Penicillin-Resistant trend of *Streptococcus pneumoniae* in Asia: A systematic review

Setareh Mamishi¹, ², Sepideh Moradkhani¹, Shima Mahmoudi¹, Reihaneh Hosseinpour - Sadeghi¹, Babak Pourakbari*¹

¹Pediatrics Infectious Diseases Research Center, Tehran University of Medical Sciences, Tehran, Iran.
²Department of Infectious Disease, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran.

Received: November 2013, Accepted: May 2014

ABSTRACT

The high prevalence of resistance to penicillin by *Streptococcus pneumoniae* is considered as a great concern, particularly in Asian countries. The aim of this study was to investigate the changing trend of penicillin-resistant *S. pneumoniae* (PRSP) in Asia over a 20 years period.

A review of the literature was conducted using the PubMed database, Google Scholar, Scopus, two Persian scientific search engines “Scientific Information Database” (www.sid.ir), and “Mag Iran” (www.magiran.com) through 1993 to 2013. Our study provides a unique chance to investigate the changing trend in PRSP in Asia over a 20 years period. Susceptibility rates among different centers in each country varied widely. In Malaysia, the PRSP rate decreased from 97.2% in 1995-1996 to 69% in 2000. In Singapore, PRSP levels decreased from 72.6% in 1997 to 30.5% in 2007-2008. In Iran, PRSP ranged from 0% to 100%. In Taiwan, the rate of PRSP was 60.3% in 1995 and <50% in other years. In Lebanon, the rate of PRSP was less than 50% (ranging from 30.1% to 50%) in all published data. In Hong Kong, the level of penicillin susceptibility decreased from 71.1% during 1993-1995 to less 42% in 2007.

Continuous surveillance of resistance data from clinical isolates as well as implementation of strict infection control policies is recommended. More studies are needed for better evaluation PRSP rate in some Asian countries such as Vietnam, Singapore, Philippines, Pakistan, Nepal, Kuwait, Korea and Indonesia.

Keywords: *S. pneumoniae*, penicillin resistant, Asia

INTRODUCTION

*Streptococcus pneumoniae* is considered as one of the most important pathogen that causes variety of serious infections such as meningitis, acute otitis media, sinusitis, sepsis, bronchitis, pneumonia and bacteriemia (1, 2). The life-threatening morbidity and mortality due to these infections commonly occur in children less than 2 years old, adults older than 65 years as well as immunocompromised individuals (3). According to the previous studies, more than 860,000 death occur annually due to *S. pneumoniae* infections in children worldwide (4-7). World Health Organization (WHO) has reported mortality rate of 700,000 to 1 million cases in children less than 5 years old due to *S. pneumoniae* infection (6, 8).

In recent years pneumococcal infections has been increased due to rapid development of antimicrobial resistance such as penicillin resistance(8). The first Penicillin Resistance *S. pneumoniae* (PRSP) was reported in Australia in 1967 (9, 10). During the past three decades, several studies have been reported different resistance pattern of *S. pneumoniae* to
penicillin particularly in developing countries. The aim of this study was to evaluate PRSP trend of *S. pneumoniae* in Asian countries.

**MATERIALS AND METHODS**

**Literature search.** A review of the literature was conducted using the PubMed database, Google Scholar, Scopus, two Persian scientific search engines “Scientific Information Database” (www.sid.ir), and “Mag Iran” (www.magiran.com) (1993 through 2013). Search strategy was a combination of the following keywords, subjects and title words: *Streptococcus pneumoniae* (pneumococcous), Penicillin-resistant *S. pneumoniae* (PRSP), Penicillin-susceptible *S. pneumoniae* (PSSP), Asia and each country independently. Articles published between January 1993 and December 2013 were included. Articles and abstracts were limited to studies written in English only.

**Inclusion criteria.** Studies that fulfilled the following criteria were included in the review article:
1. Conducted in Asia (we searched each country independently)
2. Conducted after 1993

Relevant abstracts were reviewed, and studies with any potential to meet inclusion criteria were chosen for full-text review.

**Exclusion criteria.**
1. All kind of review articles were excluded.
2. Articles including only abstract without full-text were excluded.
3. Interventional studies that showed antimicrobial resistance patterns after vaccination or antibiotic therapy.
4. Studies that described antimicrobial resistance patterns based on the serotypes were excluded.
5. Because the number of PCR method was low, this method was excluded.

**Data Extraction.** The frequency and percentage of PSSP were determined and reported for each study (Table 1).

**Analytical strategy and statistical analysis.** Studies were classified / extracted by country, year of sample collection, sources, method of antimicrobial susceptibility testing, and the percent of PSSP.

The demographic characteristics of PSSP including detailed age of the study subjects, methods, and source of specimens were extracted from Asian countries during 1993-2013. In all studies intermediate resistance was considered as resistant.

**RESULTS**

The prevalence of PSSP in the Asian regions according to different countries, time period and the using method is shown in Table 1.

A total of 21 countries including Bangladesh (n=7), China (n=15), Hong Kong (n=9), India (n=16), Indonesia (n=2), Iran (n=20), Israel (n=2), Japan (n=17), Korea (n=3), Kuwait (n=3), Lebanon (n=3), Malaysia (n=5), Nepal (n=3), Pakistan (n=1), Philippine (n=1), Saudi Arabia (n=5), Singapore (n=2), Taiwan (n=6), Thailand (n=5), Turkey (n=14) and Vietnam (n=3) were included in the study.

Based on our data, *S. pneumoniae* isolates were isolated from different clinical specimens such as blood, cerebrospinal fluid (CSF) culture, pus, nasopharyngeal swab, nasal swab, bronchoalveolar lavage, ear exudates, eye swabs, endo-tracheal tube, respiratory tract, sputum, pleural fluid, throat, and non-sterile areas.

The most methods applying in Asian region were disk diffusion and broth microdilution. Other methods such as E-test and agar dilution were less frequently used.

The following countries had the most published data on PSSP in Asia, while the others had been reported a few published data on this issue.

**Bangladesh.** According to Table 1, the least rate of penicillin susceptibility was seen during 1993-1997 in children < 5 years of age (87.3%), while in the other studies the rate of PSSP was more than 90%. However, the subject of all studies in this country was children (4, 11-16).

**China.** The least and the most rate of penicillin susceptibility was seen during 2009-2012 in children < 14 years (the rate of penicillin-susceptibility was 0%) and 2005-2011 in pediatric and adult patients (100%), respectively. In general, the frequency of PSSP has been changed according to different methods in China. The different antimicrobial susceptibility methods in this country was agar dilution (n=21, 58.3%), E-test (n=7, 19.4%), E-test
Table 1. The prevalence of PSSP in 22 countries during 1993-2013

