Special Article

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

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The National Antimicrobial Resistance Surveillance Thailand (NARST) has been initiated since 1998 to strengthen the surveillance program for antimicrobial-resistant pathogens as well as to standardize the laboratory practices in Thailand. This collaborative network was funded by the World Health Organization, and involved 33 hospitals throughout Thailand at the first phase. Nevertheless, no prior effort has been made to share the antimicrobial resistance data in the national level. In this overview, the authors provide an update on the status of antimicrobial resistance from 2000 to 2005 among important Gram-negative pathogens as well as the implication of these findings. The most striking finding appears to be the emergence of pandrug-resistant (PDR) Acinetobacter baumannii. Carbapenem-resistant A. baumannii has been dramatically increasing from 2.1% in 2000 to 46.7% in 2005. There is a trend towards the increasing incidence rates of ESBL-producing Escherichia coli from 2000 to 2005, but the incidence rates of ESBL-producing Klebseilla pneumoniae remain constant during the same period. The susceptibility of Burkholderia pseudomallei to various antibiotics, particularly ceftazidime and carbapenems, approached 100%.

In conclusions, to help strengthen the future surveillance system, NARST needs to develop the data collection tools that include some important patient characteristics and the information that can help distinguish colonizations and infections as well as community-acquired infections and hospital-acquired infections. In addition, an appropriate test for antimicrobial susceptibility including the minimal inhibitory concentration determination should be implemented and carried out for all important pathogens. The NARST data emphasized a need to strengthen the antimicrobial stewardship as well as the infection control measures at the hospital level to help reduce the transmission of antimicrobial-resistant Gram-negative bacteria in Thailand.

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

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Antimicrobial resistance, particularly among healthcare-associated infections, has been a threat to the patient's safety in both developed and developing countries. The National Antimicrobial Resistance Surveillance, Thailand (NARST) has been initiated since 1998 to strengthen the surveillance program for antimicrobial resistant pathogens as well as to standardize the laboratory practices in Thailand. This collaborative network was funded by the World Health Organization (WHO), and involved 33 hospitals throughout Thailand at the first phase. Nevertheless, no prior effort has been made to share the antimicrobial resistance data in the national level. In this overview, we provide an update on the status of antimicrobial resistance from 2000 to 2005 among important Gram-negative pathogens as well as the implication of these findings.

The most striking finding from NARST surveillance appears to be the emergence of pandrug-resistant (PDR) *Acinetobacter baumannii*[1]. *A. baumannii* has now emerged to be nearly untreatable, given that carbapenem-resistant rate has been dramatically increasing from 2.1% in 2000 to 46.7% in 2005. It is also notable that cefoperazone/sulbactam resistance rate among *A. baumannii* has increased in parallel from approximately 3% to 12% during the same period[1]. There is also an increasing trend of both carbapenem- and cefoperazone/sulbactam-resistance from 2005 to 2008, when right now approximately three-thirds of lower respiratory tract isolates become resistant to carbapenem[2]. These findings raise concern and alarm all caring physicians to urgently develop the infection control interventions at the hospital level to help reduce the occurrence of PDR *A. baumannii*. Antimicrobial stewardship program appears crucial to help reduce the selective pressure of antimicrobial resistance among various Gram-negative bacteria, as described in the recent study from a tertiary care center in Thailand[3]. An effective infection control intervention to reduce the incidence of PDR *A. baumannii* has also recently been described at the same center including the use of active surveillance, hand hygiene campaign, enhanced isolation precautions, and environmental cleaning[4]. These collective efforts emphasize that an antimicrobial stewardship program and infection control interventions are feasible and possibly effective in resource-limited settings in Thailand.

Extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella pneumoniae* remained a significant problem in Thailand as shown by the NARST surveillance data[5]. Notably, there is a trend towards the increasing incidence rates of ESBL-producing *E. coli* from 2000 to 2005, but the incidence rates of ESBL-producing *K. pneumoniae* remain constant during the same period. This trend occurred along with the increasing reports of community-onset (CO) ESBL-producing *E. coli* in Thailand[6,7], suggesting that the NARST system needs to incorporate the data collection tool to help detect this problem in the future. Since infections caused by CO ESBL-producing organisms, particularly bloodstream infections, can have an impact on the treatment outcome of the patients, an appropriate empirical therapy should be warranted to reduce the morbidity and mortality[8]. A principle of de-escalation antimicrobial therapy is also warranted to help reduce the inappropriate use of carbapenems[9]. This educational program should rely on three treatment principles. First, the choice of empirical therapy should be based on the local prevalence, antimicrobial susceptibility patterns, and risks of infections with drug-resistant organisms in each setting. Second, the procurement of pretreatment culture specimens is essential for implementation and evaluation of de-escalation antimicrobial treatment strategies. Lastly, the duration of antimicrobial treatment in accompanying with adverse drug events should be incorporated in antimicrobial treatment strategies.

