Hospital-Acquired Pneumonia and Ventilator-Associated Pneumonia in Adults at Siriraj Hospital: Etiology, Clinical Outcomes, and Impact of Antimicrobial Resistance

Peerawong Werarak MD*, Pattarachai Kiratisin MD*,
Visanu Thamlikitkul MD*

** Division of Infectious Disease, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*

Background*: Nosocomial pneumonia (NP), hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP), is an important cause of morbidity and mortality in hospitalized patients. One of the factors contributing to a high mortality rate of HAP and VAP could be antibiotic resistance among the causative agents.*

Objective*: To determine prevalence of bacterial pathogens clinical features, risk factors of HAP and VAP, antimicrobial resistance among major respiratory pathogens, clinical implication of antimicrobial resistance, antimicrobial regimens used, and treatment outcomes of adult patients with HAP and VAP at Siriraj Hospital.*

Material and Method: *This was a prospective, hospital-based, active surveillance study on HAP and VAP in hospitalized adults at Siriraj Hospital from December 2007 to March 2009. The patients with HAP and VAP were followed prospectively until they expired or were discharged from the hospital.*

Results: *One hundred and forty-six adult patients were included. Seventy percent of the patients were males with the mean age of 70.8 years. HAP was accounted for 24.7% and VAP 75.3%. Most of the patients (82.9%) had late-onset HAP or VAP with the median day of onset of pneumonia of 11 days. Two third of the patients were hospitalized in general medical wards. Bronchopneumonia was observed in 53.4% and multilobar pneumonia in 24.7%. A. baumanni was the most common isolated pathogen and 92.3% of them were multidrug-resistant (MDR) or pandrug-resistant (PDR). The other common isolated pathogens were K. pneumoniae, P. aeruginosa and methicillin-resistant S. aureus (MRSA). Carbapenem was the most commonly used initial antibiotic (45.9%) followed by colistin (21.9%) and cephalosporins (21.1%). The concordance of initial antibiotics was 58.9%. Antibiotics were modified 43.8% of the patients. Colistin was the most commonly used modified antibiotic followed by carbapenem. The modified antibiotics were concordant with isolated bacteria in 98.4%. The patients received mechanical ventilators in 81.5% with the median ventilator day of 10 days. At the initial response (72 hours after antibiotic therapy), an improvement was 56.8% and a mortality rate due to pneumonia was 14.4%. Death due to pneumonia at the end of treatment was 42.5%. The 30-day mortality from pneumonia was 45.9%. There were no significant differences in the outcomes of pneumonia between HAP and VAP. The factors associated with PDR-organisms were late-onset hospital-acquired pneumonia and previous carbapenem usage within 72 hours. Septic shock and bilateral lung involvement were significantly associated with unfavorable outcomes at 72 hours. Septic shock, severe sepsis, and previous carbapenem usage within 72 hours were significantly associated with mortality at the end of treatment and at 30 days after developing pneumonia.*

Conclusion: *HAP and VAP remain to be very important hospital-acquired infections at Siriraj Hospital. The isolated pathogens are usually multidrug-resistant and the mortality rate remains high. The local data on prevalence of the isolated pathogens and their antibiotic susceptibility may help clinicians choose more appropriate initial antibiotics in order to improve the outcome and to decrease the emergence of resistant organisms.*

Keywords: *Nosocomial pneumonia, Hospital-acquired Pneumonia, Ventilator-associated Pneumonia*

J Med Assoc Thai 2010; 93 (Suppl. 1): S126-138
Full text. e-Journal: *http://www.mat.or.th/journal*

Correspondence to: Thamlikitkul V, Division of Infectious Disease, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand. E-mail sivth@mahidol.ac.th

