Special Article

An Overview of Antimicrobial Susceptibility Patterns of Gram-Positive Bacteria from National Antimicrobial Resistance Surveillance Thailand (NARST) Program from 2000 to 2005

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In this overview, the authors summarize the antimicrobial susceptibility patterns of important Gram-positive bacteria from the National Antimicrobial Resistance Surveillance Thailand (NARST) program between 2000 and 2005 as well as the clinical implications. This collaborative network program was funded by the World Health Organization, and involved 33 hospitals throughout Thailand. There are rising trends of drug-resistant S. pneumoniae (DRSP), ampicillin-resistant enterococci, but a constant occurrence of methicillin-resistant S. aureus (MRSA) was noted during this period. The rates of penicillin and erythromycin resistances of S. pneumoniae were constantly high, ranging from 42.5% to 47.7% and 24.6% to 31.1%, respectively, whereas the rates of cefotaxime resistance were quite low, ranging from 2.1% to 8.4%. The rates of multidrug-resistant (MDR) S. pneumoniae ranged from 14.8% to 34.3%. Of all S. aureus isolates, MRSA comprised 24% to 27%, and vancomycin resistance rates of these MRSA isolates ranged from 0.1% to 0.8%. The antimicrobial resistance rates of methicillin-susceptible S. aureus isolates were very low. The rates of ampicillin and high-level gentamicin resistances of E. faecium from 2000 to 2005 have been significantly increasing from 52% to 84.1%, and from 46.9% to 75%, respectively, but vancomycin resistance was stable at the rates between 0.4% and 1.9%.

In conclusions, antimicrobial resistance rates of important Gram-positive bacteria have been increasing in Thailand. All local, national, and international surveillance data will help to set the strategic plan for control and treatment of these resistant organisms. Appropriate and accurate microbiological procedures regarding the collection and transportation of clinical specimens as well as the identification of these emerging resistant organisms are urgently needed, in collaboration with other concerned sectors.

Keywords: *Anti-infective agents, Drug resistance, Bacterial, Gram-positive bacteria, Microbial sensitivity tests, Population surveillance, Thailand*

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Bacteria are the most common causes of serious infections in human, both community-acquired and healthcare-associated infections. Although there are many available antibacterial agents as well as modern supportive measures for most bacterial infections, the morbidity and mortality from some infections are still high due to many contributing factors including clinical conditions and comorbidities of patients as well as the virulence and particularly antimicrobial resistance nature of the causative pathogen. National Antimicrobial Resistance Surveillance of Thailand (NARST) has been initiated since 1998 to strengthen the surveillance program for antimicrobial-resistant pathogens as well as to standardize the microbiology laboratory practices in Thailand. This collaborative network was initially funded by the World Health Organization (WHO) and involved 33 public and private hospitals at the first phase, and currently more than 60 hospitals throughout Thailand participated the network.

Although Gram-negative bacteria are probably the most prevalent bacterial pathogens in human worldwide as well as in Thailand, Gram-positive bacteria are also equally important. The important Gram-positive bacteria include staphylococci particularly *Staphylococcus aureus*, enterococci, *Streptococcus pyogenes*, and *Streptococcus pneumoniae*. Certain Gram-positive bacteria including staphylococci and enterococci can cause both community-acquired and healthcare-associated infections, but *S. pneumoniae* mostly causes community-acquired infections. To date, the emergence of muli-drug-resistant (MDR) Gram-positive bacteria has been reported worldwide. In Thailand, most of these Gram-positive infections are caused by methicillin-resistant *S. aureus* (MRSA), a pathogen causing healthcare-associated infections, and drug-resistant *S. pneumoniae* (DRSP), a pathogen causing community-acquired infections. In contrast, to the best of our knowledge, just only two outbreaks of infections and colonization caused by vancomycin-resistant enterococci (VRE) has recently been noted at Siriraj Hospital (unpublished data) and Rajvithi Hospital.

