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Korean Nationwide Surveillance of Antimicrobial Resistance of Bacteria in 1998

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Abstract

Antimicrobial resistance surveillance can provide information needed for empirical therapy of antimicrobial agents and for control of resistance. To determine the trend of antimicrobial resistance in Korea, in vitro susceptibility data in 1998 were collected from 25 hospitals participating to a program of Korean Nationwide Surveillance of Antimicrobial Resistance (KONSAR). The data were analyzed based upon hospital location and bed capacity. The results showed that cefoxitin-resistant *E. coli* and *K. pneumoniae* and 3rd-generation cephalosporin-resistant *K. pneumoniae* were prevalent, that 3rd-generation cephalosporin-resistant *E. cloacae, S. marcesens* and *A. baumannii* had increased, and ampicillin-resistant *S. enterica* were not rare. Oxacillin-resistant *S. aureus,* penicillin-non-susceptible pneumococci and β-lactamase-producing *H. influenzae* were prevalent even smaller hospitals surveyed, and an increase of imipenem-resistant *P. aeruginosa* and vancomycin-resistant *E. faecium* is a new obvious threat. In general, resistance rates to some old antimicrobial agents, i.e., *E. coli* to ampicillin and *S. aureus* to oxacillin were high and did not vary greatly between the different levels of hospitals, while the rates to some of the newer ones, i.e., *P. aeruginosa* to imipenem, was quite variable and depended on the hospitals, probably reflecting difference in selective pressure.

Key Words: Antimicrobial resistance, Korean resistance surveillance, pathogenic bacteria

INTRODUCTION

It has been known that bacteria resistant to antimicrobial agents are relatively more prevalent in Korea when compared to other industrialized countries.[1] Surveillance of antimicrobial resistance not only facilitates the optimal use of antimicrobial agents for the treatment of infected patients,[2] but the information obtained from it can be crucial to establish control measures for preventing the spread of resistance. Therefore, the WHO Western Pacific Regional Office has been operating a surveillance program since 1988. WHO in Geneva has initiated an international surveillance program to obtain more valuable data. WHO also recommended an organization of a national surveillance program, based on which the Korean Nationwide Surveillance of Antimicrobial Resistance (KONSAR) program was started in 1997. The KONSAR group reported the surveillance results for the year 1997.[3]

In this study, routine susceptibility data for the year 1998 were collected from hospitals participating in the KONSAR Program, and were compared to those obtained for previous years. As in 1997, particular attention, was given to trends of extended-spectrum β-lactamase-producing strains, cephamycin-resistant *Escherichia coli* and *Klebsiella pneumoniae*, imipenem-resistant *Pseudomonas aeruginosa*, ampicillin-resistant *Haemophilus infeuenzae*, fluoroquinolone-resistant gram-negative bacilli, and glycopeptide-resistant enterococci.

MATERIALS AND METHODS

Routine susceptibility test data of all isolates for the year 1998 were collected from 25 of the 65

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hospitals participating in the KONSAR program. The KONSAR laboratories have been participating WHO quality control programs to improve their performance. The data from hospitals were analyzed only when the number of isolates of a species exceeded 20. Therefore, for the following organisms the number of hospitals contributing to the analysis were: 14 for non-typhoidal *Salmonella*, 19 for *Stenotrophomonas maltophilia*, 10 for *H. influenzae*, 20 for *Streptococcus pneumoniae*, 21 for *Enterococcus faecalis* and 16 for *E. faecium*.

About one half of the participating hospitals used either the MicroScan (Dade MicroScan Inc., West Sacramento, CA) or the Vitek System (bioMerieux Vitek, Marcy-l'Etoile, France) for most of their isolates, while others only used the NCCLS disk diffusion method.[4] Antimicrobial agents used to test susceptibility of frequently isolated species were compared to estimate trends of antimicrobial use and adequacy of laboratory service. In order to access fluoroquinolone resistance, the data for ciprofloxacin, ofloxacin, levofloxacin and pefloxacin were used in combination. The rate of penicillin non-susceptible in *S. pneumoniae* included results obtained from both, broth microdilution and oxacillin disk screening tests. Some antimicrobial agents which are not recommended for the treatment of certain bacterial infections were included for purposes of comparison only.

