

Current Status of Antimicrobial Resistance in Korea

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Antimicrobial resistant bacteria have been relatively more prevalent in Korea than in other industrialized countries. During the last several years, increase of known resistance and the emergence of new resistances have been noted, both in community-acquired and nosocomial pathogens. In Korea, the majority of laboratories use the NCCLS disk diffusion method, while some large hospitals use the commercial broth microdilution tests. The data presented in this symposium are mostly from the WHO Focal Point laboratory and Nationwide surveillance program.

Resistance of staphylococci. In Korea, methicillin-resistant *S. aureus* (MRSA) was not detected in the 1960s. In the 1970s, MRSA started to be isolated and in the 1988 the proportion increased to 44%. Since early 1990s the rate became over 70%. In a 1998 nationwide surveillance, the proportion of MRSA was 72%. A study with isolates from wounds, showed that MIC₅₀ of methicillin was 512 µg/ml and most were expression class 3 or 4. Coagulase type II increased to 30%. It was noted that all isolates were susceptible to arbekacin.

In Korea, an isolate of vancomycin-intermediate *S. aureus* (VISA) was detected retrospectively. It was isolated in 1997 from a pelvic abscess specimen of a 45-year-old man. However, other workers attempts failed to detect any other VISA isolates, although Mu3-like strains were prevalent.

Resistance of streptococci and enterococci. As in other countries, *Streptococcus pyogenes* re-

mained very susceptible to β-lactam antibiotics, i.e., MIC of penicillin was 0.015 g/ml. A study showed resistance rates to erythromycin 27% and to tetracycline 56%. In a study, the MIC range of penicillin G for *S. agalactiae* was 0.03~0.06 g/ml. The resistance rates to erythromycin and tetracycline were 26% and 100%, respectively.

The penicillin non-susceptible rate of *S. pneumoniae* in a Korean tertiary care hospital rose from 3% in 1986 to 29% in 1988 and then to 77% in 1993. Similar results have been reported in other hospitals. Capsular types 19F, 23F were frequently isolated, and these types were often non-susceptible to penicillin G. The nationwide surveillance in 1998 showed the mean non-susceptible rate of 78%.

Enterococcus faecium increased to 38% of all enterococci in a tertiary care hospitals in 1999 and the ampicillin-resistance rate was 96%. The first isolation of vancomycin-resistant enterococci (VRE) in Korea was reported in 1992, but it was rare. However, in a tertiary care hospital the proportion of vancomycin-resistant *E. faecium* rose abruptly in 1998 and reached 29% in 1999. Most of the VRE were VanA type *E. faecium*.

Resistance of gonococci. A penicillinase-producing *Neisseria gonorrhoeae* (PPNG) was first reported in Korea in 1979. Since the early 1990s, the proportion of PPNG has risen to over 70%. Isolates of gonococci were often intermediate to ciprofloxacin, but high-level resistant strain started

to be isolated in 2000. Spectinomycin-resistant gonococci remained rare.

Resistance of gram-negative bacilli to β -lactams. In a nationwide surveillance in 1998, resistance rates of *Escherichia coli* were 78% to ampicillin and 44% to cephalothin. Cefotaxime resistance rates by regular NCCLS breakpoint were 8% for *E. coli* and 22% for *Klebsiella pneumoniae*, suggesting ESBL production. In 1999, 529 and 464 isolates of *E. coli* and *K. pneumoniae*, respectively, were collected from 28 hospitals and among them 8.3% and 18.1% were ESBL positive. In Korea, SHV-2, SHV-12a, TEM-4, and TEM-52 types were reported, but interestingly Toho- and Kitasato-type ESBLs were not detected.

A plasmid mediated class C β -lactamase, CMY-1, was first reported in Korea in 1988. It was noted that CMY-1b with increased resistance to ceftazidime had emerged. A survey in 1998 showed that 12% of *E. coli* and 14% of *K. pneumoniae* were resistant to ceftaxime.

In a survey in 1998, 47% and 51% of *Enterobacter cloacae* and *Serratia marcescens*, respectively, were resistant to cefotaxime. Cefepime-resistant isolates remained rare, i.e., at 1% each for *E. coli* and *E. cloacae*, 2% of *K. pneumoniae* and 4% of *S. marcescens*.

In a tertiary care hospital, imipenem-resistance rates of *P. aeruginosa* were 3% to 6% during 1994-1996, but in 1997-1999, the rates rose to 14%~15%. This tendency was also observed in other hospitals and among the imipenem-resistant isolates 8.7% produced carbapenemase. Interestingly, the metallo- β -lactamase was not IMP-type, but VIM-2. It is a great concern that metallo- β -lactamase-producing strains are increasing and that the resistance is transferable by conjugation.

