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Resistance rates to commonly used antimicrobials among pathogens of both bacteremic and non-bacteremic community-acquired urinary tract infection

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This study examined the distribution of organisms and their antimicrobial resistance in patients admitted due to acute bacteremic and non-bacteremic community-acquired urinary tract infection (UTI). During a period of 1 year and 1 month, a total of 201 patients and 253 bacterial isolates were studied. Fever higher than 38.5ºC was significantly more common in the bacteremic group than the non-bacteremic group (68% vs 48%; $p<0.05$). *Escherichia coli*, *Klebsiella pneumoniae, Pseudomonas aeruginosa,* and *Proteus mirabilis* were the most common organisms isolated. *E. coli* was the leading pathogen and it was significantly more predominant in bacteremic UTI than non-bacteremic UTI (73% vs 49%; $p<0.01$). Bacteria other than *E. coli* (i.e., *K. pneumoniae, P. aeruginosa, Proteus* spp., *Morganella morganii*, *Enterobacter cloacae*, *Citrobacter* spp., *Acinetobacter baumannii*, *Serratia marcescens*, and *Providencia* spp.) were more common in non-bacteremic UTI than bacteremic UTI (44% vs 22%; $p<0.01$). *E. coli* isolated from both bacteremic and non-bacteremic patients had a high rate of resistance to ampicillin (80%), cephalothin (59%), gentamicin (29%), piperacillin (61%), trimethoprim-sulfamethoxazole (56%), amoxicillin-clavulanic acid (34%), and ticarcillin-clavulanic acid (36%). Isolates of *P. aeruginosa*, *K. pneumoniae*, and *Proteus* spp. from the non-bacteremic group showed a higher proportion of resistance to extended-spectrum cephalosporins, aminoglycosides (netilmicin and amikacin) and ciprofloxacin. The emergence of a high rate of resistance to commonly used antimicrobials (ampicillin, cephalothin, gentamicin, trimethoprim-sulfamethoxazole, piperacillin, amoxicillin-clavulanic acid and ticarcillin-clavulanic acid) may have an impact on the antibiotic treatment of patients admitted due to acute community-acquired bacteremic or non-bacteremic UTI in Taiwan. Further studies are needed to clarify the impact of antimicrobial resistance on the outcome in these conditions.

Key words: Antibacterial agents, bacteremia, microbial drug resistance, urinary tract infection

There is growing concern about the increasing antimicrobial resistance in the causative organisms of urinary tract infection (UTI) in Taiwan and globally [1-4]. UTI-associated bacteremia represents one of the common causes of bacteremia [5]. The outcome of bacteremia is closely related to the severity of illness and appropriateness of antibiotic treatment [6,7]. Inappropriate empiric therapy has been found to be a predictor of mortality in patients who had bacteremia originating from a urinary tract source [8]. In order to determine the pattern of antimicrobial resistance, we prospectively enrolled 201 acutely hospitalized patients with bacteremic and non-bacteremic community-acquired UTI and analyzed their bacterial isolates.

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Patients and Methods

Patient population and clinical evaluation

This prospective observational study was conducted between June 1999 and June 2000 at Tri-Service General Hospital, a 1400-bed tertiary care teaching hospital in Taipei. The investigators in this study evaluated each patient admitted from the emergency room under the impression of UTI. Inclusion criteria were: (1) ≥18 years of age; and (2) symptoms of acute cystitis (frequency, dysuria, urgency, hematuria, suprapubic pain); signs of acute pyelonephritis (body temperature ≥38.0°C with or without chills, flank pain and costovertebral angle tenderness); or symptomatic patients with a urinary catheter. Exclusion criteria were children under 18 years

old and prior hospitalization 2 weeks before admission. Blood cultures and urine culture were obtained aseptically before the use of antimicrobial agents. The following data were collected using a worksheet: demographic characteristics, underlying disease, prior history of UTI, complete blood count, results of culture and antimicrobial susceptibility testing, antibiotic treatment course and clinical outcome.

Definitions

A urine culture was considered to be positive if it fulfilled 1 of the following criteria: (1) a quantitative urine culture growing a single organism in concentrations of $\geq 10^5$ colony-forming units (cfu)/mL; or (2) a quantitative urine culture growing 2 organisms each in concentrations $\geq 10^5$ cfu/mL in symptomatic patients with permanent indwelling catheters. Pyuria was defined as >10 leukocytes per high power field in the sediment of a centrifuged urine specimen. The following conditions were classified as central nervous system disorders: dementia, cerebrovascular diseases, traumatic injuries of the brain, parkinsonism, and hydrocephalus with ventriculoperitoneal shunt implantation. Prostate hyperplasia, urolithiasis, obstructive uropathy other than renal stone, and congenital urinary tract disorder were all classified as genitourinary tract disorders. Percutaneous nephrostomy, suprapubic catheter and Foley's catheter were all classified as indwelling urinary catheters.