| Country | Periods analyzed | Methods |
|---------|------------------|---------|
|         | 1993-2003 | 2003-2013 |
|         | % (References) | % (References) | Disk Diffusion | E-test | Broth micro dilution | Agar dilution |
| Bangladesh | 87.3(11), 97.0(12), 93.0(12) | 100.0(13) |
|          | 91.2(14) | 90.0(15), 97.1(16), 100.0(4) | + | + |
| China | 88.1(21), 60.1(19) | 75.0(25) | 36.9(30), 79.5(30) | + |
|         | 80.9(27), 35.7(20), 44.8(20), 59.3(31), 89.3(29), 39.3(29), 96.2(29), 48.5(29), 58.6(29), 39.7(29), 63.9(29), 49.2(29), 72.7(29), 58.3(29), 61.5(29), 53.8(29), 66.7(29), 47.6(29), 100(29), 66.7(29), 61.9(32) | + |
| Hong Kong | 62.6(38), 58.0(36) | 58.0(36) | 12.56(33), 17.2(33), 42.0(37) | + | |
|          | 71.1(39), 60.0(39), 76.1(39), 44.4(125) | 44.4(125), 35.1(35) | + |
| Indonesia | 100.0(41), 81.7(40), 84.0(40), 96.7(49), 100.0(42), 100.0(43) | 100.0(41), 100.0(44), 100.0(45), 33.3(47), 67.0(52), 100(46) | + |
|          | 75.0(42) | + |
| India | 95.0(52) | 95.5(54) | + |
|          | 93.6(48) | 84.6(50) | + | + |
|          | 25.0(55) | + | + |
|          | 86.0(51) | + | + | + |
|          | 6.7(40), 6.7(40) | + | + |
| Indonesia | 100.0(127) | + |
| Iran: | 97.8(128) | + | + |
| Tehran: | 0(56), 44.0(59), 43.3(65), 75.7(129), 34.0(60) | Tehran: 0(56), 43.3(65), 34.0(60) | + |
|         | Ahvaz: 25.0(69) | Tehran: 25.0(69) | |
|         | Tehran: 100.0(58) | Tehran: 100.0(58) | |
|         | Shahrekord: 71.1(61) | Tehran: 100.0(58) | |
|         | Tehran: 40.0(62), 90.8(63) | Tehran: 100.0(58) | |
|         | Shiraz: 40.0(71) | Tehran: 100.0(58) | |
|         | Tehran: 65.0(58) | Tehran: 65.0(58) | |
|         | Tehran: 92.0(66) | Tehran: 92.0(66) | |
|         | Isfahan: 30.0(68) | Isfahan: 30.0(68) | |
| Tehran: | 71.0(129) | Tehran: 71.0(129) | |
|         | Shahrekord: 0(57) | Tehran: 71.0(129) | |
|         | Shiraz: 66.1(70) | Tehran: 71.0(129) | |
|         | Zahedan: 68.5(1) | Tehran: 71.0(129) | |
|         | Tehran: 82.0(73) | Tehran: 82.0(73) | |
| Tehran: | 70.0(64) | Tehran: 70.0(64) | + |
| Country    | Periods analyzed | Methods                  |
|------------|------------------|--------------------------|
|            | 1993-2003        | 2003-2013                | Disk Diffusion | E-test | Broth micro dilution | Agar dilution |
|            | % (References)   | % (References)           |               |        |                      |               |
| **Pakistan** |                 |                          |               |        |                      |               |
|            | 65.0(130), 65.2\(^\circ\)(131), 63.3\(^\circ\)(131) |                          | +            | +        |                      |               |
| **Japan**   |                 |                          |               |        |                      |               |
|            | 60.0(89)         |                          | +            | +        |                      |               |
|            | 52.8 (87), 54.6 (87), 49.6 (77), 60.5 (88), 51.5 (82), 35.7 (85), 49.3 (87), 45.2 (85), 5.7 (83), 36.1 (85), 39.3 (84), 42.0 (132), 49.0 (87), 38.0 (86), 81.0 (86) | 34.9(82), 48.5(82), 42.0 (132), 81.0 (86), 38.0 (86), 53.9 (80), 30.0 (86), 35.7 (78), 100.0 (79) | +            |                      |               |
|            | 27.4(81)         |                          | +            | +        |                      |               |
|            | 39.4(75)         |                          | +            | +        |                      |               |
|            | 53.2 (76)        |                          | +            | +        |                      |               |
|            | 36.0(74)         |                          |               |        |                      |               |
| **Korea**   |                 |                          | +            |        |                      |               |
|            | 25.0(133)        | 32.0(134), 79.1(135)     | +            |        |                      |               |
| **Kuwait**  |                 |                          | +            |        |                      |               |
|            | 46.2(136)        |                          | +            |        |                      |               |
|            | 60.0(137)        | 59.0(138)                | +            | +        |                      |               |
| **Lebanon** |                 |                          |               |        |                      |               |
|            | 50.0(140), 44.4(140), 45.5(140), 38.9(140) | 40.6 (140)              | +            |        |                      |               |
|            | 30.1(141)        |                          | +            | +        |                      |               |
| **Malaysia** |               |                          |               |        |                      |               |
|            | 97.2(93)         | 99.4(91)                 | +            |        |                      |               |
|            | 89.1(142), 69.0(90) |                          | +            |        |                      |               |
|            | 93.0(92)         |                          | +            |        |                      |               |
| **Nepal**   |                 |                          | +            |        |                      |               |
|            | 96.0(143)        | 12.3(144)                | +            |        |                      |               |
|            | 100.0 (145)      |                          | +            |        |                      |               |
| **Pakistan** |               |                          | +            |        |                      |               |
|            | 83.0\(^\circ\)(146), 77.0\(^\circ\)(146) |                          | +            |        |                      |               |
| **Philippines** |             |                          | +            |        |                      |               |
|            | 97.9(147)        |                          | +            |        |                      |               |
| **Saudi Arabia** |             |                          | +            |        |                      |               |
|            | 46.0(96)         | 46.0(96)                 | +            |        |                      |               |
|            | 49.0 (97)        |                          | +            |        |                      |               |
|            | 63.4 (98)        |                          | +            |        |                      |               |
| **Singapore** |             |                          | +            |        |                      |               |
|            | 36.7(148)        |                          | +            |        |                      |               |
|            | 72.6(3)          | 30.5(3)                  | +            | +        |                      |               |
| **Taiwan**  |                 |                          | +            |        |                      |               |
|            | 60.3(149), 46.3(149) |                          | +            |        |                      |               |
|            | 45.2(99), 45.2(99) | 91.8(100), 16.8(100)     | +            |        |                      |               |
|            | 43.6 (150)       | 26.3 (103)               | +            |        |                      |               |
| **Thailand** |               |                          | +            |        |                      |               |
|            | 54.2(105), 54.4(105), 53.3 (105) | 57.2(105), 57.6(105), 52.3 (105) | +            |        |                      |               |
|            | 24.5 (104)       |                          | +            |        |                      |               |
|            | 58.0 (108)       |                          | +            |        |                      |               |
|            | 97.5 (105)       | 97.5 (105)               | +            | +        |                      |               |
|            | 82.9 (107)       |                          | +            | +        |                      |               |
|            | 48.0(109)        |                          |               |        |                      |               |
| Country | Periods analyzed | Methods |
|---------|-----------------|---------|
|         | 1993-2003 | 2003-2013 |
|         | Disk Diffusion | E-test | Broth micro dilution | Agar dilution |
| Turkey  | % (References) | % (References) | + | + |
| 1993-2003 | 70.3(151), 77.0(152), 94.0(117), 73.7(14)(117), 88.5(117), 66.6(119) | 94.0(117), 73.7(117), 88.5(117), 67.6(118) | + |
|         | 54.0(120) | 89.8(116) | + |
| Vietnam | 48.0 (153) | 26.4(154) | + |

1 The method is not determined
2 In children
3 In adults
4 Among non-meningitis isolates
5 Among meningitis isolates
6 In clinical isolates
7 In invasive isolates
8 In carriage isolates
9 The agreement between the MICs obtained by E-test and agar dilution for penicillin was >97.5%
10 In nasopharyngeal carriage isolates
11 In hospitalized and non-hospitalized cancer patients
12 In total strains
13 In older children and adults
14 In the group of sick children
15 In the control group

and agar dilution (n=4, 11.1%), broth micro dilution (n=3, 8.3%) and finally disk diffusion and E-test (n=1, 2.8%). The subject of most studies in this country was children (17-26); while only one study evaluated adults (27) and in three surveys (28-30) study subjects included both groups. However, in two studies, study subjects were not known (31, 32).

**Hong Kong.** The least and the most rate of penicillin susceptibility was reported in 2004 (33) in children<6 years (12.5%) and between 1993 and 1995 in adult patients (76.1%). The rate of PSSP was varied by different methods in Hong Kong. Several studies worked on children and adolescents (33-37). However, there are studies which evaluated both groups (38, 39).