In this overview, the authors summarize an updated NARST data on antimicrobial susceptibility patterns of most important Gram-positive bacteria isolated from clinical specimens from 2000 to 2005 as well as the clinical implication[1-3]. *S. pneumoniae* contributes to the most important bacterial pathogen causing the respiratory tract infections, both in pediatric and adult patients. Amoxicillin is one of the most commonly prescribed antimicrobial agents for those infections in Thailand, followed by macrolides including erythromycin, roxithromycin, clarithromycin, and azithromycin. The data of NARST surveillance indicated that the rates of penicillin resistance of *S. pneumoniae w*ere constantly high ranging from 42.5% to 47.7% from 2000 to 2005, and these high rates were observed in almost all regions of Thailand especially the isolates from university hospitals and from young children. Most of these isolates were intermediately resistant to penicillin. In contrast to penicillin resistance, the rates of cefotaxime resistance were quite low, ranging from 2.1% to 8.4%. In addition, the resistance rates of erythromycin were relatively high, ranging from 24.6% to 31.1% especially isolates from university and private hospitals. Although most *S. pneumoniae* isolates were still susceptible to levofloxacin, the resistance rates have been increasing during the study period. The prevalence of MDR *S. pneumoniae* isolates were in the range from 14.8% to 34.3%, consistent with those described by the ANSORP study[4]. Based on these results, non-anti pseudomonal third-generation cephalosporin should be the antibiotic of choice for empirical treatment of serious infections caused by *S. pneumoniae*, especially meningitis.

Methicillin-susceptible *S. aureus* (MSSA) is one of the most common pathogens causing community-acquired infections, whereas MRSA contributes significantly to either healthcare-associated or hospital-acquired infections in Thailand. In contrast, MRSA is also associated with community-acquired infections in western countries. The data of NARST surveillance indicated that MRSA constantly contributed 24% to 27% of all *S. aureus* clinical isolates from most hospitals during the study period, except from certain university hospitals where the percentage ranging between 30% and 60%. The rates of antimicrobial resistance of MSSA isolates were very low; the resistance rates for erythromycin, clindamycin, vancomycin, and fosfomycin ranged from 3.2% to 14%, 1.1% to 8.4%, 0% to 3.3%, and 0% to 20%, respectively. Since there have never been reported since homogeneous vancomycin-intermediate as well as heterogeneous and homogeneous vancomycin-resistance have never been reported in Thailand, appropriate and accurate microbiological investigations are urgently needed to confirm the vancomycin resistance among these isolates. In contrast to MSSA isolates, MRSA isolates were highly resistant to most antimicrobials with the rates of erythromycin and clindamycin resistance ranging from 83.3% to 100%, and 37.4% to

68.9%, respectively. Therefore, these antimicrobials should not be prescribed for empirical treatment of MRSA infections in Thailand. Regarding vancomycin and teicoplanin resistance of MRSA, the rates were very low ranging from 0.1% to 0.8% and 0.8% to 3.2%, respectively. Among MRSA, only heterogeneous vancomycin-intermediate *S. aureus* strains have been isolated from various clinical specimens at Siriraj Hospital[5], Srinagarind Hospital[6], and King Chulalongkorn Memorial Hospital[7]. Appropriate and accurate microbiological investigations are also needed to confirm the vancomycin resistance among these isolates. The rates of fosfomycin resistance were widely variable among the hospitals ranging from 0% to 100%, probably due to overuse or misuse in certain hospitals. Therefore, vancomycin and teicoplanin are still the agents of choice for empirical treatment of MRSA infections in Thailand.

Enterococcus faecalis was the most common isolates (46.5%) among *Enterococcus* spp., followed by *E. faecium* (23%). The rates of ampicillin and high-level gentamicin-resistant *E. faecalis* were constantly high in the range between 30% and 35% from 2000 to 2005. The rates of vancomycin resistance were very low, ranging between 0.5% and 4%. In contrast, the rates of ampicillin resistance of *E. faecium* have significantly increased from 52% to 84.1%. The rates of high-level gentamicin resistance of *E. faecium* have also increased from 46.9% to 75%, but vancomycin resistance rates were constantly low between 0.4% and 1.9%. Enterococci susceptible to penicillin are predictably susceptible to ampicillin. In contrast, enterococci susceptible to ampicillin cannot be assumed to be susceptible to penicillin. Therefore, either ampicillin and penicillin disks or just penicillin disk should be used to determine the susceptibility by the disk diffusion method among enterococcal isolates. Based on these data, there is a difficulty in selection of antimicrobial agents in the treatment of serious enterococcal infections especially meningitis and endocarditis that require a combination between beta-lactam and aminoglycoside antimicrobials.