A strain was classified as resistant if the susceptibility test results were reported as either resistant or intermediate. Susceptible strains were those strains which were susceptible to the antimicrobial agent tested.

Microbiological methods

During the study period, BacT/Alert 240 (Organon Teknika Corp., Durham, NC, USA) was used for the blood culture of aerobic and anaerobic bacteria. Species identification was initially performed using the Vitek GNI system (Vitek Systems, Hazelwood, MO, USA). The identification was also confirmed by conventional

Table 1. Demographic and clinical characteristics of patients with bacteremic versus non-bacteremic community-acquired urinary tract infection

Characteristic	Bacteremic group n = 60	Non-bacteremic group n = 141	Odds ratio	95% confidence interval
Male	20	52	0.87	(0.46-1.64)
Female	40	89	1.16	(0.61-2.18)
Age				
≥65 years	36	104	0.57	(0.30-1.07)
Nursing home residents	11	17	1.65	(0.72-3.78)
Underlying disease				
Malignant disorder	7	16	1.04	(0.41-2.67)
Benign prostate hyperplasia	4	11	0.85	(0.26-2.79)
Previous urinary tract infection	11	22	1.22	(0.55-2.71)
Diabetes mellitus	20	38	1.37	(0.71-2.63)
Central nervous system disorder	13	44	0.62	(0.30-1.25)
Genitourinary tract abnormality[a]	6	10	1.47	(0.51-4.24)
Bedridden	11	33	0.74	(0.35-1.59)
Chronic renal insufficiency	24	52	1.15	(0.62-2.14)
Heart disease	2	8	0.58	(0.12-2.80)
Lung disease	5	12	0.98	(0.33-2.93)
Spinal disorder	2	6	0.78	(0.15-3.99)
Indwelling urinary catheter[b]	4	32	1.05	(0.51-2.14)
Signs/symptoms at admission				
Severe sepsis	7	12	1.43	(0.534-3.83)
Temperature ≥38.5°C	39	68	2.02	(1.08-3.77)
Leukocyte count $\geq 12 \times 10^9$/L	32	58	1.66	(0.90-3.04)
Serum urea nitrogen ≥30 mg/dL	13	32	0.95	(0.46-1.97)
Creatinine ≥2.5 mg/dL	13	24	1.36	(0.64-2.89)

[a]Including urolithiasis and congenital urinary tract disorder.

[b]Including percutaneous nephrostomy, suprapubic catheter and Foley catheter.

biochemical tests. Antimicrobial susceptibility tests were performed using the Kirby-Bauer disk-diffusion test on Mueller-Hinton agar (BBL Microbiological Systems, Cockeysville, MD). The methods were as described by the National Committee for Clinical Laboratory Standards (NCCLS) [9]. *Escherichia coli* ATCC 35218 and ATCC 25922, *Staphylococcus aureus* ATCC 25923, *Pseudomonas aeruginosa* ATCC 27853, and *Enterococcus faecalis* ATCC 29212 served as controls. Interpretations were done according to the guidelines of the NCCLS [9].

Statistical analysis

All of the collected data were entered in a computer database for analysis. Independent-sample *t* test, chi-squared test or Fisher's exact test was used to assess the statistical significance of differences. A statistically significant difference was defined as a p value of <0.05. Data analysis was performed using SPSS version 9.0 for Windows, statistical software package (SPSS Inc., Chicago, Ill.).

Results

A total of 201 consecutive patients with community-acquired UTI were enrolled. Sixty patients (30%) were bacteremic and 141 patients (70%) were non-bacteremic. A total of 253 bacterial isolates were collected, of which 24% (60/253) were blood isolates, and 76% (193/253) were urine isolates. Of the bacteremic patients, 45% (27/60) had the same organism isolated from blood and urine cultures.