**India.** The least and the most rate of penicillin susceptibility was seen during 1999-2002(40) (6.7%) and in the period of 1996-2009 (41-46) from children and adults (100%), respectively. In general, the rate of PSSP was varied in India. In the most studies, study subjects were children (43-45, 47-50). However, there are some studies which worked on children and adults (41, 42, 46, 51-54) and even unknown subjects (40, 55).

**Iran.** The least and the most level of penicillin susceptibility were seen in Tehran during 1995-2005 (56), Shahrekord in 2005 (57)(0%) and between 2004-2006(58) in children (100%). Totally, the frequency of PSSP has been changed in Iran (rate of PSSP with different rates was seen during 1995-2008; then increased up to 2009; and finally decrease until 2012). The most prevalent used method in this country was disk diffusion (n= 13, 59.1%); followed by broth micro dilution (n=5, 22.7%), E-test (n=3, 13.6%) and agar dilution (n=1, 4.5%). The subjects of most studies were children and adolescents (1, 56, 58-68); while there are some reports which was evaluated both age groups (69-72). Moreover, in two studies, the study subjects were unknown (57, 73).

**Japan.** Rate of PSSP varied in Japan in the period...
of 1993-2006. In Japan, the most prevalent methods which was used for antimicrobial susceptibility was broth micro dilution (n=22, 81.5%) followed by E-test, agar dilution, disk diffusion and broth micro dilution. The subject of most studies was children (74-79); however, there are some reports that evaluated adults (80, 81), both groups (82-86) and indeterminate subjects (87-89).

Malaysia. Rate of penicillin susceptibility was the least and the most in 1999-2000 (90) (69%) and between 2009-2010 (91)(99.4%), respectively. Totally, the frequency of PSSP decreased during 1995-2000; then increased up to 2010. Among studies, two surveys evaluated children (92, 93). However, one report worked on all age groups (91).

Saudi Arabia. The least and the most rate of penicillin susceptibility was seen in 2000 (94) in children< 10 years old (40.9%) and during 2004-2005 (95) in infants and patients >50 years old (93%). The penicillin susceptibility rate in this country decreased from 2000-2005; then, increased up to 2006. The most studies worked on children (94, 96); however, two research evaluated all age groups (95, 97) and in one study, study subjects were unknown (98).

Taiwan. The least and the most rate of penicillin susceptibility was seen in the period of 2000-2001 (99) in children (4.5%) and between 2003-2006 (100) (91.8%), respectively. Rate of PSSP decreased in the period of 1995-2004; and different rates was seen until 2006. However, based on reports from 1996 to 2001, isolates from this country indicated high prevalence of penicillin susceptibility (101). Different methods which was used in this country was broth micro dilution (n=4, 44.4%) and disk diffusion and agar dilution (n=2, 22.2%), respectively. In different survey, study subjects selected from children and adolescents (102), however, some studies worked on both groups (99) and in determinate subjects (100, 103).

Thailand. The least and the most rate of penicillin susceptibility was seen during 2001-2002 (104) (24.5%) and in 2000-2005 (105)in isolates aged range <6 and >60 years old (97.5%), respectively. Surveillance researches in 11 Asian countries during 2000 to 2001 (106), estimated that the penicillin susceptibility rate was almost low in this region. The most common used methods in this country were disk diffusion (n=7, 58.3%), followed by E-test, broth micro dilution, disk diffusion and E-test and finally disk diffusion and agar dilution (n=1, 8.3%). One study worked on children (107); but three studies evaluated the both groups (105, 108, 109) and one research evaluated indeterminate subjects (104).

Turkey. The least and the most rate of penicillin susceptibility was seen between 1997 and 2001 (110) (0%) and during 1997-1998 (111) among adults (97%). In general, the frequency of PSSP changed by different methods in this region. In this country, rate of PSSP evaluate by using E-test (n=7, 36.8%), agar dilution (n=5, 26.3%), disk diffusion (n=3, 15.8%), broth micro dilution (n=2, 10.5%), disk diffusion altogether E-test (n=1, 5.3%), respectively. The most studies worked on children (112-116); one report worked on adults (111); but two survey applied the both groups (117, 118). However, in two studies, study subjects were not known (119, 120).

DISCUSSION

This study describes the changing trends in antimicrobial resistance of pneumococcal isolates collected from Asian countries during 1993 to 2013. Our review confirms that PRSP is a significant health problem among children in the most Asian countries. Although comparisons among countries are difficult due to differences in study design and methods, we evaluated 155 studies in Asia.

Our study provides a unique chance to investigate the changing trend in PSSP in Asia over a period of 20 years. Susceptibility rates among different centers in each country varied widely. Regards to current research, in children, prevalence of PSSP was as low as 0% in China (24) and Iran (56) while the highest susceptibility rate was seen in Bangladesh (4), India (43, 45), Iran (58) and Japan (79)(100%). As documented in previous report, children younger than age 5 years are more frequently infected with penicillin resistant strains (106).

In large countries, it is more likely that the resistance rates differ between one region and another. Therefore, due to great variation in resistance rates by hospital and patient type within countries good laboratory facilities and qualified personnel are needed for each region.

In Malaysia, the PSSP rate decreased from 97.2% in 1995-1996 to 69% in 2000. In Singapore, PSSP levels
susceptibility among S. pneumoniae isolates from Nepal was only 96% in 2000-2001, but decreased to 2.3% in 2009-2010.

More studies are needed for better evaluation of PSSP rate in countries such as Vietnam, Singapore, Philippines, Pakistan, Nepal, Kuwait, Korea and Indonesia. In addition, the leading factors associated with low susceptibility rate of penicillin in countries such as Hong Kong, Iran, Japan, Lebanon, Taiwan, and Vietnam should be evaluated in the future.

There were different rates of penicillin susceptibility in some countries such as Japan, Iran, China, Hong Kong, India, Saudi Arabia and Thailand based on the age groups, types of isolates, used methods and periods analyzed. It has been reported that the spread of PRSP strains in Saudi Arabia and Kuwait might be derived by the selective pressure created by excessive use, misuse of antimicrobial agents or even easy availability of these agents (121). Song et al. reported that the rates of PSSP in Asia are decreasing in 11 countries in Asia and the Middle East during 2000-2001 (106). Recent data collected by the Asian Network for Surveillance of Resistant Pathogen (ANSORP) with respect to pneumococcal isolates from clinical specimens, reported a low prevalence of penicillin and multidrug susceptibility in some Asian countries such as Korea, Japan and Vietnam (106). Totally, the prevalence of susceptibility to commonly used antimicrobial agents in S. pneumoniae isolates in far East countries is less than in European and North/South American countries (122).

The high prevalence of resistance to penicillin, particularly in Asian countries, is of great concern. Developing countries face substantial problems of antimicrobial resistance due to several factors including self-medication, absence of diagnostic tools, over-the-counter use, inadequate storage or even use of expired drugs (123).

Prior antibiotic use is considered as the leading risk factor associated with drug-resistant S. pneumoniae (124). Therefore, it should be another possible factor in frequency of penicillin resistance in some countries with low rate of PRSP.

According to this study, some countries had the most published data on PSSP, while some other Asian countries have been reporting a few published data on this issue. With regard to microbiological methods, few studies mentioned application of quality assurance in identification and susceptibility testing. In addition, quantitative susceptibility data (e.g. MICs or inhibition diameters) were only rarely available.

In conclusion, the current study has provided updated information and changing trends in penicillin resistance of S. pneumoniae in Asian countries. Continuous surveillance of resistance data from clinical isolates as well as implementation of strict infection control policies, evaluation of the new generation of conjugate vaccines and enhanced public health efforts to reduce transmission are required to diminish the progression of antimicrobial resistance.