The hospitals were grouped according to their bed capacity: Hospitals with over 1,000 beds were designated as "large" and those with less than 1,000 beds as "medium". There were four large hospitals, three in Seoul and one in Pusan. Similarly, of the 21 "medium" hospitals, seven were located in Seoul and 14 in non-Seoul areas. The mean resistance rate was calculated from the resistance rates in each hospitals. This was done to minimize the influence of the larger number of isolates from the larger hospitals on the resistance rates.

RESULTS

Antimicrobial agents used to test susceptibilities in over 80% of laboratories were: *Enterobacteriaceae* to ampicillin, cephalothin, 3rd-generation cephalosporin, imipenem, amikacin, gentamicin, tobramycin and fluoroquinolone; *P. aeruginosa* to piperacillin, ceftazidime, imipenem, amikacin, gentamicin, tobramycin and fluoroquinolone; staphylococci to penicillin, oxacillin, clindamycin, erythromycin, teicoplanin and

Table 1. Number of Laboratories Which Tested Susceptibility of Bacteria to Indicated Antimicrobial Agents

Enterobacteriaceae		*P. aeruginosa*		Staphylococci	
Antimicrobial agent	No. of Lab	Antimicrobial agent	No. of Lab	Antimicrobial agent	No. of Lab
Ampicillin	22	Piperacillin	22	Penicillin	22
Piperacillin	13	Ceftazidime	23	Oxacillin	24
Cephalothin	24	Aztreonam	19	Clindamycin	22
3rd-generation cephalosporin	25	Imipenem	25	Erythromycin	24
Aztreonam	11	Piperacillin-tazobactam	6	Fluoroquinolone	18
Cefotetan	8	Cefoperazone-sulbactam	11	Gentamicin	14
Cefoxitin	10	Amikacin	25	Cotrimoxazole	14
Imipenem	24	Gentamicin	24	Tetracycline	15
Aminopencillin-BLI*	12	Netilmicin	5	Fusidic acid	4
Piperacillin-tazobactam	6	Tobramycin	21	Teicoplanin	20
Cefoperazone-sulbactam	5	Fluoroquinolone	25	Vancomycin	23
Amikacin	24				
Gentamicin	24				
Netilmicin	4				
Tobramycin	22				
Fluoroquinolone	25				
Cotrimoxazole	17				
Tetracycline	10				

* BLI, β-lactamase inhibitor.

vancomycin (Table 1).

The total number of organisms analyzed for susceptibility were 127,180 and the proportions were: *E. coli, K. pneumoniae, E. cloacae,* and *Serratia marcescens,* 30.5%; non-typhoidal *Salmonella,* 0.8%; *Acinetobacter baumannii,* 9.3%; *S. maltophilia,* 1.8%; *P. aeruginosa,* 16%; *H. influenzae,* 0.6%; *Staphylococcus aureus,* 20.5%; coagulase-negative staphylococci, 10.9%; *E. faecalis,* 5.6%; *E. faecium,* 2.3%; *S. pneumoniae,* 1.7% (Table 2).

Among the *E. coli* isolates, over 50% were resistant to ampicillin, piperacillin, cotrimoxazole and tetracycline, while less than 10% were resistant to 3rd-generation cephalosporin, aztreonam, cefoperazone-sulbactam, cefotetan, piperacillin-tazobactam, imipenem and amikacin (Table 3). The resistance rate of *K. pneumoniae* to cefotaxime was 22% when conventional, but not ESBL, breakpoint was applied. Less than 10% of the *Klebsiella* isolates were resistant to cefoperazone-sulbactam, cefotetan, imipenem, amikacin and fluoroquinolone. The resistance rates for *E. cloacae* to cefoperazone-sulbactam, amikacin, imipenem and fluoroquinolone, and for *S. marcescens* to aztreonam cefotetan and imipenem, and for *A. baumannii* to ampicillin-sulbactam, cefoperazone-sulbactam and imipenem, were all less than 20%. *S. maltophilia* showed relatively low resistance rates only to cefoperazone-

Table 2. Species and Number of Isolates Analyzed for Antimicrobial Resistance in 1997 and 1998