Clinical characteristics of patients

The patients' ages ranged from 20 to 94 years, with a median of 74 years. Most (140/201; 70%) were ≥65 years of age and 55% were women. Among the bacteremic patients, 60% were ≥65 years old. The underlying diseases were not significantly different between the bacteremic and non-bacteremic groups. An indwelling urinary catheter was more frequently used in patients in the non-bacteremic group (n = 32) than in the bacteremic group (n = 4). The only significant difference in clinical characteristics between the bacteremic and non-bacteremic groups was the higher percentage of fever ≥38.5°C in the bacteremic group (68% vs 48%; p<0.05) [Table 1].

Distribution of organisms

The pathogens causing bacteremic versus non-bacteremic UTI are listed in Table 2. Gram-negative organisms constituted 94% (237/253) and Gram-positive organisms constituted 6% (16/253) of all isolates. *E. coli* was significantly more common in patients in the bacteremic group than in the non-bacteremic group (73% vs 49%; p<0.01).

Table 2. Distribution of organisms in bacteremic and non-bacteremic community-acquired urinary tract infection

	Bacteremic group n = 60 (%)	Non-bacteremic group n = 164 (%)
Gram-negative organisms		
Escherichia coli	44 (73)	80 (49)
Pseudomonas aeruginosa	3 (5)	27 (16)
Klebsiella pneumoniae	5 (8)	11 (7)
Morganella morganii	1 (2)	4 (2)
Proteus mirabilis and other *Proteus* species	3 (5)	11 (7)[a]
Enterobacter cloacae	1 (2)	6 (4)
Citrobacter freundii and other *Citrobacter* species	0	6 (4)[b]
Acinetobacter baumannii	0	4 (2)
Serratia marcescens	0	2 (1)
Providencia species	0	1 (1)
Gram-positive organisms		
Staphylococcus saprophyticus	2 (3)	0
Staphylococcus aureus	1 (2)	7 (4)
Group B *Streptococcus*	0	2 (1)
Enterococcus	0	3 (2)

[a]One was other *Proteus* species.

[b]Three were other *Citrobacter* species.

Antimicrobial resistance pattern

The antimicrobial resistance patterns of the 4 most common pathogens isolated from patients with bacteremic and non-bacteremic UTI are shown in Table 3. *E. coli* strains exhibited a high proportion of antimicrobial resistance to ampicillin (80%), cephalothin (59%), gentamicin (29%), piperacillin (61%), trimethoprim-sulfamethoxazole (56%), amoxicillin-clavulanic acid (34%), and ticarcillin-clavulanic acid (36%).

Non-bacteremic *E. coli*, *K. pneumoniae*, and *Proteus* species had various rates of resistance to extended-spectrum cephalosporins (9 to 18%), netilmicin (9 to 36%), and ciprofloxacin (9 to 36%). *P. aeruginosa* from non-bacteremic patients showed resistance to the following antipseudomonal agents: gentamicin (56%), netilmicin (33%), amikacin (19%), piperacillin (15%), ticarcillin-clavulanic acid (33%), ciprofloxacin (33%), ceftazidime (15%), aztreonam (26%), and cefepime (7%) [Table 3].

Table 3. Comparison of the antimicrobial resistance patterns between isolates from patients with bacteremic and non-bacteremic urinary tract infection (UTI)

	Escherichia coli (%)		*Pseudomonas aeruginosa* (%)		*Klebsiella pneumoniae* (%)		*Proteus* species (%)	
	Bacteremic UTI (n = 44)	Non-bacteremic UTI (n = 80)	Bacteremic UTI (n = 3)	Non-bacteremic UTI (n = 27)	Bacteremic UTI (n = 5)	Non-bacetremic UTI (n = 11)	Bacteremic UTI (n = 3)	Non-bacteremic UTI (n = 11)
Ampicillin	79	80	ND	ND	100	100	67	82
AM-CL	39	31	ND	ND	20	18	33	9
Piperacillin	59	62	0	15	40	55	33	36
TC-CL	30	39	0	33	ND	ND	0	0
TMP-SMX	55	57	ND	ND	40	64	0	64
Cephalothin	59	59	ND	ND	40	36	33	36
Cefuroxime	5	9	0	ND	40	18	0	9
Ceftriaxone	2	9	75	70	20	18	0	18
Ceftazidime	0	6	0	15	0	18	0	0
Cefepime	2	4	0	7	0	0	0	0
Aztreonam	5	10	0	26	0	18	0	0
Moxalactam	2	2	100	100	20	9	0	0
Ciprofloxacin	5	17	0	33	20	36	0	9
Gentamicin	23	32	0	56	20	36	67	36
Netilmicin	2	10	0	33	0	36	0	9
Amikacin	0	0	0	19	0	27	0	9
Imipenem	0	2	0	0	0	0	0	0