Resistance of gram-negative bacilli to fluoroquinolones and aminoglycosides. In a Korean hospital, only 5% of *E. coli* and 1% of *K. pneu-*

moniae were resistant to ofloxacin in 1991, but the rates rose rapidly to 26% and 19%, respectively in 1994. The resistance rate of *E. coli* was 33% in 1999. A 1998 surveillance showed that resistance is more prevalent in large hospitals, particularly of *E. coli*. Fluoroquinolone resistance rates of *P. aeruginosa* and *Acinetobacter baumannii* were 24% to 39% and 23% to 58%, respectively, depending on the hospital groups.

In 1998, amikacin resistance rates of *E. coli* and *K. pneumoniae* were relatively low, 5% and 9%, respectively. The rates were 16% for *E. cloacae*, 20% for *S. marcescens*, 60% for *A. baumannii* and 30% for *P. aeruginosa*. Gentamicin resistance rates were 32% for *E. coli*, 28% for *K. pneumoniae*, 48% for *S. marcescens*, 79% for *A. baumannii* and 50% for *P. aeruginosa*. Tobramycin resistance rates were similar to those to gentamicin.

Resistance of *Salmonella* and *Shigella*. Ampicillin-resistant non-typhoidal *Salmonella* was rare until the early 1980s, i.e., only 4 of 211 isolates were resistant during 1979-1983. In 1986, resistance rates of *Salmonella* serovar Typhimurium were 77% to ampicillin, 65% to chloramphenicol and 0% to cotrimoxazole. During 1995-1997, 5 strains of *S. enterica* producing TEM-52 ESBL were isolated in a hospital.

Typhoid fever was prevalent until the early 1980s in Korea, but since the early 1980s, isolation of *Salmonella* Typhi has rapidly decreased and non-typhoidal *Salmonella* has increased. Ampicillin or chloramphenicol-resistant *Salmonella* Typhi was not known to exist until an isolate was detected in 1992 from a patient who traveled to South East Asian countries. Two resistant isolates were again isolated at the same hospital in 1995. In 1997, 11% and 15% of the isolates collected by the National Institute of Health Korea were resistant to ampicillin and chloramphenicol, respectively.

Bacillary dysentery was very prevalent in the past, but now it occurs much less frequently. It was reported that among the *Shigella* strains isolated in 1998, 8% were *S. flexneri* and 92% were *S. sonnei*. *S. flexneri* is well known for its antimicrobial resistance. Among the *S. sonnei* isolates in 1998, 99% were resistant to cotrimoxazole and 71% to ampicillin.

Resistance of *Haemophilus influenzae* to β -lactams. In the early 1980s, 9% of *H. influenzae* isolates were resistant to ampicillin by β -lactamase production. The rate gradually rose and in a 1998 surveillance it was 56%. The β -lactamase-positive rates were similar in large and medium hospitals. β -lactamase-negative ampicillin-resistant (BLNAR) strain and β -lactamase-positive aminopenicillin/clavulanate-resistant (BLPACR) strain has not been studied in Korea, yet.

Resistance of *Bacteroides fragilis*. Only 1% of *B. fragilis* isolated in 1995-1996 showed resistance to cefoxitin, but the clindamycin resistance rate was 43%, which was much higher than in

other countries. During 1989-1996, none of the isolates of *B. fragilis* were resistant to imipenem, metronidazole, or chloramphenicol, but the resistance rates to piperacillin and cefotaxime rose remarkably from 12% to 25% and from 17% to 33%, respectively. In general the resistance rates of the non-*fragilis B. fragilis* group species were higher than those of *B. fragilis*.

Summary. MRSA, erythromycin-resistant *S. pyogenes*, penicillin non-susceptible pneumococci, PPNG, ESBL-producing *E. coli* and *K. pneumoniae*, class C β -lactamase-producing *E. coli*, fluoroquinolone-resistant *E. coli*, aminoglycoside-resistant *A. baumannii* and *P. aeruginosa* are all prevalent in Korea, which suggest the presence of high levels of antimicrobial selective pressure and nosocomial spread of resistant bacteria. Rapid increase of VRE and emergence of fluoroquinolone-resistant gonococci and VIM-2 metallo- β -lactamase-producing *P. aeruginosa* are recently observed new threats in Korea.