Organism	No. (%) of isolates tested in:	
	1997	1998
*Enterobacteriaceae**	31,985 (32.5)	38,788 (30.5)
Non-typhoidal *Salmonella*	539 (0.5)	962 (0.8)
A. baumannii	7,875 (8.0)	11,866 (9.3)
S. maltophilia	2,128 (2.2)	2,322 (1.8)
P. aeruginosa	16,125 (16.4)	20,370 (16.0)
H. influenzae	721 (0.7)	746 (0.6)
S. aureus	22,049 (22.4)	26,042 (20.5)
Coagulase-negative staphylococci	8,533 (8.7)	13,854 (10.9)
E. faecalis	5,069 (5.2)	7,075 (5.6)
E. faecium	1,633 (1.7)	2,968 (2.3)
S. pneumoniae	1,649 (1.7)	2,187 (1.7)
Total	98,306 (100)	127,180 (100)

* Includes *E. coli, K. pneumoniae, E. cloacae* and *S. marcescens.*

Table 3. Antimicrobial Resistance Rates of Gram-negative Bacilli Frequently Isolated from Clinical Materials

Antimicrobial agents	% of isolates resistant (No. of isolates tested)*					
	E. coli (20604)	*K. pneumoniae* (9079)	*E. cloacae* (5781)	*S. marcescens* (3324)	*A. baumannii* (11866)	*S. maltophilia* (2322)
Ampicillin	78	96	96	95	96	97
Aminopenicillin-BLI†	29	25	67	93	14	89
Cephalothin	44	38	98	99	99	96
Cefotaxime	8	22	47	51	83	91
Ceftazidime	7	25	48	25	64	50
Aztreonam	3	20	46	17	78	88
Cefoperazone-sulbactam	5	7	18	21	4	22
Cefoxitin	12	14	97	74	98	99
Cefotetan	5	4	57	9	82	20
Piperacillin	61	35	54	38	75	76
Piperacillin-tazobactam	5	10	35	37	43	52
Ticarcillin-clavulanate	22	18	53	56	55	22
Imipenem‡	0	0	0.8	1.1	5.2	96
Amikacin	5	9	16	20	60	65
Gentamicin	32	28	47	48	79	76
Tobramycin	25	32	51	62	78	78
Fluoroquinolone	25	8	16	22	71	21
Cotrimoxazole	55	31	47	51	65	29
Tetracycline	68	26	49	92	76	83

* Intrinsic resistance of *K. pneumoniae, E. colacae, S. marcescens, A. baumannii* and *S. maltophilia* to ampicillin, cephalothin, or cefoxitin are included just for comparison. † BLI, β-lactamase inhibitor. ‡ Rare, but important, antibiotic resistance was expressed as decimals to show subtle differences.

sulbactam (22%), cefotetan (20%), ticarcillin-clavulanate (22%), and fluoroquinolone (21%). Resistance rates of *E. cloacae*, *S. marcescens*, *A. baumannii*, and *S. maltophilia* to cefotaxime were high (Table 3, Fig. 1).

The resistance rate for non-typhoidal *Salmonella* was 13.1% to ampicillin and less than 1% to ceftazidime and fluoroquinolone (Table 4).

Among the *P. aeruginosa* isolates, 17% were resis-

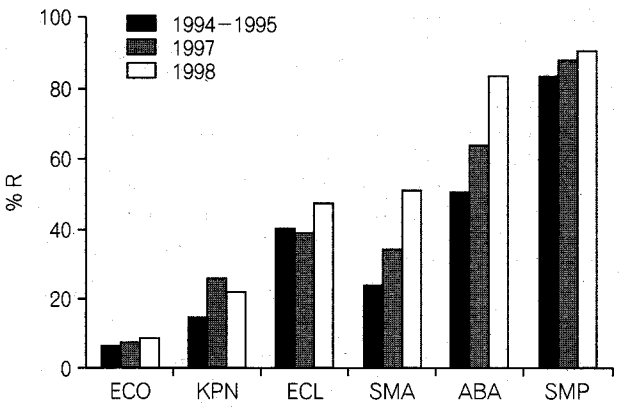

Fig. 1. Rising cefotaxime resistance rates of gram-negative bacilli during 1994 to 1998.