Abbreviations: AM-CL = amoxicillin-clavulanic acid; TC-CL = ticarcillin-clavulanic acid; TMP-SMX = trimethoprim-sulfamethoxazole; ND = not done

Risk factors for resistance to both cephalothin and gentamicin in *E. coli* isolates

Since empiric antibiotic regimens for acute community-acquired UTI usually contain cephalothin and gentamicin, we further analyzed the risk factors for UTI caused by *E. coli* resistant to both cephalothin and gentamicin. The following risk factors were identified: bed-ridden, previous UTI, use of in-dwelling urinary catheter, and nursing home resident (Table 4).

Table 4. Risk factors for resistance to both cephalothin and gentamicin in *Escherichia coli* causing urinary tract infection

Risk factor	Two drugs resistant	Two drugs susceptible	Odds ratio	95% confidence interval
Age				
≥65 years	24	22	2.73	0.98-1.85
<65 years	6	15	0.25	0.1-0.89
Gender				
Female	22	30	0.64	0.69-1.18
Male	8	7	1.56	0.58-3.44
Underlying disease				
Central nervous system disorder	10	9	1.56	0.64-2.93
Diabetes mellitus	8	5	2.33	0.72-5.41
Neoplasm	3	2	1.94	0.33-10.36
Benign prostate hyperplasia	1	1	1.24	0.08-18.91
Bedridden	13	3	8.67	1.68-17.04
Chronic renal insufficiency	9	12	0.89	0.45-1.90
Previous urinary tract infection	16	8	4.14	1.23-4.96
Use of urinary catheter[a]	11	3	6.56	1.39-14.75
Nursing home resident	8	2	6.36	1.13-21.52

[a]Including percutaneous nephrostomy, suprapubic bladder catheter or Foley catheter.

Mortality

The overall mortality rate was 8% (16/201); 7 patients had bacteremia and all were older than 65 years. All patients with bacteremic UTI received parenteral extended-spectrum cephalosporin as the empirical treatment. Among them, one patient's bacteremic isolates were resistant to cephalothin, cefuroxime, gentamicin, piperacillin, trimethoprim-sulfamethoxazole and amoxicillin-clavulanic acid.

Discussion

This study found a high rate of resistance to commonly used antimicrobials in pathogens isolated from patients with bacteremic and non-bacteremic community-acquired UTI. Isolates from bacteremic patients were somewhat less resistant than those from non-bacteremic patients. *E. coli* isolates were more predominant in bacteremic patients than in non-bacteremic patients (73% vs 49%; $p<0.01$). *E. coli* from both bacteremic and non-bacteremic patients exhibited high resistance rates to ampicillin, cephalothin, gentamicin, piperacillin, trimethoprim-sulfamethoxazole, and amoxicillin-clavulanic acid. A review of the antimicrobial resistance rates of *E. coli* in UTI among various countries highlights the seriousness of the resistance situation in Taiwan (Table 5). Resistance to extended-spectrum cephalosporins, aminoglycosides (netilmicin and amikacin), and ciprofloxacin was common in non-bacteremic *E. coli*, *K. pneumoniae*, *P. aeruginosa*, and *Proteus* spp.

The greatest concern arising from the results of this study is the increasing resistance of *E. coli* isolates from bacteremic UTI patients to commonly used empirical antimicrobial agents. According to a study from France, 36.8% of bacteremic *E. coli* was resistant to amoxicillin, 26.3% to amoxicillin-clavulanic acid, 5.3% to cephalothin, 0% to gentamicin, 5.3% to nalidixic acid, 5.3% to nitrofurantoin, 5.3% to trimethoprim-sulfamethoxazole, 5.3% to ceftazidime, and 5.3% to pefloxacin [10]. Our study indicated an even worse situation in the high rate of resistance of *E. coli* isolates from patients with bacteremic UTI. Two reasons may account for the high resistance identified in our study. First, antibiotic resistance is linked to prior exposure to antibacterial drugs [10,11]. Liu et al demonstrated that β-lactams (85%; including first- or second-generation cephalosporins and penicillin) and aminoglycosides (53.8%) were commonly prescribed for hospitalized patients in Taiwan [12]. Second, prior UTI and multiple admissions to the hospital were the risk factors for resistance to antimicrobial agents [13]. In our study, 30% of patients had a previous UTI history, and this may have been underestimated. Prior studies reported risk factors for multidrug resistance of urinary isolates included urinary catheter use, age ≥65 years, diabetes mellitus, and antibiotic use [14,15].