Nosocomial pneumonia (NP), hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP), is an important cause of morbidity and mortality in hospitalized patients despite advances in antimicrobial therapy and better supportive care modalities[1,2]. The common pathogens causing NP include aerobic gram-negative bacilli, such as *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Acinetobacter* species[3,4]. NP due to *Staphylococcus aureus*, particularly methicillin-resistant *S. aureus* (MRSA), has been rapidly emerging. Inappropriate antimicrobial therapy of NP, particularly in the ICU setting, is increasingly being recognized as a potential cause of morbidity and mortality. Treatment of NP is usually supportive, along with the administration of antibiotics. Various antimicrobial options used for treatment of NP included not only classical regimens such as cephalosporins, aminoglycosides, or fluoroquinolones but also some newer broad-spectrum antibiotics such as piperacillin/tazobactam, carbapenems, linezolid or ceftobiprole[1,5,6]. The selection of antimicrobial agents active against the microorganisms associated with NP seemed to be an important determinant of hospital mortality[7-9]. Appropriate antimicrobial therapy, when initiated early, was shown to reduce mortality among critically-ill patients with NP[7,8,10,11]. The common pathogens associated with administration of inappropriate antimicrobial treatment to patients with NP were *P. aeruginosa*, *S. aureus*, and *Acinetobacter species*[7,8]. Most episodes of inappropriate antimicrobial treatment were attributed to potentially antibiotic-resistant gram-negative bacteria, including *P. aeruginosa*, *Acinetobacter* species, *Klebsiella pneumoniae*, and *Enterobacter* species as well as MRSA[7,8,12].

The recent document, prepared by a joint committee of the American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA), focused on the epidemiology and pathogenesis of bacterial pneumonia in adults and emphasized modifiable risk factors for infection[5]. In addition, the microbiology of HAP/VAP was reviewed, with an emphasis on multidrug-resistant (MDR) bacterial pathogens, such as *P. aeruginosa*, *Acinetobacter* species, and MRSA. While many clinicians follow the general recommendations of the ATS/IDSA guidelines, others follow institutional recommendations, or national guidelines, where available. The frequency of specific pathogens causing HAP/VAP may vary by hospital, region, patient population, exposure to antibiotics, and changes over time, emphasizing the need for timely, local surveillance data. Therefore, a local data study of etiology and outcomes of HAP/VAP are required for setting more appropriate guidelines for management of NP in the future. To clarify the therapeutic efficacy of these older and newer therapeutic options, etiologic distribution, antimicrobial resistance of major pathogens and clinical outcomes of HAP and VAP should be investigated. The objectives of the study were to determine prevalence of bacterial pathogens of HAP and VAP, clinical features, risk factors of HAP and VAP, antimicrobial resistance among major respiratory pathogens, clinical implication of antimicrobial resistance, antimicrobial regimens used, and treatment outcomes of adult patients with HAP and VAP at Siriraj Hospital.

Material and Method

This was a prospective, hospital-based, active surveillance study on NP in hospitalized adults at Siriraj Hospital from December 2007 to March 2009. The study protocol was approved by Siriraj Ethics Committee on Human Research.

The subject was included if he/she had all of the following criteria; 1) age $\geq$ 18 years, 2) had infection that was developed at $\geq$ 48 hours after admission and was not incubating at the time of admission, 3) two or more serial chest radiographs with at least one of the following features-new or progressive and persistent infiltrate, consolidation, cavitation, 4) at least one of the following features: temperature > 38°C with no other recognized cause, leukocytosis ($\geq$ 12,000 WBC mm^3) or leukopenia (< 4,000 WBC/mm^3), altered mental status with no other recognized cause for adults aged $\geq$ 70 years, 5) at least two of the following features: new onset of purulent sputum, or change in character of sputum, or increased respiratory secretions, or increased suctioning requirements, new onset or worsening cough, or dyspnea, or tachypnea, rales or bronchial breath sounds, worsening gas exchange (*e.g.* oxygen desaturation [$PaO_2/FiO_2 \leq 240$], increased oxygen requirements, or increased ventilation demand).

A patient with any one of the following criteria was excluded: 1) immunocompromised patient (absolute neutrophil < 500/mm^3, leukemia, lymphoma, known HIV infection with CD4 count < 200, splenectomy, one who is in his/her transplant hospital stay, cytotoxic chemotherapy, high dose steroids daily for > 2 weeks, daily use of immunosuppressive agent for > 2 weeks); 2) patient on clinical trial which does not allow the relevant data to be used, 3) infection caused by confirmed non-bacterial pathogens such as fungus and virus.