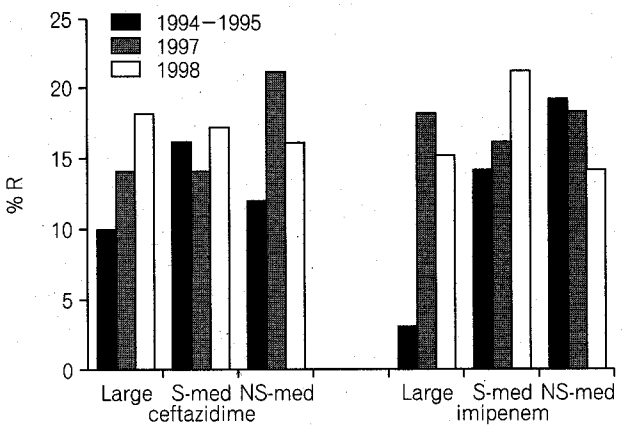

Fig. 2. Comparison of ceftazidime and imipenem resistance rates of P. aeruginosa in different group of hospitals.

Table 4. Antimicrobial Resistance Rates of Non-typhoidal *Salmonella* by Hospital Group

Antimicrobial agents	% of isolates resistant by hospital group (No. tested):			
	Large (407)	Seoul-Medium (164)	Non-Seoul-Medium (391)	Mean (962)
Ampicillin	8	13	18	13
Ceftazidime*	0.7	0	0	0.2
Cotrimoxazole	1	2	2	2
Fluoroquinolone	1	1	2	1

* Rare, but important, antibiotic resistance was expressed as decimals to show subtle differences.

Table 5. Antimicrobial Resistance Rates of *P. aeruginosa* by Hospital Group

Antimicrobial agents	% of isolates resistant by hospital group (No. tested):			
	Large (5547)	Seoul-Medium (5531)	Non-Seoul-Medium (9292)	Mean (20370)
Piperacillin	40	43	46	43
Piperacillin-tazobactam	49	29	NT*	35
Ticarcillin-clavulanate	46	32	45	41
Aztreonam	24	25	24	24
Ceftazidime	18	17	16	17
Cefoperazone-sulbactam	15	34	37	29
Imipenem	15	21	14	17
Amikacin	26	38	26	30
Gentamicin	53	49	48	50
Tobramycin	48	48	47	48
Fluoroquinolone	42	45	37	42

* NT, not tested.

Table 6. Ampicillin Resistance Rates of *H. influenzae* by Hospital Group

Test	% of isolates resistant by hospital group (No. tested):			
	Large (438)	Seoul-Medium (79)	Non-Seoul-Medium (235)	Mean (746)
Ampicillin	60	58	56	58
β-lactamase	57	52	58	56

Table 7. Antimicrobial Resistance Rates of Staphylococci by Hospital Group

Antimicrobial agents	% of isolates resistant by hospital group (No. tested):							
	S. aureus				Coagulase-negative staphylococci			
	Large (7764)	Seoul-Medium (6000)	Non-Seoul-Medium (12278)	Mean (26042)	Large (3344)	Seoul-Medium (3640)	Non-Seoul-Medium (6870)	Mean (13854)
Penicillin	99	97	96	97	94	91	90	92
Oxacillin	73	73	70	72	65	62	62	63
Clindamycin	63	59	64	63	40	37	38	38
Erythromycin	75	75	74	75	60	58	60	59
Fluoroquinolone	63	68	64	66	36	33	28	32
Cotrimoxazole	3	4	1	3	43	40	36	40
Gentamicin	74	76	78	76	54	59	67	60
Tetracycline	79	71	71	74	37	57	53	49
Fusidic acid	3	3	5	4	30	12	7	16
Teicoplanin*	0	0.1	0.1	0.1	1.9	0.3	0.7	0.9
Vancomycin*	0	0	0	0	0.4	0	0.5	0.2

* Rare, but important, antibiotic resistance was expressed as decimals to show subtle differences.