Compared to other studies [16-19], our results demonstrated the highest reported rate of resistance to these commonly used antibiotics. On the other hand, resistance to extended-spectrum cephalosporins, aminoglycosides (netilmicin and amikacin), and ciprofloxacin was more common in non-bacteremic isolates. Multi-resistant strains such as *P. aeruginosa*, *K. pneumoniae*, and *Proteus* spp. were significantly more common in the non-bacteremic group than the bacteremic group although the number in the latter group was small. These urinary isolates may have presented greater resistance patterns due to their ability to generate bacterial biofilms which may adhere to the bladder cells in some patients with neurogenic bladder or in those using an indwelling urinary catheter [20,21]. These adherent bacteria are viable and are not killed by antibiotic exposure. It is difficult for antibiotics to eradicate bacteria which are adherent to tissues or to penetrate biofilms on tissues. Repeated treatment with antibiotics must encourage the emergence of drug-resistant pathogens in Taiwan. Therefore, antibiotic selective pressure may contribute to the emergence of reduced susceptibility and resistance to fluoroquinolones in *E. coli* in Taiwan [22].

Table 5. Antimicrobial resistance rates of *Escherichia coli* in urinary tract infection in studies from various countries

Country [reference]	Ampicillin	Cefazolin	Gentamicin	TMP-SMX	AM-CL
Israel [18]	65%	9%	ND[c]	30%	17%
France [19]	41%	33%	1%	22%	37%
Latin America [16]	59%	16%	15%	47%	33%
North America [17]	43%	12%	2%	25%	26%
Taiwan [this study]	80%	59%	29%	56%	34%

Abbreviations: TMP-SMX = trimethoprim-sulfamethoxazole; AM-CL = amoxicillin-clavulanic acid; ND = not done

A previous study found that the outcome of community-acquired bacteremic UTI was a direct function of poor general medical status and advanced age [6]. In our study, death in 1 patient was caused by bacteremia with resistant strains. Elderly patients (≥65 years) are recognized to have a high frequency of chronic diseases and are at greatest risk for death and complications from infections. All patients with bacteremic UTI who died in this study were aged ≥65 years. All of them received a parenteral extended-spectrum cephalosporin at the time of admission. This study illustrates the critical importance of host factors as the major determinant of death caused by bacteremic UTI. On the other hand, our study also demonstrated a lack of correlation between mortality and resistant strains.

Although we were not able to demonstrate a close correlation between antibiotic use and the development of resistant strains, the widespread use of antibiotics has been reported to predispose patients to multi-drug resistant bacterial infections [10,23]. In order to combat the emergence of antibiotic resistance, efforts should be made to provide data on local antimicrobial resistance to the hospital physicians, and educate them to prescribe antibiotics prudently.

In conclusion, a high proportion of *E. coli* isolated from both bacteremic and non-bacteremic UTI patients exhibited resistance to ampicillin, cephalothin, gentamicin, piperacillin, trimethoprim-sulfamethoxazole, and amoxicillin-clavulanic acid. Empiric antibiotic treatment for community-acquired UTI should be justified according to the disease severity and its potential to increase rates of antibiotic resistance. Further studies to clarify the impact of antimicrobial resistance on the outcome of community-acquired UTI are warranted.