Despite an increasing resistance rate among *A. baumannii* and ESBL-producing organisms[1,5], there was no significant increase in the trend of antimicrobial resistance among *Pseudomonas aeruginosa*[10]. Notably, cefeporazone/sulbactam resistance rates were in the range between 10% and 15%, while carbapenem resistance rates remained constant from 12% to 16% from 2000 to 2005[10]. There was no increasing trend of carbapenem resistance from 2006 to 2008. In addition, piperacillin resistance rates were in the range between 15% and 25% during the same period. The data regarding the susceptibility of *P. aeruginosa* to both piperacillin/tazobactam and meropenem were not available in this study. Since piperacillin/tazobactam and carbapenem are antibiotics commonly prescribed for an empirical treatment of hospital-acquired infections in Thailand, caring physicians need to balance the risk of inappropriate antimicrobial therapy when selecting empirical regimen and the risk of development of antimicrobial-resistant organisms in each setting.

Burkholderia pseudomallei are regarded as endemic to Southeast Asia and Northern Australia. The susceptibility of *B. pseudomallei* to various antibiotics,

particularly ceftazidime and carbapenems, approached 100%[11]. This supports our national treatment guidelines that recommend ceftazidime with or without trimethoprim/sulfamethoxazole (TMP/SMX) as the first-line antibiotic for the treatment of melioidosis in Thailand. There are some limitations to determine the susceptibility of *B. pseudomallei* to most antimicrobials in this study. Since there are no current standards for antimicrobial susceptibility testing determined by the disk diffusion method on interpretation of the inhibition zone for *B. pseudomallei*, we have applied the interpretative criteria of *P. aeruginosa* in the present study. The antimicrobial susceptibility of *B. pseudomallei* to TMP/SMX carried out by the disk diffusion method is not a reliable method[11], and hence the susceptibility determined by the minimal inhibitory concentration (MIC) test must be incorporated in the future NARST program. In addition, the lack of clinical information makes it impossible for us to distinguish clinical infections from colonizations or to distinguish community-acquired infections from hospital-acquired infections.

This overview regarding the antimicrobial resistance patterns among Gram-negative bacteria in Thailand provides some insights for both NARST and caring physicians in clinical practice in Thailand. To help strengthen the future surveillance system, NARST needs to develop the data collection tools that include some important patient characteristics and the information that can help distinguish colonization and infections as well as community-acquired and hosital-acquired infections. Duplicate isolates from a single patient must be counted as a single isolate, and an appropriate test for antimicrobial susceptibility testing should be implemented and carried out for all important pathogens. The NARST data emphasized a need to strengthen the antimicrobial stewardship as well as the infection control measures at the hospital level to help reduce the transmission of antimicrobial-resistant Gram-negative bacteria in Thailand.

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บทสรุปของแบบแผนการทดสอบความไวของยาต้านจุลชีพในแบคทีเรียแกรมลบจากโปรแกรม National Antimicrobial Resistance Surveillance Thailand (NARST) ในช่วงปี พ.ศ. 2543 ถึง 2548

อนุชา อภิสารธนรักษ์, วันชัย บุพพันเหรัญ, สุรภี เทียนกริม, ปฐม สวรรค์ปัญญาเลิศ,นลินี อัศวโภคี

แม้นว่ากรมวิทยาศาสตร์การแพทย์ในประเทศไทยได้ทำการสืบเสาะเชื้อดื้อยามาตั้งแต่ปี พ.ศ. 2541 การเผยแพร่องค์ความรู้เกี่ยวกับเชื้อดื้อยาในภาพรวมของประเทศไทยยังมีอยู่จำกัด โดยภาพรวมแล้วเชื้อดื้อยากรัมลบหลายชนิดในประเทศไทย มีแนวโน้วที่จะเพิ่มมากขึ้นเมื่อเทียบกับประเทศสหรัฐอเมริกาหรือประเทศในแถบยุโรป ในบทความนี้เรานำเสนอภาพรวมของระบาดวิทยาของเชื้อดื้อยาประเภทกรัมลบในประเทศไทยที่มีความสำคัญ พร้อมทั้งข้อเสนอแนะในการทำการสืบเสาะแสวงหาเชื้อยาที่ควรทำสำหรับกรมวิทยาศาสตร์การแพทย์ในอนาคต รวมถึงการรักษาและการป้องกันเชื้อดื้อยาประเภทกรัมลบสำหรับแพทย์เวชปฏิบัติ