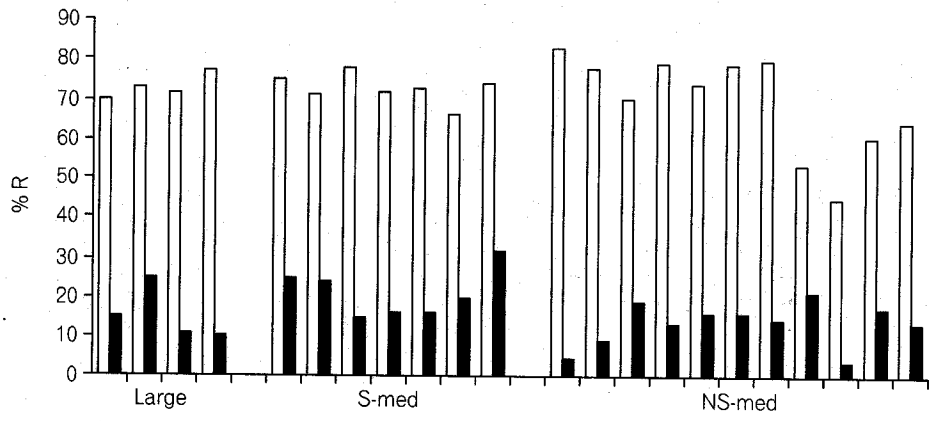

***Fig. 3.** Prevalence of oxacillin-resistant S. aureus and imipenem-resistant P. aeruginosa in each hospitals (□, oxacillin; ■, imipenem).*

tant to ceftazidime and imipenem. The resistance rates to ceftazidime were similar in all hospital groups, but those to imipenem were higher in the medium-sized hospitals of Seoul (Table 5, Fig. 2). The rates of ampicillin resistance and β-lactamase production, for *H. influenzae* were 58% and 56%, respectively, and were similar in all hospital groups (Table 6).

Almost all *S. aureus* isolates were resistant to penicillin. The resistance rate to oxacillin was 72% and the rates were not significantly different in all hospital groups (Table 7, Fig. 3). Resistance rates to cotrimoxazole and fusidic acid were 3% and 4%,

Table 8. Antimicrobial Resistance Rates of Enterococci by Hospital Group

Antimicrobial agents	% of isolates resistant by hospital group (No. tested):							
	E. faecalis				E. *faecium*			
	Large (2954)	Seoul-Medium (1420)	Non-Seoul-Medium (2701)	Mean (7075)	Large (1493)	Seoul-Medium (698)	Non-Seoul-Medium (777)	Mean (2968)
Ampicillin	4	6	5	5	82	80	77	80
Fluoroquinolone	29	34	36	33	77	77	70	75
Tetracycline	81	85	80	82	45	64	48	52
Teicoplanin*	0.8	0	0.1	0.3	6.9	11.6	10.2	9.7
Vancomycin*	0.8	0.3	0.6	0.6	8.4	14.4	10.0	10.9

* Rare, but important, antibiotic resistance was expressed as decimals to show subtle differences.

Table 9. Antimicrobial Resistance Rates of Pneumococci by Hospital Group

Antimicrobial agents	% of isolates resistant by hospital group (No. tested):			
	Large (762)	Seoul-Medium (676)	Non-Seoul-Medium (749)	Mean (2187)
Penicillin*	84	81	71	78
Erythromycin	73	77	65	72
Cotrimoxazole	78	65	59	67
Fluoroquinolone	6	3	2	4
Tetracycline	80	71	69	73

* Includes results of oxacillin disk screening.

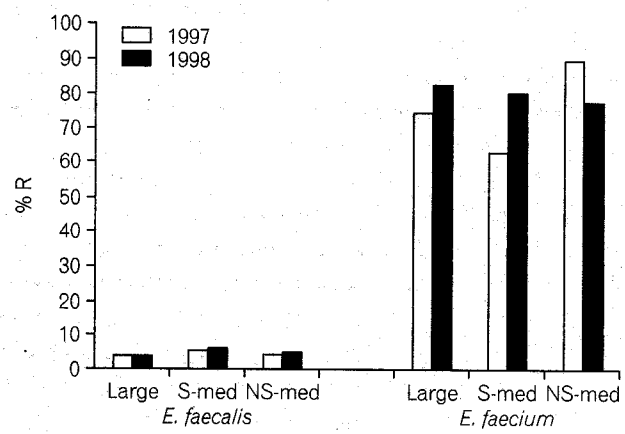

Fig. 4. Comparison of ampicillin resistance rates of E. faecalis and E. faecium in different group of hospitals.