References

1. Ho M, McDonald LC, Lauderdale TL, Yeh LL, Chen PC, Shiau YR. Surveillance of antibiotics resistance in Taiwan, 1998. J Microbiol Immunol Infect 1999;32:239-49.
2. Ho P, Yuen K, Yam W, Sai-Yin Wong S, Luk W. Changing patterns of susceptibilities of blood, urinary and respiratory pathogens in Hong Kong. J Hosp Infect 1995;31:305-17.
3. Igari J, Shitara M, Shitara M, Shitara M, Yoshimoto K, Hayashi Y. Susceptibilities of uropathogenic bacteria to ampicillin, cefazolin, cefmetazole and gentamicin. Nine-year survey of changing patterns of susceptibilities. Jpn J Antibiot 1990;43: 1530-7.
4. Weber G, Riesenberg K, Schlaeffer F, Peled N, Borer A, Yagupsky P. Changing trends in frequency and antimicrobial resistance of urinary pathogens in outpatient clinics and a hospital in southern Israel, 1991-1995. Eur J Clin Microbiol Infect Dis 1997;16:834-8.
5. Korvick JA, Bryan CS, Farber B, Beam TR Jr, Schenfeld L, Muder RR, et al. Prospective observational study of *Klebsiella* bacteremia in 230 patients: outcome for antibiotic combinations versus monotherapy. Antimicrob Agents Chemother 1992;36: 2639-44.
6. Bryan CS, Reynolds KL. Community-acquired bacteremic urinary tract infection: epidemiology and outcome. J Urol 1984; 132:490-3.
7. Weinstein MP, Murphy JR, Reller LB, Melvin P, James R, Kenneth A, et al. The clinical significance of positive blood cultures: a comprehensive analysis of 500 episodes of bacteremia and fungemia in adults, II: clinical observations with special reference to factors influencing prognosis. Rev Infect Dis 1983;5:54-70.
8. Bishara J, Leibovici L, Huminer D, Drucker M, Samra Z, Konisberger H, et al. Five-year prospective study of bacteraemic urinary tract infection in a single institution. Eur J Clin Microbiol Infect Dis 1997;16:563-7.
9. National Committee for Clinical Laboratory Standards. Performance standards for antimicrobial disk susceptibility tests. 6th and 7th ed. Approved Standard M2-A7. Wayne, Pennsylvania. National Committee for Clinical Laboratory Standards 1999 and 2000.
10. Lepelletier D, Caroff N, Reynaud A, Richet H. *Escherichia coli*: epidemiology and analysis of risk factors for infections caused by resistant strains. Clin Infect Dis 1999;29:548-52.
11. Steinke DT, Seaton RA, Phillips G, MacDonald TM, Davey PG. Factors associated with trimethoprim-resistant bacteria isolated from urine samples. J Antimicrob Chemother 1999; 43:841-3.
12. Liu YC, Huang WK, Huang TS, Kunin CM. Detection of antimicrobial activity in urine for epidemiologic studies of antibiotic use. J Clin Epidemiol 1999;52:539-45.
13. Allen UD, MacDonald N, Fuite L, Chan F, Stephens D. Risk factors for resistance to "first-line" antimicrobials among urinary tract isolates of *Escherichia coli* in children. Can Med Assoc J 1999;160:1436-40.
14. Wright SW, Wrenn KD, Haynes M, Hass DW. Prevalence and risk factors for multidrug resistant uropathogens in ED patients. Am J Emerg Med 2000;18:143-6.
15. Arstila T, Huovinen S, Lager K, Lehtonen A, Huovinen P. Positive correlation between the age of patients and the degree of antimicrobial resistance among urinary strains of *Escherichia coli*. J Infect 1994;29:9-16.
16. Gales AC, Jones RN, Gordon KA, Sader HS, Wike WW, Beach ML, et al. Activity and spectrum of 22 antimicrobial agents

tested against urinary tract infection pathogens in hospitalized patients in Latin America: report from the second year of the SENTRY antimicrobial surveillance program (1998). J Antimicrob Chemother 2000;45:295-303.

17. Jones RN, Kugler KC, Pfaller MA, Winokur PL, and the SENTRY surveillance group, North America. Characteristics of pathogens causing urinary tract infections in hospitals in North America: results from the SENTRY antimicrobial surveillance program, 1997. Diag Microbiol Infect Dis 1999; 35:55-63.
18. Finkelstein R, Kassis E, Reinhertz G, Gorenstein S, Herman P. Community-acquired urinary tract infection in adults: a hospital viewpoint. J Hosp Infect 1998;38:193-202.
19. Goldstein FW. Antibiotic susceptibility of bacterial strains isolated from patients with community-acquired urinary tract infection in France. Multicenter study group. Eur J Clin Microbiol Infect Dis 2000;19:112-7.
20. Tsukamoto T, Matsukawa M, Sano M, Takahashi S, Hotta H, Itoh N, et al. Biofilm in complicated urinary tract infection. Int J Antimicrob Agents 1999;11:233-9.
21. Gregor R. Do antibiotics clear bladder infections? J Urol 1994; 152:865-7.
22. McDonald LC, Chen FJ, Lo HJ, Yin HC, Lu PL, Huang CH, et al. Emergence of reduced susceptibility and resistance to fluoroquinolones in *Escherichia coli* in Taiwan and contributions of distinct selective pressures. Antimicrob Agents Chemother 2001;45:3084-91.
23. Thomas FE, Jackson RT, Melly MA, Alford RH. Sequential hospital wide outbreaks of resistant *Serratia* and *Klebsiella* infections. Arch Intern Med 1977;137:581-4.