REFERENCES

1. Bokaeian M, Khazaee H, Javadimehr M. Nasopharyngeal Carriage, Antibiotic Resistance and serotype distribution of Streptococcus pneumoniae among healthy adolescents in Zahedan. Iran Red Crescent Med J 2011;13(5):328-333.
2. Bogaert D, De Groot R, Hermans P. Streptococcus pneumoniae colonisation: the key to pneumococcal disease. J Lancet Infect Dis 2004;4(3):144-154.
3. Vasoo S, Singh K, Hsu LY, Chiew YF, Chow C, Lin RT, et al. Increasing antibiotic resistance in Streptococcus pneumoniae colonizing children attending day-care centres in Singapore. J Respir Med 2011;16(8):1241-1248.
4. Saha SK, Naheed A, El Arifeen S, Islam M, Al-Emran H, Amin R, et al. Surveillance for invasive Streptococcus pneumoniae disease among hospitalized children in Bangladesh: antimicrobial susceptibility and serotype distribution. J Clin Infect Dis 2009;48(Supplement 2):S75-S81.
5. Williams BG, Gouws E, Boschi-Pinto C, Bryce J, Dye C. Estimates of world-wide distribution of child deaths from acute respiratory infections. J Lancet Infect Dis 2002;2(1):25-32.
6. O’Brien KL, Wolfson LJ, Watt JP, Henkle E, Deloria-Knoll M, McCall N, et al. Burden of disease caused by Streptococcus pneumoniae in children younger than 5 years: global estimates. J Lancet (London, England)
infections (2000–2005). Among Beijing children with upper respiratory nasopharyngeal isolates of Serogroup distribution and antimicrobial resistance of Chemother agar dilution and E-Test methods.

16. Alam K, Saha SK, Nasreen T, et al. Antibiotic resistance patterns of Streptococcus pneumoniae isolates that cause invasive disease among Chinese children. J Clin Infect Dis 2010;50(3):340-343.

17. Saha SK, Ruhulamin M, Masaki H, Hanif M, Al Arifeen S, et al. Comparison of antibiotic resistance and serotype composition of carriage and nasopharyngeal strains of Streptococcus pneumoniae in Shenzhen, China. J Commun Dis Intell 2013;374(9693):893-902.

18. Varon M, Roytman Y, et al. Penicillin-resistant trend of Streptococcus pneumoniae Carriage in the Gaza Strip. J Pone 2012;7(4): 1-6.

19. Yau S, Yao K, Shen X, Yu S, Lu Q, Deng L, Ye Q, et al. Antimicrobial resistance and serotypes of nasopharyngeal strains of Streptococcus pneumoniae in Chinese children with acute respiratory infections. J Int Med Res 2007;35(2):253-267.

20. Liu Y, Wang H, Chen M, Sun Z, Zhao R, Zhang L, et al. Serotype distribution and antimicrobial resistance patterns of Streptococcus pneumoniae isolated from children in China younger than 5 years. J Diagn Microbiol Infect Dis 2008;61(3):256-263.

21. Wang M, Zhang Y, Zhu D, Wang F. Prevalence and phenotypes of erythromycin-resistant Streptococcus pneumoniae in Shanghai, China. J Diagn Microbiol Infect Dis 2001;39(3):187-189.

22. Xue L, Yao K, Xie G, Zheng Y, Wang C, Shang Y, et al. Serotype distribution and antimicrobial resistance of Streptococcus pneumoniae isolates that cause invasive disease among Chinese children. J Clin Infect Dis 2010;50(3):741-744.

23. Chen R, Chen Y, Black S, Hao CL, Ding YF, Zhang T, et al. Antibiotic resistance patterns and serotype distribution in Streptococcus pneumoniae from hospitalized pediatric patients with respiratory infections in Suzhou, China. J Trop Pediatr 2010;56(3):204-205.

24. Ma X, Zhao R, Ma Z, Yao K, Yu S, Zheng Y, et al. Serotype distribution and antimicrobial resistance of Streptococcus pneumoniae isolates causing invasive diseases from Shenzhen Children's Hospital. J Pone 2013;8(6): 1-7.

25. Huang HH, Zhang YY, Xiu QY, Zhou X, Huang SG, Lu Q, et al. Community-acquired pneumonia in Shanghai, China: microbial etiology and implications for empirical therapy in a prospective study of 389 patients. Eur J Clin Microbiol Infect Dis 2006;25(6):369-374.

26. Hua CZ, Shang SQ, Li JP, Xu S, Chen ZM, Yu HM. Antimicrobial resistance of Streptococcus pneumoniae isolated from children and genetic background of penicillin-resistant strains. World J Pediatr 2005;1(1):384-388.

27. Tao LL, Hu BJ, He LX, Wei L, Xie HM, Wang BQ, et al. Etiology and antimicrobial resistance of community-acquired pneumonia in adult patients in China. Chin Med J(Engl) 2012;125(17):2967-2972.

28. Ding JJ, Xu S, Guo FM, Shi Y, Shao HF, Meng XZ. Comparison of three different PCR-based methods to predict the penicillin nonsusceptible Streptococcus pneumoniae isolates from China. J Lett Appl Microbiol 2009;48(1):105-111.

29. Zhao C, Zhang F, Chu Y, Liu Y, Cao B, Chen M, et al. Phenotypic and genotypic characteristic of invasive pneumococcal disease burden from both children and adult Patients from a Multicenter Surveillance in China 2005–2011. J Pone 2013;8(12): 1-9.

30. Yang F, Xu XG, Yang MJ, Zhang YY, Klugman KP, McGee L. Antimicrobial susceptibility and molecular epidemiology of Streptococcus pneumoniae isolated from children and adult patients in China. J Clin Microbial Infect 2009;37(4):649-655.
31. Xiao Y, Wang J, Li Y. Bacterial resistance surveillance in China: a report from Mohanarin 2004–2005. Eur J Clin Microbiol Infect Dis 2008;27(8):697-708.

32. Ye F, He LX, Cai BQ, Wen FQ, Chen BY, Hadiarto M, et al. Spectrum and antimicrobial resistance of common pathogenic bacteria isolated from patients with acute exacerbation of chronic obstructive pulmonary disease in mainland of China. Chin Med J (Engl) 2013;126(12):2207-2214.

33. Ho PL, Lam KF, Chow FK, Lau YL, Wong SS, Cheng SL, et al. Serotype distribution and antimicrobial resistance patterns of nasopharyngeal and invasive Streptococcus pneumoniae isolates in Hong Kong children. J Vaccine 2004;22(25-26):3334-3339.

34. Boost M, O'Donoghue M, Dooley J. Prevalence of carriage of antimicrobial resistant strains of Streptococcus pneumoniae in primary school children in Hong Kong. J Epidemiol Infect 2001;127(1):49-55.

35. Ip M, Nelson EAS, Cheuk ES, Sung RY, Li A, Ma H, et al. Serotype distribution and antimicrobial susceptibilities of nasopharyngeal isolates of Streptococcus pneumoniae from children hospitalized for acute respiratory illnesses in Hong Kong. J Clin Microbiol 2007;45(6):1969-1971.

36. Chan JMC, Ng DKK, Miu TY, Lam P, Tse CWS, Chan CH, et al. Invasive pneumococcal disease in Hong Kong children. J Pediatr Respirology Critic Care 2013; 9 (2): 4-8.

37. Ho P, Wong RC, Chow FK, Cheung MY, Wong SS, Yam W, et al. Application of a multiplex pbp2b and pbp2x PCR for prediction of penicillin resistance in Streptococcus pneumoniae. J Antimicrob Chemother 2004;53(5):890-891.