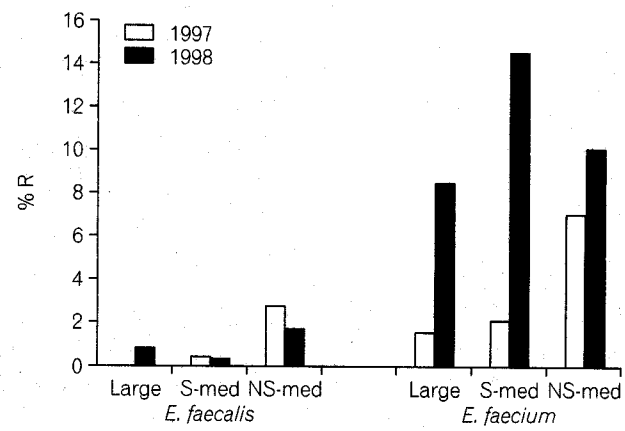

Fig. 5. Comparison of vancomycin resistance rates of E. faecalis and E. faecium in different group of hospitals.

respectively. Among the *S. aureus*, 0.1% were resistant to teicoplanin, but none were to vancomycin. Among the coagulase-negative staphylococci, 63% were resistant to oxacillin and 40% to cotrimoxazole. Teicoplanin and vancomycin resistance rates were 0.9% and 0.2%, respectively.

Ampicillin resistance rates of *E. faecalis* and *E. faecium* were 5% and 80%, respectively (Table 8, Fig 4). Similarly, rates to teicoplanin and vancomycin resistance for *E. faecalis* were 0.3% and 0.6%, respec-

tively, and 9.7% and 10.9%, respectively for *E. faecium*. The teicoplanin and vancomycin-resistance rates of *E. faecium* were higher in the medium-sized hospitals of Seoul (Table 8, Fig. 5). The penicillin-non-susceptible rate for *S. pneumoniae* was 78%, with slightly higher rate in the large hospital group. The resistance rate to fluoroquinolone was 4%, but the rates to erythromycin, cotrimoxazole and tetracycline were 72%, 67% and 73%, respectively (Table 9).

DISCUSSION

In this surveillance, the number of participating laboratories increased to 25 from 20 in 1997. We made a slight change in the hospital groups to simplify comparison of the results. As the resistance rates in a large hospital in Pusan and the three in Seoul were similar, they were grouped together. Also, hospitals with less than 500 beds were included to those with 500 to 1,000 beds.

With the increased incidence of multi-resistant bacteria, and ever increasing number of new antimicrobial agents, clinical laboratories are confronted with the need to provide adequate data regarding the selection of suitable antimicrobial agents.[2] The selection of antimicrobial agents for testing may also depend upon, the kind of microdilution panel being used, and the availability of antimicrobial disks. It may also not be adequate to test susceptibility to available antimicrobial agents in a hospital pharmacy, as a drug committee needs current susceptibility data to introduce new antimicrobial agents. In this surveillance, it was shown that the kind of antimicrobial agents used for susceptibility testing were similar to those used in 1997, except that some laboratories have started to use cefoperazone-sulbactam (Table 1).[3] As in 1997, many laboratories tested susceptibility of *Enterobacteriaceae* and *P. aeruginosa* to 3rd-generation cephalosporin and imipenem, but not many tested to β-lactam and β-lactamase inhibitor combinations or to cephamycins. This situation may lead to over use of 3rd-generation cephalosporin and imipenem, resulting in increase of strains with ESBL and derepressed AmpC β-lactamase as well as strains with imipenem resistance.

With the increase of participating laboratories, the number of isolates tested increased by 29% (Table 2). Compared to 1997, a slight increase in *A. baumannii*, coagulase negative staphylococci, and enterococci isolates was noted.[3] It is interesting to note that the number of isolates of *E. faecium* increased by 81.8%, while *E. faecalis* only increased by 39.5% only. The increase can probably be ascribed to increased resistance of these organisms.