The eligible patients were followed until they were discharged from the hospital or they expired. The data collected included age, gender, underlying illnesses, clinical features, severity of illness, type of isolated bacteria, antibiotic susceptibility profiles of the isolated bacteria, antimicrobial regimen, clinical courses and outcomes of therapy. Assessment of clinical response was performed at 72 hours after initial antibiotic treatment, at the end of treatment (EOT), and at 7-14 days (test-of-cure, TOC) after the end of treatment. Microbiological outcome was assessed at the end of treatment. Overall 30-day mortality and infection (pneumonia)-related mortality were also determined. The data were collected and enter into the case report forms and they were analyzed by descriptive statistics, Chi-square statistics, Fisher-Exact test, student t test, Mann-Whitney U test and logistic regression analysis where appropriate. A p-value of ≤ 0.05 was considered statistically significant difference.

Definitions

Hospital-acquired pneumonia (HAP) is defined as pneumonia that occurs $\geq$ 48 hours after admission to the hospital in non-ventilated patients. Ventilator-associated pneumonia (VAP) is defined as pneumonia that arises $\geq$ 48 hours after mechanical ventilation. Early onset of HAP/VAP is defined as HAP/VAP that occurs within 4 days of hospitalization or tracheal intubation. The severity of primary diseases of the patients was classified as rapidly fatal (fulminant, irreversible disease with death expected within the next several weeks despite optimum therapy), ultimately fatal (irreversible disease with death expected within the next 4 years despite optimum therapy), and non-fatal (chronic or acute reversible disease with death not expected within the next 4 years). Septic shock is defined as sepsis associated with evidence of organ hypoperfusion and a systolic blood pressure < 90 or > 30 mm Hg less than the baseline or a requirement for the use of vasopressor to maintain the blood pressure. Etiologic bacteria of HAP/VAP were determined according to the results of microbiological evaluation performed before initiation of antibiotic therapy. The pathogens were classified as follows: 1) definite pathogen-presence of bacteria isolated from blood culture matching with that from culture of the lower respiratory tract specimens or presence of bacteria isolated from pleural fluid culture, 2) probable pathogen-presence of bacteria isolated from the culture of blind bronchial/tracheal aspirates with $\geq 10^5$ CFU/ml in a quantitative culture or presence of bacteria isolated from the culture of bronchoscopic BAL with $\geq 10^4$ CFU/ml in a quantitative culture or presence of bacteria isolated from blood that mismatched with that of respiratory tract specimens, 3) possible pathogen-presence of bacteria isolated from the lower respiratory tract specimens meeting the criteria for adequate sputum specimen *i.e.* WBC $\geq$ 25/LPF and epithelial cell < 10/LPF. The resistance to antibiotics is classified as multi-drug resistance (MDR) and pan-drug resistance (PDR). MDR is defined as resistance to at least 3 classes of anti-pseudomonas antibiotics and PDR is defined as resistance to all classes of anti-pseudomonas antibiotics except polymyxins. The antimicrobial therapies are classified into empirical and definitive, the former being defined as the initial therapy before the culture results are available, and the latter as therapy after the result of antibiotic susceptibility tests are available. The antimicrobial therapy is considered 'concordant' if no isolated bacteria are resistant to the empirical antibiotics used in the case.

Results

Characteristics of patients

There were 146 patients included in the study. The characteristics of the patients are shown in Table 1. Seventy percent of the patients were males with a mean age of all patients of 70.8 years. One hundred and ten patients (75.3%) had VAP and thirty six (24.7%) had HAP. Most of the patients (82.9%) had late-onset pneumonia with a median day of onset after admission of 11 days. The median day of VAP onset after mechanical ventilation was 9 days. The major diagnoses of the patients on admission included neurological disorders (26%), respiratory disorders (24.7%), cardiovascular diseases (13.7%), and sepsis (11.6%). Most of the patients were hospitalized at general medical wards (67.1%) and intensive care units, ICUs (17.2%). The common co-morbid conditions included proton-pump inhibitor usage (61%), diabetes mellitus (16.4%), hemiplegia or quadriplegia (33.6%), and cerebrovascular diseases (30.8%). The severity of primary diagnoses of the patients was ultimately fatal in 45.9%, rapidly fatal in 42.5% and non-fatal in 11.6%. Many patients received endotracheal intubation or tracheostomy (75.3%), nasogastric intubation (69.9%) and urinary catheterization (69.2%). The significant differences in the characteristics of the patients between the HAP group and VAP group were that the VAP patients had more severe underlying diseases and received endotracheal intubation or tracheostomy, nasogastric intubation and urinary catheterization more often than the HAP patients, and were less likely to be hospitalized in

