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Current epidemiology of pneumococcal resistance: is it worsening?

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Streptococcus pneumoniae is one of the most important pathogens causing various types of mucosal and invasive infections with significant mortality worldwide. Emergence and spread of antimicrobial resistance in *S. pneumoniae* has become a serious concern worldwide, particularly in Asian countries where antibiotics are widely abused or misused and pneumococcal conjugate vaccine (PCV) is not widely applied[1]. Pneumococcal resistance is influenced by several factors including the increased use of antimicrobial agents, dissemination of resistant clones, and introduction of PCV[2,3]. The introduction of 7-valent PCV (PCV7) comprising 7 serotypes, 4, 6B, 9V, 14, 18C, 19F, and 23F has contributed to a decrease in the prevalence rates of antimicrobial resistance in pneumococci as well as the incidence of invasive pneumococcal infections caused by vaccine serotypes[4]. However, emergence of non-vaccine serotypes, particularly serotype 19A, has been shown to be associated with increasing prevalence of antimicrobial resistance and has become a prominent problem worldwide[5].

High prevalence of macrolide resistance in pneumococci is an increasing concern in many parts of the world, particularly in Asian countries where resistance rate to macrolides in pneumococci was reported to be >70%[6]. According to the Asian Network for Surveillance of Resistant Pathogens (ANSORP) study, the overall rate of erythromycin resistance has significantly increased from 46.1% in 1996-1997 to 72.7% in 2008-2009 in Asian countries[6,7,8]. In addition, macrolide-resistant pneumococci carrying both *erm*B and *mef*A genes, which show resistance to multiple antimicrobials in addition to a high level of resistance to macrolides, have increased in many parts of the world including Asian countries[6,9]. Particularly, the prevalence of 19A pneumococcal isolates carrying both genes have also increased.

According to the revised Clinical and Laboratory Standards Institute (CLSI) breakpoints for penicillin in non-meningeal pneumococcal isolates, many studies have reported very low rate of non-susceptibility to penicillin among non-meningeal isolates[10]. However, increasing prevalence of pneumococcal isolates with high penicillin minimum inhibitory concentrations (MICs) has been noted in some countries, suggesting that changing trends in penicillin resistance should be continuously monitored.

Most pneumococcal isolates remain susceptible to fluoroquinolones in most countries despite wide use of fluoroquinolones for the treatment of respiratory tract infections. In Asia, the overall rates of non-susceptibility to fluoroquinolones have been persistently low (1.7% and 2.4% in 2000-2001 and 2008-2009, respectively)[6,8]. However, relatively high prevalence of fluoroquinolone resistance was found in some Asian countries such as Taiwan and Korea and some isolates showed high-level fluoroquinolone resistance (MIC ≥ 16 mg/L)[6], which suggests that given a frequent use of respiratory fluoroquinolones in the clinical practice, emergence of highly-resistant pneumococcal strains to fluoroquinolones can lead to treatment failure in pneumococcal infections in the future.

Multidrug resistance (MDR) in *S. pneumoniae* has increased worldwide[11]. In particular, the emergence and spread of multidrug-resistant *S. pneumoniae* clones of serotype 19A is an increasing concern. ANSORP study showed that 86.0% of serotype 19A isolates were resistant to macrolide and 79.8% showed MDR, suggesting that the increasing prevalence of serotype 19A would be one of the major reasons for the increasing prevalence of macrolide resistance and MDR in *S. pneumoniae*[6].

Introduction of PCV13, which contains 6 additional serotypes including serotype 19A, may contribute to reduce of antimicrobial resistance in pneumococci with non-vaccine serotypes, especially multidrug-resistant 19A *S. pneumoniae* strains. However, antimicrobial resistance in pneumococcal strains with other serotypes that are not covered by the PCV13 such as 6C, 11, 15A, 33A, or 35B can be emerged. Therefore, pneumococcal resistance should be continuously monitored. Also, given the impact of pneumococcal resistance, appropriate use of antibiotics and

wide application of pneumococcal vaccination would be important to reduce the burden of pneumococcal infections due to antimicrobial resistance.

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