Surveillance of Antimicrobial Resistance among Bacterial Pathogens Isolated from Hospitalized Patients at Chiang Mai University Hospital, 2006-2009

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ABSTRACT

Background: Conducting surveillance of multidrug-resistant organisms leads to identifying changes in the pathogens causing healthcare-associated infections (HAIs) of specific sites, and the antimicrobial susceptibility patterns. This surveillance study aimed to characterize the pattern of nosocomial multidrug-resistant pathogens.

Methods: Clinical laboratory reports from Chiang Mai University hospital were reviewed from 2006 to 2009.

Results: During the 4-year period, gram-negative bacteria were the majority of clinical isolates. A. baumannii was the most common pathogen isolated from sputum. E. coli was the most common pathogen isolated from blood and urine. Carbapenem resistance among A. baumannii isolates was 67.1%, 74.2%, 68.9%, and 74.2% in 2006, 2007, 2008, and 2009, respectively. Carbapenem resistance among P. aeruginosa was 35.0%, 33.8%, 27.0%, and 26.8% in 2006, 2007, 2008, and 2009, respectively. Extended-spectrum β-lactamase producing strains accounted for 35.2% and 49.2% among E. coli and K. pneumoniae, respectively in 2006 and 53.2% and 56.5% in 2009. Gram-positive bacteria accounted for 25% of all isolates for all 4 years. S. aureus and Enterococci were the most common gram-positive pathogens. Among S. aureus, 35% and 44% were methicillin-resistant strains in 2006 and 2009, respectively.

Conclusions: The surveillance data showed that gram-negative bacteria are the major problems in our hospital. Multidrug-resistant Acinetobacter baumannii is a particularly important problem. Continued surveillance is essential to monitor the trend of these multidrug-resistant bacteria. (J Infect Dis Antimicrob Agents 2011;28:35-44.)

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INTRODUCTION

Nosocomial infections caused by antimicrobial-resistant pathogens have an impact on clinical outcomes including morbidity, mortality, length of hospital stays and costs.¹ The Centers for Disease Control and Prevention (CDC) announced 4 strategies which include 12 steps to prevent antimicrobial resistance.² These strategies are as follows: prevent infection, diagnose and treat infection effectively, use antimicrobials wisely, and prevent transmission. Understanding antimicrobial susceptibility patterns at our own institution leads to appropriate empirical antimicrobial therapy.

Conducting surveillance for antimicrobial resistance among nosocomial pathogens has multiple purposes: to detect clustering in time and space of infections i.e. outbreaks, to convince clinicians and administrators that there is a potential problem (that may require additional resources), to guide treatment (e.g. the choice of antimicrobial agents) and/ or prevention strategies, to reduce the incidence of healthcare-associated infections (HAIs), and to make comparisons within and between hospitals or healthcare systems.³

There are networks and organizations conducting surveillance in many regions e.g. the National Health Safety Network (NHSN) in the United States,⁴ the International Nosocomial Infection Control Consortium (INICC) among limited resources countries,⁵ the Study for Monitoring Antimicrobial Resistance Trends (SMART) in Europe and Asia-Pacific,⁶⁷ and the National Antimicrobial Resistance Center, Thailand (NARST) in Thailand.⁸

We, therefore, conduct the surveillance of antimicrobial resistance among nosocomial pathogens at our hospital to identify changes in pathogens causing HAIs at specific sites, and the antimicrobial susceptibility patterns over time.

MATERIALS AND METHODS

We analyzed data reported from the central diagnostic laboratory (CDL), Chiang Mai University Hospital. Chiang Mai University Hospital is an 1,800-bed, teaching hospital in Northern Thailand which serves over 400,000 out-patients and over 50,000 in-patients each year. There are 7 intensive care units: medical (3), surgical (1), neurosurgical (1), cardiothoracic (1), pediatric (1); 7 intermediate care units: medical (3), surgical (3), pediatric (1), obstetrics and gynecology (1).

All clinical specimens either from infected or colonized hospitalized patients submitted to the CDL for bacterial cultures between January 1, 2006 and December 31, 2009 were included. The methods used for pathogen identification and antimicrobial susceptibility testing were those put out by the Clinical and Laboratory Standards Institute (CLSI).⁹ The susceptibility results were categorized into three groups: sensitive (S), intermediate resistant (I), and resistant (R). For fluoroquinolone susceptibility testing, CDL sometimes tested different antimicrobial agents within the class according to availability at the time of testing; resistance was defined using data from at least one of several agents within the class. We defined resistance to fluoroquinolone among Pseudomonas aeruginosa and Escherichia coli as resistant to either ciprofloxacin, levofloxacin, or ofloxacin.