38. Ho PL, Que TL, Chiu SS, Yung RW, Ng TK, Tsang DN, et al. Fluoroquinolone and other antimicrobial resistance in invasive pneumococci, Hong Kong, 1995-2001. J Emerg Infect Dis 2004;10(7):1250-1257.

39. Kam KM, Lucy KY, Fung SM, Yiu PP, Harden TJ, Cheung MM. Emergence of multiple-antibiotic-resistant Streptococcus pneumoniae in Hong Kong. J Antimicrob Agents Chemother 1995;39(12):2667-2670.

40. Goyal R, Singh N, Kaur M, Talwar V. Antimicrobial resistance in invasive and colonising Streptococcus pneumoniae in North India. Indian J Med Microbiol 2007;25(3):256-259.

41. Mani R, Pradhan S, Nagarathna S, Wasuilla R, Chandramukhi A. Bacteriological profile of community acquired acute bacterial meningitis: a ten-year retrospective study in a tertiary neurocare centre in South India. Indian J Med Microbiol 2007;25(2):108-114.

42. Kapoor MR, Nair D, Aggarwal P, Gupta B. Rapid diagnosis of community-acquired pneumonia using the Bac T/Alert 3D system. Brazilian J Infec Dis 2006;10(5):352-356.

43. Kar UK, Satpathy G, Nayak N, Das BK, Panda SK. Serotype distribution of Streptococcus pneumoniae isolates from ophthalmic and systemic infections and of commensal origin. Indian J Med Res 2006;124(1):99-104.

44. Zakariya BP, Bhat V, Harish BN, Babu TA, Joseph NM. Neonatal sepsis in a tertiary care hospital in South India: bacteriological profile and antibiotic sensitivity pattern. Indian J Pediatr 2011;78(4):413-417.

45. Sonavane A, Baradkar V, Mathur M. Pattern and antibiotic susceptibility of bacteria isolated in clinically suspected cases of meningitis in children. J Pediatr Neurosci 2008;3(2):131-133.

46. Alam M, Pillai P, Kapur P, Pillai K. Resistant patterns of bacteria isolated from bloodstream infections at a university hospital in Delhi. J Pharm Bioallied Sci 2011;3(4):525-530.

47. Dhakal R, Sujatha S, Parija S, Bhat B. Asymptomatic colonization of upper respiratory tract by potential bacterial pathogens. Indian J Pediatr 2010;77(7):775-778.

48. Larsson C, Kanungo R, Kalmeter G, Rao RS, Krantz I, Norrby SR, et al. High frequency of multiresistant respiratory tract pathogens at community level in South India. J Clin Microbiol Infect 1999;5(12):740-747.

49. Jain A, Kumar P, Awasthi S. High nasopharyngeal carriage of drug resistant Streptococcus pneumoniae and Haemophilus influenzae in North Indian schoolchildren. J Trop Med IntHealth 2005;10(3):234-239.

50. Wattal C, Oberoi J, Pruthi P, Gupta S. Nasopharyngeal carriage of Streptococcus pneumoniae. Indian J Pediatr 2007;74(10):905-907.

51. Chawla K, Gurung B, Mukhopadhyay C, Bairiy I. Reporting emerging resistance of Streptococcus pneumoniae from India. J Glob Infect Dis 2010;2(1):10-14.

52. Shariff M, Choudhary J, Zahoor S, Deb M. Characterization of Streptococcus pneumoniae isolates from India with special reference to their sequence types. J Infect Dev Ctries 2013;7(02):101-109.

53. Kanungo R, D Lima D, Rajalakshmi B, Kumar A, Badrinath S. Emerging antibiotic resistant pneumococci in invasive infections in south India: Need for monitoring. Indian J Pharmacol 2002;34(1):38-43.

54. Molander V, Elisson C, Balaji V, Backhaus E, John J, Vargheese R, et al. Invasive pneumococcal infections in Vellore, India: clinical characteristics and distribution of serotypes. JBMCS Infect Dis 2013;13:52-53.

55. Sourav S, Patricia A, Sharma S, Kanungo R, Jayachandran S, Prashanth K. Detection of pneumolysin and autolysin genes among antibiotic resistant Streptococcus pneumoniae in invasive infections. Indian J Med Microbiol 2010;28(1):34-39.

56. Kalantari N, Taheri-kalani M, Parvaneh N, Mamishi S. Etiology and antimicrobial susceptibility of bacterial septic arthritis and osteomyelitis. Iran J Publ Health 2007;36(3): 27-32 .
penicillin-resistant trend of streptococcus pneumoniae