Table 1. Characteristics of patients with HAP and VAP

	Total (n = 146)	HAP (n = 36)	VAP (n = 110)	p-value
Gender Male	103 (70.5%)	24 (66.7%)	79 (71.8%)	0.71
Female	43 (29.5%)	12 (33.3%)	31 (28.2%)	
Mean age, years (SD)	70.8 (15.6)	72.5 (13.1)	70.3 (16.3)	0.45
Onset of pneumonia				
Early-onset	25 (17.1%)	6 (16.7%)	19 (17.3%)	1.00
Late-onset	121 (82.9%)	30 (83.3%)	91 (82.7%)	
Median day of pneumonia onset after admission (range)	11 (2-176)	13.5 (2-131)	10 (2-176)	0.61
Median day of VAP onset after mechanical ventilation (range)		-	9 (2-171)	
Diagnosis on admission				
Neurological disorders	38 (26.0%)	8 (22.2%)	30 (27.3%)	0.7
Respiratory disorders	36 (24.7%)	7 (19.4%)	29 (26.4%)	0.54
Cardiovascular diseases	20 (13.7%)	9 (25%)	11 (10%)	0.05
Sepsis	17 (11.6%)	3 (8.3%)	14 (12.7%)	0.57
Gastrointestinal disorders	12 (8.2%)	4 (11.1%)	8 (7.3%)	0.49
Trauma	10 (6.8%)	1 (2.8%)	9 (8.2%)	0.45
Solid tumor	7 (4.8%)	2 (5.6%)	5 (4.5%)	1
Malignancy	4 (2.7%)	0	4 (3.6%)	
Other conditions	2 (1.4%)	2 (5.6%)	0	
Location of the patient at diagnosis of pneumonia				
General medical ward	98 (67.1%)	23 (63.9%)	75 (68.2%)	0.79
Surgical ICU	16 (11.0%)	2 (5.6%)	14 (12.7%)	0.36
General surgical ward	14 (9.6%)	7 (19.4%)	7 (6.4%)	0.04
Medical ICU	9 (6.2%)	0	9 (8.2%)	
Emergency room	5 (3.4%)	2 (5.6%)	3 (2.7%)	
Others	4 (2.7%)	2 (5.6%)	2 (1.8%)	
Co-morbid condition				
Use of proton-pump inhibitor	89 (61.0%)	24 (66.7%)	65 (59.1%)	0.54
Chronic renal failure	50 (34.2%)	10 (27.8%)	40 (36.4%)	0.46
Hemiplegia/quadriplegia	49 (33.6%)	10 (27.8%)	39 (35.5%)	0.52
Cerebrovascular disease	45(30.8%)	8 (22.2%)	37 (33.6%)	0.28
Diabetes mellitus	24 (16.4%)	7 (19.4%)	17 (15.5%)	0.76
Enteral feeding	24 (16.4%)	3 (8.3%)	21 (19.1%)	0.21
Chronic lung disease	17 (11.6%)	2 (5.6%)	15 (13.6%)	0.24
Non-abdominal postoperative surgery	16 (10.9%)	4 (11.1%)	12 (10.9%)	1.00
Solid tumors other than lung	15 (10.3%)	5 (13.9%)	10 (9.1%)	0.53
Congestive heart failure	10 (6.8%)	3 (8.3%)	7 (6.4%)	0.98
Liver cirrhosis	7 (4.8%)	2 (5.6%)	5 (4.5%)	1.00
Dementia	5 (3.4%)	0	5 (4.5%)	0.33
Acute renal failure	5 (3.4%)	0	5 (4.5%)	0.33
Hemodialysis	4 (2.7%)	0	4 (3.6%)	0.57
Metastatic tumor with lung involvement	4 (2.7%)	1 (2.8%)	3 (2.7%)	1.00
Post-abdominal surgery	4 (2.7%)	0	4 (3.6%)	0.57
Heavy alcohol drinking	3 (2.1%)	3 (8.3%)	0	0.01
Peritoneal dialysis	2 (1.4%)	1 (2.8%)	1 (0.9%)	0.43
Lung cancer	2 (1.4%)	1 (2.8%)	1 (0.9%)	0.43
Acute myocardial infarction	1 (0.7%)	0	1 (0.9%)	1.00
Heavy Smoking	1 (0.7%)	0	1 (0.9%)	1.00
Adrenal insufficiency	1 (0.7%)	0	1 (0.9%)	1.00
Severity of primary diagnosis				
Ultimately fatal	67 (45.9%)	21 (58.3%)	46 (41.8%)	<0.01
Rapidly fatal	62 (42.5%)	7 (19.4%)	55 (50%)	
Non-fatal	17 (11.6%)	8 (22.2%)	9 (8.2%)	
Presence of indwelling devices				
Nasogastric tube	102 (69.7%)	15 (41.7%)	87 (79.1%)	<0.01
Urinary catheter	101 (69.2%)	13 (36.1%)	88 (80%)	<0.01
Endotracheal tube	78 (53.4%)	0	78 (70.9%)	<0.01
Tracheostomy	32 (21.9%)	1 (2.8%)	31 (28.2%)	<0.01
Central venous catheter	10 (6.8%)	1 (2.8%)	9 (8.2%)	0.45
Others	6 (4.1%)	1 (2.8%)	5 (4.5%)	1.00
Prior admission within last 90 days	24	8 (22.2%)	16 (14.5%)	0.41
Previous mechanical ventilation within 90 days	10	2 (5.6%)	8 (7.3%)	1.00