Statistical analysis

Data were presented in number (%). All statistical analyses were performed using Stata statistical software version 10.0 (Stata Statistical Software: Release 10.0, Stata Corporation, College Station, TX, 2007).

RESULTS

Distribution of clinical specimens

There were 13,654, 14,314, 14,976, and 16,970
clinical specimens submitted to CDL for bacterial cultures during the 4-year period. The majority of specimens were sputum or respiratory specimens including bronchoalveolar lavage (BAL) (31.6%), followed by urine (29.3%), pus (22.8%), blood (7.8%), and cerebrospinal fluid (0.7%).

Majority of clinical specimens were sent from medical units (39.7%) and surgical units (27.4%). (Table 1)

Pathogen distribution

Gram-negative bacilli were the majority pathogens isolated from clinical specimens (75%). The three most common pathogens were E. coli, P. aeruginosa, and Acinetobacter baumannii. The most common pathogen isolated from sputum, urine, pus, and blood were A. baumannii, E. coli, Staphylococcus aureus, and E. coli, respectively. (Figure 1)

The distribution of pathogens from particular units is shown in Table 1.

Antimicrobial Resistance

Ceftazidime-resistant P. aeruginosa was found in 41.8%, 36.0%, 33.3%, and 34.9% in 2006, 2007, 2008, and 2009, respectively (Figure 2). Carbapenem-resistant A. baumannii was found in 67.1%, 74.2%, 68.9%, and 74.3% in 2006, 2007, 2008, and 2009, respectively (Figure 2). Among carbapenem-resistant A. baumannii, the isolates were susceptible to cefoperazone/sulbactam in 66.0% and 93.4% in 2006 and 2007, and then declined to 37.4% and 20.5% in 2008 and 2009 (Figure 3). Extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae was more prevalent in E. coli than in K. pneumoniae (Figure 4). Carbapenem-resistant E. coli was found in 0.1, 0.7, 0.5, and 0% in 2006, 2007, 2008, and 2009, respectively. Carbapenem-resistant K. pneumoniae was found in 2.3%, 2.0%, 0.7%, and 0.9% in 2006, 2007, 2008, and 2009, respectively.

Methicillin-resistant Staphylococcus aureus was found in 34.8%, 34.8%, 39.5%, and 44.3% in 2006,
Figure 1. Percentages of most common pathogens isolated from sputum (a), urine (b), and blood (c).
2007, 2008, and 2009, respectively. Vancomycin-resistant enterococci were isolated in 1, 2, and 5 clinical specimens in 2006, 2007, and 2009, respectively.

Clinical isolates from the intensive care units (ICUs) and intermediate care units had higher rates of resistance to various antimicrobial agents than clinical isolates from general units (Table 2). Among medical units, susceptibility to various antimicrobial agents for *A. baumannii* and *P. aeruginosa* differed by units and years as shown in Figure 5.

**DISCUSSION**

These surveillance data revealed that the most common pathogen from respiratory specimens were *A. baumannii*. This finding corresponded to the national report from the NARST.\(^8\) Approximately 67-75% of *A. baumannii* isolates were resistant to carbapenems, which is a broad-spectrum antibiotic covering most of gram-negative and gram-positive bacteria, including anaerobes. This rate was much higher than that reported to the NHSN, the Centers for Disease Control and Prevention, which was 29.2-36.8%.\(^9\) Sulbactam has an intrinsic activity against *A. baumannii*.\(^10\) However, we do not have sulbactam alone, but in combination with cefoperazone or ampicillin. Cefoperazone/sulbactam had less activity
against *A. baumannii* in the recent years as shown in Figure 2. Carbapenem-resistant *A. baumannii* were susceptible to cefoperazone/sulbactam in only 20% in the year 2009. Susceptibility to colistin was preserved in almost 100% for *A. baumannii*. While waiting for respiratory culture results of hospitalized patients who developed lower respiratory infections in our hospital and whose Gram stain showed gram-negative coccobacilli, coverage of *A. baumannii* is needed.

*P. aeruginosa* was the second most common pathogen isolated from respiratory specimens. Antimicrobial susceptibility for *P. aeruginosa* was not as bad as *A. baumannii*.

Carbapenem-resistant was found in around 30% of clinical isolates, which was higher than the national report of 10%, and was similar to the NHSN and the International Nosocomial Infection Control Consortium (INICC) report. However, the activity of ceftazidime, which had an excellent activity against *P. aeruginosa* in the past, was diminished. Piperacillin/tazobactam remained to have good activity against *P. aeruginosa*.