resistance among bacteria isolates of lower respiratory tract infection in COPD Shahrekord-Iran, 2005. Pak J Med Sci 2007;23(3):438-440.
58. Fahimzad A, Mamaishi S, Noorbakhsh S, Siadati A, Hashemi F, Tabatabaei S, et al. Study of antibiotics resistance in pediatric acute bacterial meningitis with E-Test method. Iran J Pediatr 2006;16(2):149-156.
59. Mamishi S, Pourakbari B, Ashtiani MH, Hashemi FB. Frequency of isolation and antimicrobial susceptibility of bacteria isolated from bloodstream infections at Children's Medical Center, Tehran, Iran, 1996–2000. Int J Antimicrob Agents 2005;26(5):373-89.
60. Pourakbari B, Sadr A, Ashtiani MTH, Mamishi S, Dehghani M, Mahmoudi S, et al. Five-year evaluation of the antimicrobial susceptibility patterns of bacteria causing bloodstream infections in Iran. J Infect Dev Ctries 2011;6(02):120-125.
61. Khoshdel A IR, Saedi A, Kheire S, Hamidi M, Kasiri K, et al. The prevalence of Streptococcus pneumoniae and its penicillin resistance pattern in children less than five years old from Shahrekord, Iran, 2007. J Shahrekord Univ Med Sci 2009;10(4):89-95.
62. Mirnejad R, Jeddi F, Kiani J, Khoshdel M. Etiology of spontaneous bacterial peritonitis and determination of their antibiotic susceptibility patterns in Iran. Asian Pacific J Trop Dis 2011;1(2):116-118.
63. Sanac-Dashita A, Abdinia B, Karimi A. Nasopharyngeal carrier rate of Streptococcus pneumoniae in children: serotype distribution and antimicrobial resistance. J Arch Iran Med 2012;15(8):500-503.
64. Aligholi M, Emaneini M, Jabalameli F, Shavasvan S, Abdolmalekzi S, Sedaghat H, et al. Antibiotic susceptibility pattern of gram-positive cocci cultured from patients in three university hospitals in Tehran, Iran during 2001-2005. Acta Medica Iranica 2009;47(4):329-334.
65. Rezaeizadeh G, Pourakbari B, Ashtiani MH, Asgari F, Mahmoudi S, Mamishi S. Antimicrobial susceptibility of bacteria isolated from cerebrospinal fluids in an Iranian referral pediatric center, 1998-2005. J Maedica (Buchara) 2012;7(2):131-137.
66. Noorbakhsh S, Siadati S, Rimaz S, Mamishi S. Determination of appropriate antibiotic in bacterial Meningitis of children based on MIC. Tehran Univ Med J 2005;63(1).
67. Behnaz F, Firoussabzi L, Babaei-Zadeh A, Mohammadzadeh M. Prevalence of pharyngeal pneumococcal carriers and susceptibility patterns among children of day care centers in yezd district, Iran. J shahid sadoughi univ Med Sci Health Services2004;12(1):65-69.
68. Mostafavizadeh K, Khourvash F, Abousefaei H, Fasihidastjerdi M, Mobasherzadeh S, Izadi Morteza JJN. Determination of Streptococcus pneumoniae resistant to penicillin and ceftriaxone by e-test method. Kowsar Med J 2008;12(4):325-330.
69. Kalantar E, Mosaei M, Ekrami A, Pedram M. Isolation and antimicrobial susceptibility of bacteria from external ear canal of cancer patients at Shafa Cancer Hospital-Ahwaz. J Cancer Res Ther 2006;2(1):17-19.
70. Kohanteb J, Sadeghi E. Penicillin-resistant Streptococcus pneumoniae in Iran. J Med Princ Pract 2007;16(1):29-33.
71. Kargar M, Baghernejad M, Dalini SG. The Role of ppb1a, ppb2b and ppb2x Genes in Penicillin Resistance in Streptococcus pneumoniae Strains Isolated from ICUs. J Isfahan MedSch 2012;30(176):1-8.
72. Rahbar M, Gra-Agaji R, Hashemi S. Nosocomial blood stream infections in Imam Khomeini Hospital, Urmia, Islamic Republic of Iran, 1999-2001. East Mediterr Health J 2005;11(3):478-484.
73. Habibian S, Mehrabi-Tavana A, Ahmadi Z, Izadi M, Jonaidi N, Darakshanpoure J, et al. Serotype distribution and antibiotics susceptibility pattern of Streptococcus. Iran Red Crescent Med J 2013;15(10):1-9.
74. Hotomi M, Billal DS, Kamide Y, Kanesaka K, Uno Y, Kudo F, et al. Serotype distribution and penicillin resistance of Streptococcus pneumoniae isolates from middle ear fluids of pediatric patients with acute otitis media in Japan. J Clin Microbiol 2008;46(11):3808-3810.
75. Masuda K, Masuda R, Nishi JI, Tokuda K, Yoshinaga M, Miyata K. Incidences of nasopharyngeal colonization of respiratory bacterial pathogens in Japanese children attending day-care centers. J Pediatr Int 2002;44(4):376-380.
76. Nagai K, Matsuo Y, Tsumura N, Sakata Y, Kato H. Antimicrobial susceptibilities and serotypes of Streptococcus pneumoniae in southwestern Japan and correlation of penicillin-binding protein 2b and 2x mutations in susceptibilities of penicillin G and cefotaxime. J Diagn Microbiol Infect Dis 2000;37(2):107-113.
77. Suzuki K, Nishimura T, Baba S. Current status of bacterial resistance in the otolaryngology field: results from the Second Nationwide Survey in Japan. J Infect Chemother 2003;9(1):46-52.
78. Ishiwada N, Kurosaki T, Terashima I, Kohno Y. The incidence of pediatric invasive pneumococcal disease in Chiba prefecture, Japan (2003–2005). J Infect 2008;57(6):455-458.
79. Hishiki H, Ishiwada N, Fukasawa C, Abe K, Hoshino T, Aizawa J, et al. Incidence of bacterial coinfection with respiratory syncytial virus bronchopulmonary infection in pediatric inpatients. J Infect Chemother 2011;17(1):87-90.
80. Ishida T, Maniwa K, Kagioka H, Hirabayashi M, Onaru K, Tomioka H, et al. Antimicrobial susceptibilities of Streptococcus pneumoniae isolated from adult patients with community-acquired pneumonia in Japan. J Respirology 2008;13(2):240-246.
81. Qin L, Masaki H, Watanabe K, Furumoto A, Watanabe H. Antimicrobial susceptibility and genetic characteristics of Streptococcus pneumoniae isolates indicating possible nosocomial transmission routes in a community hospital in Japan. J Clin Microbiol 2007;45(11):3701-3706.
82. Suzuki K, Nishimaki K, Okuyama K, Katoh T,

http://ijm.tums.ac.ir

IRAN. J. MICROBIOL. Vol. 6, No. (August 2014), 198-210 207
MAMISHI ET AL.