In general, resistance rates of *E. coli* in 1998 were quite similar to those reported for 1997, and the resistance rate to cefotaxime was 8% by conventional breakpoint, suggesting persistence of ESBL-producing strains (Table 3). New TEM- and SHV-type ESBLs emerge continuously.[5,6] It is interesting to note that in Korea, only TEM- and SHV-type β-lactamases are prevalent, as opposed to Japan where these types are rare.[7] Among the *E. coli* isolates, 12% were resistant to cefoxitin. In Korea, plasmid-mediated CMY-1-producing *E. coli* is widespread.[8] Recently, a new mechanism of resistance in *E. coli* due to chromosomal AmpC β-lactamase hyperproduction, has been reported in other country.[9]

Third-generation cephalosporin-resistance was more prevalent in *K. pneumoniae*.[10] This can probably be ascribed to the ability of this organism to acquire resistance determinants relatively easily. Recently, a novel AmpC β-lactamase production was reported as a mechanism of resistance in *K. pneumoniae*.[11] *E. cloacae, S. marcescens, A. baumannii* and *S. maltophilia* are frequently encountered multiresistant nosocomial pathogens. Cefotaxime-resistance rates in these organisms were already very high in 1994−1995, and given the findings of this survey, it would appear that resistance in these strains is still on the increase (Fig. 1).[12] These results may suggest the prevalence of derepressed AmpC β-lactamase-producing strains. Future surveillance on the susceptibility to 4th-generation cephalosporin, such as cefepime and cefpirome, may provide valuable information on these nosocomial pathogens. *A. baumannii* is a problem nosocomial pathogen with frequent multi-resistance. It was found that the fluoroquinolone resistance rate rose significantly from 56% in 1997 to 71% in this study, and the fact that imipenem resistance rate had risen to 5.2% is particularly alarming (Table 3). It has recently been reported that imipenem resistance rate of *A. baumannii* increased to 5.1% in a tertiary hospital.[13]

Antimicrobial resistance of *S. enterica* is a problem in many countries.[14] In this study, serovars of the *Salmonella* isolates were not determined, but Kim et

al.[15] reported that the *S. enterica* serovar Typhimurium, was the second most frequently isolated (25.7%) in Korea between 1995-1997, 54% of which were resistant to aminopenicillin. In Korea even ESBL-producing *S. enterica* have been reported.[16]

In this study, a few strains were resistant to ceftazidime, suggesting they were ESBL producers (Table 4). *S. enterica* enteritis may not require antimicrobial treatment, but when extraintestinal sites become infected, antimicrobial therapy becomes necessary.

In *P. aeruginosa*, the mean ceftazidime-resistance rate rose from 12% to 17% between 1994 and 1998,[3,12] while that of imipenem-resistance rose from 11% to 17%. It is noteworthy that, in 1998, the rate was higher in the medium sized hospitals of Seoul, than in the other hospitals surveyed (Fig. 2). It is likely that stricter control of imipenem use in the larger teaching hospitals, or effective control of nosocomial infections may have had some effect in limiting the spread of resistance. In a study, it was reported that imipenem resistance in *P. aeruginosa* was mostly due to loss of OprD.[17] The rates of ampicillin-resistance and β-lactamase production of *H. influenzae* remained high in this study (Table 6). The β-lactamase-positive rate of 56% was much higher than the 31% to 38% reported in a 5-year American survey.[18]

With the exception of slight decrease of fusidic acid resistance, from 8% in 1997 to 4% in this survey, resistance rates of *S. aureus* were similar to those reported in 1997. High rates of oxacillin resistance in *S. aureus,* 72% (Table 7), was the same as that in 1997, and this trend has been continuing for many years.[19] While a cotrimoxazole resistance rate for *S. aureus* was 3%, it was 40% in coagulase-negative staphylococci. A strain of vancomycin-intermediate *S. aureus* (VISA) was reported in a Korean hospital.[20] The significance of VISA is unclear, but we should not ignore this organism as Moellering has warned not to.[21] Given that routine tests may not be sensitive enough to detect VISA, presence of VISA was not surveyed in this study. Presence of teicoplanin-resistant coagulase-negative staphylococci was reported in Korea,[22] and the resistance rate in this surveillance was 0.9%.

