 2 summarize the percentage resistance of gram-negative bacilli isolated from hospitalized and outpatients.

Discussion

Before discussing the antimicrobial susceptibilty results reported in this study, it should be mentioned that many patients, especially outpatients with urinary tract infections, are treated empirically,[8] and, therefore, neither the organisms implicated nor their antimicrobial susceptibilities are ever known.

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TABLE 1. *Pattern of antimicrobial resistance among urinary tract isolates of Enterobacteriaceae at Almana General Hospital over two years (1998-1999).*

		Percent of resistant isolates against								
Bacteria	No. of isolates	TRI	NIT	AMX	AUG	CL	CXM	CAZ	CIP	GN
Esch. coli (overall)	1145	43.4	0.3	52.2	21.7	5.1	3.1	2.0	13.7	5.8
Inpatients	345	47	1.2	61.2	30.4	11	8.7	6.1	22.6	11
Outpatients	800	41.9	0	48.4	18	2.5	0.8	0.25	9.9	3.5
Klebsiella spp. (overall)	270	25.9	1.9	100	13.7	7.4	5.2	5.2	6.7	3.0
Inpatients	103	29.1	3.9	100	19.4	11.7	11.7	11.7	12.6	7.8
Outpatients	167	22.8	0.6	100	10.2	4.8	1.2	1.2	3.0	0
Proteus spp. (overall)	92	67.4	100	42.4	6.5	8.7	7.6	5.4	8.7	22.8
Inpatients	41	65.9	100	36.6	7.3	14.6	14.6	12.2	19.5	26.8
Outpatients	51	68.6	100	47.1	5.9	3.9	2.0	0	0	19.6
Enterobacter spp. (overall)	75	38.7	4.0	90.7	82.6	54.7	18.7	12	9.3	5.3
Inpatients	37	46	8.1	94.6	78.4	67.6	27	16.2	10.8	8.1
Outpatients	38	31.6	0	86.8	86.8	42.1	10.5	7.9	7.9	2.6
Citrobacter spp. (overall)	33	24.2	3.0	78.8	30.3	30.3	21.2	21.2	21.2	21.2
Inpatients	17	29.4	0	70.6	41.2	29.4	29.4	29.4	29.4	23.5
Outpatients	16	18.8	6.3	87.5	18.8	31.3	12.5	6.3	12.5	18.8

TRI=trimethoprim; NIT=nitrofurantoin; AMX=amoxycillin; AUG=amoxycillin-clavulanate; CL=cephalexin; CXM=cefuroxime; CAZ=ceftazidime; CIP=ciprofloxacin; GN=gentamicin.

TABLE 2. *Pattern of antimicrobial resistance among urinary tract isolates of non-Enterobacteriaceae at Almana General Hospital over two years (1998-1999).*

	No. of	Percentage of resistant isolates against		
Bacteria	isolates	CAZ	CIP	GN
Pseudomonas aeruginosa				
Overall	165	4.2	10.3	10.3
Inpatients	128	5.5	12.5	13.3
Outpatients	37	0	2.7	0
Acinetobacter spp.				
Overall	54	59.3	20.4	11.1
Inpatients	32	62.5	21.9	15.6
Outpatients	22	54.5	18.2	4.5

CAZ=ceftazidime; CIP=ciprofloxacin; GN=gentamicin.

In the present study, *E. coli* was by far the most frequently isolated bacterium, both in outpatients and in hospitalized patients (47.8%). The overall rate of resistance of *E. coli* isolates to amoxycillin was 43.3%. In a study by Ahmad et al.[9] in Buraidah, Saudi Arabia, 86% of the *E. coli* isolated from urine were resistant to ampicillin. The resistance rates for strains of *E. coli* isolated from hospitalized patients (61.2% to amoxycillin, 30.4% to amoxycillin-clavulanate, 47% to trimethoprim, 22.6% to ciprofloxacin, and 11% to cephalexin and gentamicin) were higher than those from outpatients (48.4%, 18%, 41.9%, 9.9%, 2.5%, and 3.5%, respectively). However, resistance of *E. coli* to amoxycillin and trimethoprim among outpatients' isolates was still high (48.4% and 41.9%, respectively). While resistance to amoxycillin and trimethoprim among the gram-negative isolates of the *Enterobacteriaceae* group were more than 42% and 25%, respectively, nitrofurantoin showed the lowest resistance rate (<5%), with the exception of the *Proteus* species. The high rate of resistance to amoxycillin and trimethoprim renders these antimicrobial organisms inappropriate for empirical therapy.