Yasujima J, Chihara J, et al. Trends in antimicrobial susceptibility of Streptococcus pneumoniae in the Tohoku district of Japan: a longitudinal analysis from 1998 to 2007. Tohoku J Exp Med 2010;220(1):47-57.
83. Hoshino K, Watanabe H, Sugita R, Asoh N, Ntabaguzi SA, Watanabe K, et al. High rate of transmission of penicillin-resistant Streptococcus pneumoniae between parents and children. J Clin Microbiol 2002;40(11):4357-4359.
84. Kasahara K, Maeda K, Mikasa K, Uno K, Takahashi K, Konishi M, et al. Clonal dissemination of macrolide-resistant and penicillin-susceptible serotype 3 and penicillin-resistant Taiwan 19F-14 and 23F-15 Streptococcus pneumoniae isolates in Japan: a pilot surveillance study. J Clin Microbiol 2005;43(4):1640-1645.
85. Inoue M, Kaneko K, Akizawa K, Fujita S, Kaku M, Igari J, et al. Antimicrobial susceptibility of respiratory tract pathogens in Japan during PROTEK years 1–3 (1999–2002). J Infect Chemother 2006;12(1):9-21.
86. soguchi N, Tano J, Nasu Y, Koyama M, Narui K, Kamishima H, et al. Antimicrobial susceptibilities and distribution of resistance genes for beta-lactams and macrolides in Streptococcus pneumoniae isolated between 2002 and 2004 in Tokyo. Int J Antimicrob Agents 2007;29(1):26-33.
87. Yamaguchi K, Ohno A. Investigation of the susceptibility trends in Japan to fluoroquinolones and other antimicrobial agents in a nationwide collection of clinical isolates: a longitudinal analysis from 1994 to 2002. J Diagn Microbiol Infect Dis 2005;52(2):135-143.
88. Tanoue S. Clinical and laboratory evaluation of penicillin resistant Streptococcus pneumoniae in relation to the mutations of pbp 1a, pbp2b and pbp2x. Kurume Med J 2001;48(1):1-8.
89. Kojima F, Nakagami Y, Takemori K, Iwatani Y, Fujimoto S. Penicillin susceptibility of non-serotypeable Streptococcus pneumoniae from ophthalmic specimens. J Microb Drug Resist 2006;12(3):199-202.
90. Desa MN, Lin TK, Yasin RM, Parasakthi N. Penicillin susceptibility and molecular characteristics of clinical isolates of Streptococcus pneumoniae at the University of Malaya Medical Center, Kuala Lumpur, Malaysia. Int J Infect Dis 2003;7(3):190-197.
91. Alasal SM, Omar R, Ismail S, Yusof MY, Dhabaan GN, Abdulla MA. Evidence of bacterial biofilms among infected and hypertrophied tonsils in correlation with the microbiology, histopathology, and clinical symptoms of tonsillar diseases. Int J Otolaryngol 2013;2013:1-11.
92. Rohani M, Raudzah A, Ng A, Ng P, Zaidatul A, Asmah I, et al. Epidemiology of Streptococcus pneumoniae infection in Malaysia. J Epidemiol Infect 1999;122(1):77-82.
93. Malik AS, Ismail A, Pennie RA, Naidu JV. Susceptibility pattern of Streptococcus pneumoniae among pre-school children in Kota Bharu, Malaysia. J Trop Pediatr 1998;44(1):10-14.
94. Memish ZA, Balkhy HH, Shibi AM, Barrozo CP, Gray GC. Streptococcus pneumoniae in Saudi Arabia: antibiotic resistance and serotypes of recent clinical isolates. Int J Antimicrob Agents 2004;23(1):32-38.
95. Asghar AH. Frequency and antimicrobial susceptibility patterns of bacterial pathogens isolated from septicemic patients in Makkah hospitals. Saudi Med J 2006;27(3):361-367.
96. Shibi A. Distribution of serotypes and antibiotic resistance of invasive pneumococcal disease isolates among children aged 5 years and under in Saudi Arabia (2000–2004). J Clin Microbiol Infect 2008;14(9):876-879.
97. Shibi A. Patterns of macrolide resistance determinants among S. pyogenes and S. pneumoniae isolates in Saudi Arabia. J Int Med Res 2005;33(3):349-355.
98. Asaad AM, Al Yousef S. Surveillance of antimicrobial resistance in a Military Hospital, Saudi Arabia using WHONET 5 program. Egyptian J Med Microbiol 2007;16(1):79-94.
99. Lee CY, Chiu CH, Huang YC, Chung PW, Su LH, Wu TL, et al. Invasive pneumococcal infections: a clinical and microbiological analysis of 53 patients in Taiwan. J Clin Microbiol Infect 2003;9(7):614-618.
100. Hsieh Y-C, Chang K-Y, Huang Y-C, Lin H-C, Ho Y-H, Huang L-M, et al. Clonal spread of highly β-lactam-resistant Streptococcus pneumoniae isolates in Taiwan. J Antimicrob Agents Chemother 2008;52(6):2266-2269.
101. Hsueh PR, Teng LJ, Lee LN, Yang PC, Ho SW, Luh KT. Extremely high incidence of macrolide and trimethoprim-sulfamethoxazole resistance among clinical isolates of Streptococcus pneumoniae in Taiwan. J Clin Microbiol 1999;37(4):897-901.
102. Lin WJ, Lo WT, Chou CY, Chen YY, Tsai SY, Chu ML, et al. Antimicrobial resistance patterns and serotype distribution of invasive Streptococcus pneumoniae isolates from children in Taiwan from 1999 to 2004. J Diagn Microbiol Infect Dis 2006;56(2):189-196.
103. Hsieh YC, Wang JT, Lee WS, Hsueh PR, Shao PL, Chang LY, et al. Serotype competence and penicillin resistance in Streptococcus pneumoniae in Taiwan. J Emerg Infect Dis 2006;12(11):1709-1714.
104. Chayakul P, Hortiwakul R. In vitro activities of penicillin G, cefotaxime, fosfomycin, fucidic acid and vancomycin against Streptococcus pneumoniae. J Infect Dis Antimicrob Agents 2004;21(2):41-46.
105. Dejsirilert S, Tienkrim S, Ubonyaem N, Sawanpanyalert P, Aswapokee N, Suankratay C. National antimicrobial resistance surveillance among clinical isolates of Streptococcus pneumoniae in Thailand. J Med Assoc Thailand 2009;92 Suppl 4:S193-33.
106. Song JH, Jung SI, Ko KS, Kim NY, Son JS, Chang HH, et al. High prevalence of antimicrobial resistance among clinical Streptococcus pneumoniae isolates in Asia (an ANSORP study). J Antimicrob Agents Chemother 2004;48(6):2101-2107.
107. Chup-Uppakarn S. Antimicrobial resistance of S.
pneumoniae and H. influenzae at Hat Yai Hospital. J Infect Dis Antimicrob Agents 1998;15:5-8.
108. Pruexprasert P, Tunyanapit W, Kaewjungwad L, Kaewpaiboon S. In vitro susceptibility of Streptococcus pneumoniae to penicillin and seven other antimicrobial agents: a study from Southern Thailand. J Infect Dis Antimicrob Agents 2001;18(3):108-111.
109. Srifeungfung S, Chokephaibulkit K, Tribuddharat C. Serotypes and antimicrobial susceptibilities of Streptococcus pneumoniae isolated from hospitalized patients in Thailand. Southeast Asian J Trop Med Public Health 2007;38(3):469-477.
110. Pinar A, Köseoğlu Ö, Yenişehirli G, Şener B. Molecular epidemiology of penicillin-resistant Streptococcus pneumoniae in a university hospital, Ankara, Turkey. J Clin Microbiol Infect 2004;10(8):718-723.
111. Yurdakul A, Çalışhr H, Atasever M, Orduš L, Öğretensoy M. Resistance to penicillin among the Streptococcus pneumoniae in Turkey. Eur Respir J 2001;18(2):436.
112. Çiftçi E, Doğru Ü, Aysev D, Ince E, Güriz H. Nasopharyngeal colonization with penicillin-resistant Streptococcus pneumoniae in Turkish children. J Pediatr Int 2000;42(5):552-556.
113. Bayraktar MR, Durmaz B, Kalcioglu MT, Durmaz R, Cizmeci Z, Aktas E. Nasopharyngeal carriage, antimicrobial susceptibility, serotype distribution and clonal relatedness of Streptococcus pneumoniae isolates in healthy children in Malatya, Turkey. J Antimicrob Agents 2005;26(3):241-246.
114. Percin D, Bozdoğan B, Ayangil D, Sümerkan B, Appelbaum PC. Molecular Epidemiology and antibacterial susceptibility of streptococci isolated from healthy children attending day care units. Balkan Med J 2011;28(4):414-419.
115. Latife İ. The characteristics of nasopharyngeal Streptococcus pneumoniae in children attending a daycare unit. J New Microbiol 2008;31:357-362.
116. Karakaş A, Öncü O, Acar A, Turhan V, Çavuşlu Ş, Görenek L. The effect of day care centres to nasopharyngeal Streptococcus pneumoniae colonization and penicillin resistance. Anatol J Clin Investig 2010;4(1): 11-14.
117. Percin D, Altintop YA, Sümerkan B. Ten-year surveillance of invasive Streptococcus pneumoniae isolates in central Turkey prior to the introduction of a conjugate vaccine. J Infect Dev Ctries 2010;4(09):560-565.
118. Şener B, Tunçkanat F, Ulusoy S, Tünger A, Soylerir G, Müalıźmoğlu L, et al. A survey of antibiotic resistance in Streptococcus pneumoniae and Haemophilus influenzae in Turkey, 2004–2005. J Antimicrob Chemother 2007;60(3):587-593.
119. Zarakolu P, Soylerir G, Gur D, Unal S. Antimicrobial resistance patterns of respiratory pathogens: a local report from Turkey. J Clin Microbiol Infect 2003;9(12):1257-1258.
120. Öncü S, Punar M, Eraksoy H. Comparative activities of β-lactam antibiotics and quinolones for invasive Streptococcus pneumoniae isolates. J Chemother 2004;50(2):98-100.
121. Memish ZA, Osoba AO, Shibli AM, Mokaddas E, Venkatesh S, Rotimi VO. Emergence and trends of penicillin non-susceptible Streptococcus pneumoniae in Saudi Arabia and Kuwait - perspective and outstanding issues. J Chemother 2007;19(5):471-481.
122. Felmingham D, Cantor R, Jenkins SG. Regional trends in beta-lactam, macrolide, fluoroquinolone and telithromycin resistance among Streptococcus pneumoniae isolates 2001-2004. J Infect 2007;55(2):111-118.
123. Byarugaba DK. A view on antimicrobial resistance in developing countries and responsible risk factors. Int J Antimicrob Agents 2004;24(2):105-110.
124. Lynch JP, 3rd, Zhanel GG. Streptococcus pneumoniae: does antimicrobial resistance matter? Semin Respir Crit Care Med 2009;30(2):210-238.
125. Ip M, Chau SS, Chi F, Cheuk ES, Ma H, Lai RW, et al. Longitudinally tracking fluoroquinolone resistance and its determinants in penicillin-susceptible and -nonsusceptible Streptococcus pneumoniae isolates in Hong Kong, 2000 to 2005. J Antimicrob Agents Chemother 2007;51(6):2192-2194.
126. Ip M, Lyon DJ, Yung RW, Chan C, Cheng AF. Evidence of clonal dissemination of multidrug-resistant Streptococcus pneumoniae in Hong Kong. J Clin Microbiol 1999;37(9):2834-2839.
127. Yuliarti K, Hadingoro SR, Supriyatno B, Karuniawati A. Invasive pneumococcal disease among hospitalized children aged 28 days to 60 months in Jakarta. Southeast Asian J Trop Med Public Health 2012;43(1):136-144.
128. Soewignjo S, Gessner BD, Sutanto A, Steinhoff M, Prijanto M, Nelson C, et al. Streptococcus pneumoniae nasopharyngeal carriage prevalence, serotype distribution, and resistance patterns among children on Lombok Island, Indonesia. J Clin Infect Dis 2001;32(7):1039-1043.
129. Jahanmehr S, Rajabi A, Radd MS, Nejad GB. The resistance of Streptococcus pneumoniae against penicillin and other antibiotics. J Acta Medica Iranica 2004;42(3):223-227.
130. Greenberg D, Dagan R, Muallem M, Porat N. Antibiotic-resistant invasive pediatric Streptococcus pneumoniae clones in Israel. J Clin Microbiol 2003;41(12):5541-5545.
131. Regev-Yochay G, Raz M, Dagan R, Porat N, Shainberg B, Pinco E, et al. Nasopharyngeal carriage of Streptococcus pneumoniae by adults and children in community and family settings. J Clin Infect Dis 2004;38(5):632-639.
132. Harimaya A, Yokota S-i, Sato K, Koizumi J-i, Yamazaki N, Himi T, et al. Alterations of pbp1a, pbp2b, and pbp2x in Streptococcus pneumoniae isolates from children with otolaryngological infectious disease in the Sapporo district of Japan. J Infect Chemother 2006;12(6):366-371.
133. Chong Y, Lee K, Park YJ, Jeon DS, Lee MH, Kim MY, et al. Korean nationwide surveillance of
antimicrobial resistance of bacteria in 1997. *Yonsei Med J* 1998;39(6):569-577.

