Application of antimicrobial stewardship and infection control program to control PDR-*A. baumannii* in resource-limited setting

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Multi-drug resistant (MDR) Gram-negative pathogens have become a threat to many countries in Western Pacific Region [1]. The ESKAPE pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species) are responsible for a substantial percentage of healthcare-associated infections and represent the vast majority of isolates with resistance to antimicrobial agents, thus creating serious therapeutic dilemmas for physicians [2]. These microorganisms are difficult to treat and pose challenges for prevention and control strategies, particularly in setting where resources are limited [3-4]. Much of the emergence and spread of MDR pathogens can be contributed to the non-judicious use of broad-spectrum antibiotics. From the institutional perspective, antimicrobials account for upwards of 30% of hospitals' pharmacy budgets [5]. It has been recognized for several decades that up to 50% of antimicrobial use is inappropriate, adding considerable cost to patient care. In addition to direct pharmacy acquisition costs, numerous reports suggest that inappropriate and unnecessary antimicrobial use leads to increased selection of resistant pathogens. Once antimicrobial resistance emerges, it can have a significant impact on patient morbidity and mortality, as well as increased health care costs [6].

Antimicrobial stewardship is a key component of a multifaceted approach to preventing the emergence of MDR pathogens. Good antimicrobial stewardship involves selecting an appropriate drug and optimizing its dose and duration to treat an infection while minimizing toxicity and conditions for selection of resistant bacterial strains [7]. Several strategies, including prescriber education, formulary restriction, prior approval, streamlining, antibiotic cycling, and computer-assisted programs have been proposed to improve antibiotic use in developed countries [7]. Although rigorous, clinical data in support of these strategies are lacking, the most effective means of improving antimicrobial stewardship will most likely

involve a comprehensive program that incorporates multiple strategies and collaboration among various specialties within a given healthcare institution. Often, multiple interventions have been bundled or made simultaneously, making it difficult to assess the benefit attributable to any one specific intervention. However, a comprehensive program that includes active monitoring of resistance, fostering of appropriate antimicrobial use, and collaboration with an effective infection control program to minimize secondary spread of resistance is considered to be optimal [6-7]. A comprehensive evidence-based stewardship program to combat antimicrobial resistance includes elements chosen from among the above mentioned strategies, which are based on local antimicrobial use and resistance problems, and on available resources that may differ depending on the size of the institution or clinical setting.

Application of antimicrobial stewardship to resource-limited setting can be challenging. The antimicrobial stewardship program at Thammasat University Hospital, which has been associated with appropriateness of antibiotic use and improved treatment rates, decreased failure rates, and reduced healthcare-related costs, is an example of this multifaceted, multidisciplinary approach [8]. The components of our antimicrobial stewardship program include continuous education, introduction of the antibiogram, antibiotic guideline, and antibiotic prescription forms with an antimicrobial stewardship team to continuously monitor the consumption of and audit the use of antibiotics with real-time, bed-side discussion with prescribing physicians. This antimicrobial stewardship program began in 2004 and appears to have been sustained over a 7-year period [8-9]. At this time, data from well-controlled studies examining the associations of antibacterial stewardship and the emergence of resistance in resource-limited are limited, but available data suggest that good antibiotic stewardship reduces rates of methicillin-resistant *Staphylococcus aureus*, resistant gram-negative bacilli including MDR-*Acinetobacter baumannii*, extended spectrum beta-lactamases producing *Escherichia coli* and *Klebsiella pneumoniae* [8]. Nevertheless, to sustain or even further improve these results, lasting and repeated efforts will be needed. Integrating infection control efforts into educational and antimicrobial stewardship programs is warranted [10]. Active infection control program in resource-limited settings for MDR-pathogens may include modified active surveillance, contact isolation, cohorting patients with MDR-pathogens, 5 moment hand hygiene, environmental cleaning, as well as monitoring healthcare workers and providing prompt feedback [11]. These strategies must be modified to fit the local setting, organizational culture, and infrastructure. Intensified efforts in infection control programs and

antibiotic stewardship serve as key components for long-term success [12]. Given the limited information of antimicrobial stewardship in resource-limited setting, additional well-designed studies are needed to explore various aspects of outcomes of antimicrobial stewardship in resource-limited settings.

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