*E. coli* was the most common pathogen isolated from urine. Over half of them were ESBL-producing
surviving isolates of carbapenem-resistant *E. coli*. Fortunately, we had only sporadic isolates of carbapenem-resistant *E. coli*. However, CDL could not perform tests to identify whether these isolates expressed carbapenemase enzyme.

*E. coli* was also the most common pathogens isolated from blood. This is different from the national report where coagulase-negative staphylococci were the most common pathogens isolated from blood.\(^8\) The surveillance data from the NHSN also reviewed that coagulase-negative staphylococci was the most common pathogen responsible for central-line associated bloodstream infection (CLABSI).\(^10\) Due to the fact that these were surveillance data, we did not explore whether they were primary or secondary bloodstream infections, and whether or not they were catheter-related bloodstream infection.

Gram-positive bacteria were not a major problem in our hospital. However, over 30% of *S. aureus* isolates were methicillin-resistant. This rate is slightly higher than the national report which was 23-28% between the years 2006-2008.\(^8\) However, this rate is much lower than that reported from the

Table 2. Percentages of antimicrobial susceptibility by departments.

<table>
<thead>
<tr>
<th>Pathogens</th>
<th>CTZ</th>
<th>SUL</th>
<th>TZ</th>
<th>IMP</th>
<th>MER</th>
<th>AMK</th>
<th>CPO</th>
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<td>27</td>
<td>28</td>
<td>28</td>
<td>22</td>
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*Total isolates from all departments; ICU, intensive care units; CTZ, ceftazidime, SUL, cefoperazone/sulbactam, TZ, piperacillin/tazobactam, IMP, imipenem; MER, meropenem; AMK, amikacin; CPO, ciprofloxacin; CO, colistin
Figure 5. Percentages of various antimicrobial susceptibility for *A. baumannii* (1a-3a), and *P. aeruginosa* (1b-3b) in the Department of Medicine, (a) represent general units, (b) represent intensive care units, (c) represent intermediate-care units. CTZ, ceftazidime; SUL, cefoperazone/sulbactam; TZ, piperacillin/tazobactam; IMP, imipenem; MER, meropenem; AMK, amikacin.
INICC, which was as high as 80%\textsuperscript{12}. Vancomycin-resistant \textit{S. aureus} has never been reported in our hospital. Vancomycin-resistant enterococci (VRE) were reported in sporadic cases, although the number of isolates increased over 4 years. VRE were much more common in the USA\textsuperscript{10}.

Clinical isolates from the medical and surgical units appeared to be the main source of Gram-negative bacilli. This might be explained by the large number of patients admitted to these units and the fact that these patients were more likely to be in severe conditions than patients admitted to other units. Clinical isolates from the ICUs and intermediate care units were more resistant to various antimicrobial agents than isolates from the general units in both medical and surgical units. This may reflect the selective pressure from higher rate of antimicrobial prescription in these units.\textsuperscript{13}

Knowing the susceptibility patterns for particular units where patients are hospitalized e.g. ICUs, intermediate care units, or general units is helpful in antimicrobial selection for empirical therapy while waiting for the culture results.

The differences in multidrug-resistant pathogens among various reports depends on the study population, the data source reviewed, the study methods, and patterns of antimicrobial use in each setting. These surveillance data identified changes in the pathogens causing HAIs of specific sites, and the antimicrobial susceptibility patterns over time. These data need to be reported to healthcare personnel and also the hospital administrators to convince them to support the strategies to decrease the occurrence and to prevent the transmission of these multidrug-resistant bacteria. This is the first step for a further management plan including 1) to establish the infection prevention and control measures for multidrug-resistant bacteria, 2) to develop antimicrobial treatment guideline for specific units, 3) to implement intervention to reduce the incidence of HAIs, and 4) to conduct research to fulfill the knowledge gap that may arise.

This study does have some limitations. Firstly, these surveillance data were retrieved from the CDL with no clinical information incorporated. Therefore, we did not differentiate between infected and colonized patients. However, this study was focused on the trend of antimicrobial resistance among clinical isolates in the same fashion as NARST, which also do not differentiate between infected and colonized patients. Secondly, some specimens sent from hospitalized patients might represent community-acquired pathogens. However, majority of the pathogens i.e. \textit{P. aeruginosa}, \textit{A. baumannii}, ESBL-producing enterobacteriaceae are more likely to represent nosocomial pathogens.

**CONCLUSIONS**

The surveillance data showed that gram-negative bacteria are the major problems in our hospital. Multidrug-resistant \textit{A. baumannii} is an important problem. Carbapenem-resistant Enterobacteriaceae and vancomycin-resistant enterococci were reported sporadically. Continued surveillance is essential to monitor the trend of these multidrug-resistant bacteria, and guide physicians to appropriately prescribe empirical therapy.

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**References**