134. Lee K, Lim CH, Cho JH, Lee WG, Uh Y, Kim HJ, et al. High prevalence of cefazidime-resistant Klebsiella pneumoniae and increase of imipenem-resistant Pseudomonas aeruginosa and Acinetobacter spp. in Korea: a KONSAR program in 2004. *Yonsei Med J* 2006;47(5):634-645.

135. Kim H-J, Lee NY, Kim S, Shin HJ, Kim M-N, Kim E-C, et al. Characteristics of microorganisms isolated from blood cultures at nine university hospitals in Korea during 2009. *Korean J Clin Microbiol* 2011;14(2):48-54.

136. Ahmed K, Wilson S, Jamal WY, Martinez G, Oishi K, Nagatake T, et al. Causative bacteria of respiratory tract infections in Kuwait by quantitative culture of sputum. *J Infect Chemother* 1999;5(4):217-219.

137. Dimitrov TS, Panigrahi D, Emara M, Al-Nakkas A, Awni F, Passadilla R. Incidence of bloodstream infections in a speciality hospital in Kuwait: 8-year experience. *J Med Princ Pract* 2005;14(6):417-421.

138. Al Sweih N, Mokkadas E, Jamal W, Phillips OA, Rotimi VO. In vitro activity of linezolid and other antibiotics against Gram-positive bacteria from the major teaching hospitals in Kuwait. *J Chemother* 2005;17(6):607-613.

139. Daoud Ghafray Z, Kourani M, Saab R, Nader MA, Hajjar M. Resistance of *Streptococcus pneumoniae* isolated from Lebanese patients between 2005 and 2009. *J Rev Exp de Quimioterapia* 2011;24(2):84-90.

140. Daoud Z, Coccozaki A, Hakime N. Antimicrobial susceptibility patterns of Haemophilus influenzae and *Streptococcus pneumoniae* isolates in a Beirut general university hospital between 2000 and 2004. *J Clin Microbiol Infect* 2006;12(1):86-90.

141. Uwaydah M, Mokhbat JE, Karam-Sarkis D, Baroud-Nassif R, Rohban T. Penicillin-resistant *Streptococcus pneumoniae* in Lebanon: the first nationwide study. *Int J Antimicrob Agents* 2006;27(3):242-246.

142. Rohani M, Parasakthi N, Raudzah A, Yasim M. In vitro susceptibilities of *Streptococcus pneumoniae* strains isolated in Malaysia to six antibiotics. *J Antimicrob Chemother* 1999;44(6):852-853.

143. Khanal B, Sharma S, Deb M, Bhattacharya S. Pneumococcal infections: Report of a hospital based study. *J Nepal Med Assoc* 2002;41:397-400.

144. Sihapat P, Tuladhar N, Marasini S, Khoju U, Thapa G. Bacterial conjunctivitis and use of antibiotics in Dhulikhel Hospital-Kathmandu University Hospital. *Kathmandu Univ Med J* 2012;9(2):69-72.

145. Joshi HH, Gertz RE, da Gloria Carvalho M, Beall BW. Use of silica desiccant packets for specimen storage and transport to evaluate pneumococcal nasopharyngeal carriage among Nepalese children. *J Clin Microbiol* 2008;46(9):3175-3176.

146. Rubab S, Awan H, Khan WA. Comparison of indigenous microbial flora of the eye to that found in conjunctival and corneal infections in a hospital based study. *Pak J Ophthalmol* 2006;22(2):97-107.

147. Sombrero L, Niissinen A, Esparar G, Lindgren M, Siira L, Virolainen A. Low incidence of antibiotic resistance among invasive and nasopharyngeal isolates of *Streptococcus pneumoniae* from children in rural Philippines between 1994 and 2000. *Eur J Clin Microbiol Infect Dis* 2008;27(10):929-935.

148. Soh SWL, Poh CL, Lin RTVP. Serotype distribution and antimicrobial resistance of *Streptococcus pneumoniae* isolates from pediatric patients in Singapore. *J Antimicrob Agents Chemother* 2000;44(8):2193-2196.

149. Chang SC, Hsieh WC, Liu CY. High prevalence of antibiotic resistance of common pathogenic bacteria in Taiwan. *J Diagn Microbiol Infect Dis* 2000;36(2):107-112.

150. Fung CP, Hu BS, Lee SC, Liu PY, Jang TN, Leu HS, et al. Antimicrobial resistance of *Streptococcus pneumoniae* isolated in Taiwan: an island-wide surveillance study between 1996 and 1997. *J Antimicrob Chemother* 2000;45(1):49-55.

151. Gür D, Ozalp M, Sümerkan B, Kaygusuz A, Töreci K, Kıksal If, et al. Prevalence of antimicrobial resistance in *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Moraxella catarrhalis* and *Streptococcus pyogenes*: results of a multicentre study in Turkey. *Int J Antimicrob Agents* 2002;19(3):207-211.

152. Esel D, Sümerkan B, Kocagöz S. Epidemiology of penicillin resistance in *Streptococcus pneumoniae* isolates in Kayseri, Turkey. *J Clin Microbiol Infect* 2001;7(10):548-552.

153. Bogaert D, Ha N, Sluiter M, Lemmens N, De Groot R, Hermans P. Molecular epidemiology of pneumococcal carriage among children with upper respiratory tract infections in Hanoi, Vietnam. *J Clin Microbiol* 2002;40(11):3903-3908.

154. Bogaert D, Ha N, Sluiter M, Lemmens N, De Groot R, Hermans P. Molecular epidemiology of pneumococcal carriage among children with upper respiratory tract infections in Hanoi, Vietnam. *J Clin Microbiol* 2002;40(11):3903-3908.

155. Watanabe K, Anh DD, Huong PLT, Nguyet NT, Anh NTH, Thi NT, et al. Drug-resistant pneumococci in children with acute lower respiratory infections in Vietnam. *J Pediatr Int* 2008;50(4):514-518.

156. Schulz C, Vien le M, Campbell JJ, Chau NV, Diep TS, Hoang NV, et al. Changes in the nasal carriage of drug-resistant *Streptococcus pneumoniae* in urban and rural Vietnamese schoolchildren. *J Trans R Soc Trop Med Hyg* 2007;101(5):484-492.