Amoxycillin resistance in *E. coli* was associated with marked resistance to trimethoprim, and to a lesser extent, to amoxycillin-clavulanate and ciprofloxacin. Of the 345 *E. coli* isolated from hospitalized patients, 39 (11.3%) were multidrug resistant. They were resistant to amoxycillin, trimethoprim, amoxycillin-clavulanate, and either ciprofloxacin or gentamicin. Many of these multidrug-resistant strains of *E. coli* showed high minimum inhibitory concentration (MIC >256 mg/L) to amoxycillin, amoxycillin-clavulanate, and ciprofloxacin. In a recent study from this hospital, high rates of resistance to amoxycillin (58%), amoxycillin-clavulanate (36%) and ciprofloxacin (23.6%) were observed in *E. coli* isolated from blood cultures.[10] Resistance to these antimicrobial agents is likely to be related to their widespread use, as it has occurred with quinolones in countries such as Spain, where quinolones are used widely.[5] Prudent use of these antimicrobial agents is advised to prevent or minimize the development of resistant strains.

Among the gram-negative isolates from hospitalized patients, more than 12% of *Proteus* spp., *Citrobacter* spp., and *Acinetobacter* spp. showed resistance to ceftazidime, ciprofloxacin and gentamicin. More than 10% of the *Pseudomonas aeruginosa* isolates were resistant to ciprofloxacin and gentamicin. *Pseudomonas*, *Enterobacter* and *Acinetobacter* species are gram-negative organisms which are known to be associated with hospital infections.[11,12]

This study has revealed high rates of antimicrobial resistance among many of the gram-negative organisms isolated from urine specimens examined at Almana General Hospital over a two-year period, with the most significant findings being high amoxycillin, trimethoprim and amoxycillin-clavulanate resistance among *E. coli* strains. The antimicrobial resistance rate of urinary isolates from hospitalized patients was higher than that of outpatients.

This report also shows that the problem of antibiotic resistance is not restricted to inpatients only.

To address the problem of increasing antimicrobial resistance, which is becoming serious worldwide,[13] antimicrobial surveillance programs are necessary both locally and nationally. Antimicrobial susceptibility surveys from different hospitals will allow comparisons between resistance rates at the national level. Collectively, antimicrobial susceptibility data derived from microbiology laboratories all over the Kingdom could be used for the reliable and rapid detection and surveillance of antimicrobial resistance, especially if these data are stored in some form of computerized laboratory information system.

References

1. Neu HC. The crisis in antibiotic resistance. Science 1992;257:1064-73.
2. Gold SG, Moellering RC. Antimicrobial drug resistance. N Engl J Med 1996;335:1445-53.
3. Kunin CM. Resistance to antimicrobial drugs: a worldwide calamity. Ann Intern Med 1993;118:557-61.
4. Tolmasky ME, Chamorro RM, Crosa JH, Marini PM. Transposon-mediated amikacin resistance in *Klebsiella pneumoniae*. Antimicrob Agents Chemother 1988;32:1416-20.
5. Aguiar JM, Chacon J, Canton R, Baquero F. The emergence of highly fluoroquinolone-resistant *Escherichia coli* in community-acquired urinary tract infections. J Antimicrob Chemother 1992;29: 349-50.
6. Cowan SF, Steel KJ. Manual for identification of medical bacteria. 3rd edition. Cambridge: Cambridge University Press, 1993:140-3.
7. PM Hawkey, DA Lewis. Medical bacteriology: a practical approach. Oxford: Oxford University Press, 1989:170-8.
8. Carlson KJ, Mulley AG. Management of acute dysuria: a decision analysis model for alternative strategies. Ann Intern Med 1985;102: 244-9.
9. Ahmad S, Ahmad F. Urinary tract infection at a specialist hospital in Saudi Arabia. Banglad Med Res Council Bull 1995;21:95-8.
10. Kader AA, Nassimuzzaman M, Dass SM. Antimicrobial resistance pattern of microorganisms isolated from blood cultures in a Saudi Arabian hospital. BMJ (Middle East) 2000;7:6-7.
11. Goetz A, Yu VL. The intensive care unit: the hottest zone. Curr Opin Infect Dis 1997;10:319-23.
12. Hilf M, Yu VL, Sharp J, et al. Antibiotic therapy for *Pseudomonas aeruginosa* bacteremia: outcome correlations. Am J Med 1989;87: 540-6.
13. American Society for Microbiology. Report of the ASM Task Force on Antibiotic Resistance. Washington DC, 1994.