The resistance rate to ampicillin differs significantly between different species of enterococci. Ampicillin-resistant *E. faecalis* is rare in any country. Therefore, the rate of 5% reported in this study (Table 8) might not be accurate. In a study, to determine presence of ampicillin-resistant strain, 23 isolates of "ampicillin-resistant *E. faecalis*" were collected from 9 hospitals in 1998.[23] It was found that of these 10 were species other than *E. faecalis*, 12 were susceptible to ampicillin (MIC $\leq 4\ \mu$g/ml) and only one was resistant (MIC 16 μg/ml). The ampicillin resistance rate of *E. faecium* has risen further from 70% in 1997 to 80% in 1998 (Fig. 4). Vancomycin resistance is a great concern in many countries, particularly in the United States. In Korea, VRE remained rare until quite recently. Vancomycin-resistant *E. faecalis* was only 0.6% in this surveillance, however, a significant increase in the rate was noted in *E. faecium* from 2.9% in 1997 to 11% in 1998. Although the rise was particularly dramatic in both large and medium hospitals in Seoul (Fig. 5), resistance rates were higher in medium hospitals. As mentioned previously, this can probably be attributed to sticter control in the use of vancomycin in large teaching hospitals. Recently, it was reported that mean rectal carriage rates of VanA type VRE was 23% in ICU patients, but that these rates varied significantly, from 0% to 48% between hospitals.[24]

Overall, 78% of pneumococci in this study were penicillin non-susceptible (Table 9). Although oxacillin disk screening may slightly overestimate prevalence of penicillin-non-susceptible pneumococci, the high prevalence of such strains in Korea has been well documented.[25-27] Song et al.[28] reported a rate of 79.7% in 1996-1997. It is noteworthy that the high resistance rates were observed in all 3 groups of hospitals. Therefore, empirical selection of penicillins for the treatment of pneumococcal meningitis should have risk in all levels of hospitals. Treatment of other site infections may also be difficult with antimicrobial agents like erythromycin, cotrimoxazole and tetracycline. However, fluoroquinolone resistance rate remained low.

It was noted that the resistance rates to some old antimicrobial agents were high, and similar, in all hospitals levels (Fig. 3). For example, the ranges of resistance rates were: *E. coli* to ampicillin (76-80% for large hospitals, 75-84% for Seoul medium hospitals, 70-89% for non-Seoul medium hospitals), *S. aureus* to penicillin, (98-100% for large hospitals, 97-99% for Seoul medium hospitals, 90-99% for non-Seoul medium hospitals) and *S. aureus* to oxacillin (70-77% for large hospitals, 66-78% for Seoul

medium hospitals, 45−83% for non-Seoul medium hospitals). However, the resistance rates to some other antimicrobial agents were more variable, even between hospitals in the same group (Fig. 5). For example, the ranges of resistance rates were: *E. coli* to fluoroquinolone (24−34% for large hospitals, 17−29% for Seoul medium hospitals, 13−36% for non-Seoul medium hospitals), *K. pneumoniae* to ceftazidime (17−42% for large hospitals, 19−37% for Seoul medium hospitals, 2−31% for non-Seoul medium hospitals), *P. aeruginosa* to imipenem (10−25% for large hospitals, 15−32% for Seoul medium hospitals, 4−26% for non-Seoul medium hospitals). These facts may indicate that resistant bacteria to old antimicrobial agents are wide spread, while prevalence of resistance with relatively new mechanism varies greatly depending on hospitals, which probably reflect difference in selective pressure. These results also indicate need for analysis of trends in each hospital. For this purpose, WHO distributed convenient WHONET software to analyze individual hospital data.

In conclusion, in Korea, cefoxitin-resistant *E. coli* and *K. pneumoniae* and 3rd-generation cephalosporin-resistant *K. pneumoniae* are prevalent, 3rd-generation cephalosporin-resistant *E. cloacae, S. marcesens* and *A. baumannii* have increased, and ampicillin-resistant *S. enterica* are not rare. Oxacillin-resistant *S. aureus,* penicillin-non-susceptible pneumococci and β-lactamase-producing *H. influenzae* are prevalent in all levels of hospitals, and an increase of imipenem-resistant *P. aeruginosa* and vancomycin-resistant *E. faecium* are new obvious threats. Future surveillance need to focus on the trend of cephamycin-resistance in *E. coli*, ESBL-producing *Enterobacteriaceae*, fluoroquinolone-resistant gram-negative bacilli, penicillin-resistant pneumococci, vancomycin-resistant *E. faecium* and imipenem-resistant *P. aeruginosa*.

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