Conclusion

There have been increasing rates of antimicrobial resistance among most common Gram-positive bacteria including *S. pneumoniae*, *S. aureus*, and enterococci in Thailand. Therefore, appropriate use of antimicrobials and the effective infection control measures should be implemented to reduce these antimicrobial-resistant Gram-positive bacteria in Thailand.

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บทสรุปของแบบแผนการทดสอบความไวของยาต้านจุลชีพในแบคทีเรียแกรมบวกจากโปรแกรม National Antimicrobial ResistanceSurveillance Thailand (NARST) ในช่วงปี พ.ศ. 2543 ถึง 2548

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จากการศึกษาทั้งหมดนี้ เราสามารถสรุปแบบแผนการทดสอบความไวของยาต้านจุลชีพในแบคทีเรียแกรมบวกที่สำคัญจากโปรแกรม National Antimicrobial Resistance Surveillance Thailand (NARST) ระหว่างปี พ.ศ. 2543-2548 และผลกระทบทางคลินิก โดยโปรแกรมนี้ถูกสนับสนุนโดยองค์การอนามัยโลก และมี 33 โรงพยาบาลทั่วประเทศเข้าร่วม ผลการศึกษาพบมีแนวโน้มสูงขึ้นของความชุกในแต่ละปีของ drug-resistant S. pneumoniae และ enterococci ที่ดื้อ ampicillin แต่ความชุกของ S. aureus ที่ดื้อ methicillin มีอัตราคงที่ สำหรับ S. pneumoniae ที่ดื้อ penicillin และ erythromycin มีความชุกที่สูงคงที่ในช่วงร้อยละ 42.5-47.7 และร้อยละ 24.6-31.1 ตามลำดับ ในขณะที่อัตราการดื้อ cefotaxime ในระดับต่ำมากระหว่างร้อยละ 2.1-8.4 สำหรับ S. pneumoniae ที่ดื้อยาหลายชนิด (multidrug-resistant) มีความชุกระหว่างร้อยละ 14.8-34.3 กรณี S. aureus พบความชุกของ S. aureus ที่ดื้อ methicillin ระหว่างร้อยละ 24-27 ดื้อ vancomycin ระหว่างร้อยละ 0.1-0.8 และอัตราการดื้อยาใน S. aureus สายพันธุ์ที่ไวต่อ methicillin อยู่ในระดับต่ำ นอกจากนั้น E. faecium ที่ดื้อ ampicillin และ high-level gentamicin มีความชุกสูงขึ้นจากปี พ.ศ. 2543-2548 ในอัตราร้อยละ 52 เป็นร้อยละ 84.1 และจากร้อยละ 46.9 เป็นร้อยละ 75 ตามลำดับ แต่การดื้อ vancomycin อยู่ในอัตราคงที่ระหว่างร้อยละ 0.4-1.9

โดยสรุป อัตราการดื้อยาต้านจุลชีพในแบคทีเรียแกรมบวกที่สำคัญมีแนวโน้มสูงขึ้นในประเทศไทย ข้อมูลการเฝ้าระวังการดื้อยาต้านจุลชีพในระดับท้องถิ่น ชาติ และนานาชาตินี้ จะช่วยในการวางแผนสำหรับการควบคุมและการรักษาการติดเชื้อจากจุลชีพที่ดื้อยาเหล่านี้ กระบวนการทางจุลชีววิทยาที่ถูกต้องและเหมาะสมในการเก็บและการส่งสิ่งส่งตรวจทางคลินิก ตลอดจนการวินิจฉัยชนิดของจุลชีพดื้อยาเหล่านี้เป็นสิ่งที่จำเป็นอย่างเร่งด่วน โดยความร่วมมือกันของทุกฝ่ายที่เกี่ยวข้อง