the general surgical wards than the HAP patients.

Clinical manifestations and Laboratory Findings

The clinical manifestations and laboratory findings of the patients are shown in Table 2. Most of the patients had fever, tachypnea, tachycardia, leukocytosis, anemia, elevated BUN and liver enzymes and hypoalbuminemia. Hypoxemia was observed in 20% of the patients at diagnosis of pneumonia. All patients had sepsis syndrome from pneumonia with septic shock in 7.5% of them. The radiological findings on chest X-rays were unilateral lesions (76.7%), bronchopneumonia (53.4%) and pleural effusion (15.1%). The significant difference in the clinical manifestations of the patients between the HAP group and VAP group was that the HAP patients had hypoxemia more often than the VAP patients.

Microbiological Results

The microbiological results are shown in Table 3. The microbiological cultures at diagnosis of pneumonia were positive for bacteria in 96% of the patients. Only 6 patients (3 in HAP and 3 in VAP groups) had definite pathogens whereas the rest were possible pathogens. The bacterial isolates were found in endotracheal aspirates (81.5%), expectorated sputum samples

Table 2. Clinical manifestations and laboratory findings at diagnosis of HAP and VAP

	Total (n = 146)	HAP (n = 36)	VAP (n = 110)	p
Vital sign				
Mean temperature ^{O}C (SD)	38.96 (0.86)	38.88 (0.73)	38.99 (0.90)	0.33
Mean respiratory rate/min. (SD)	28.5 (5.2)	27.1 (5.2)	28.9 (5.1)	0.19
Mean systolic BP, mmHg (SD)	119.9 (24.7)	115.9 (23.8)	121.3 (25.0)	0.24
Mean diastolic BP, mmHg (SD)	68.5 (13.2)	64.9 (13.6)	69.6 (12.8)	0.46
Mean pulse rate/min. (SD)	117.6 (17.0)	115.8 (16.2)	118.2 (17.3)	0.17
CBC				
Mean WBC cells/mm3 (SD)	15,346 (5,986)	16,307 (5,501)	15,031 (6,127)	0.27
Mean Hct, % (SD)	31.5 (4.9)	31.7 (5.4)	31.4 (4.9)	0.77
Mean Platelets x 1000/mm3 (SD)	254 (142)	295 (153)	240 (136)	0.04
Serum Electrolytes				
Mean sodium, mmol/L (SD)	138.9 (6.4)	136.9 (7.7)	139.6 (5.9)	0.03
Mean potassium, mmol/L (SD)	3.9 (0.7)	3.9 (0.7)	3.9 (0.7)	0.98
Mean bicarbonate, mmol/L (SD)	22.6 (5.6)	22.6 (4.4)	22.7 (5.9)	0.93
Mean BUN, mg/dL (SD)	38.1 (25.9)	37.3 (28.8)	38.3 (25.0)	0.85
Mean Creatinine, mg/dL (SD)	1.5 (1.2)	1.4 (1.2)	1.5 (1.2)	0.93
Median AST, IU/L (min-max)	39 (10-920)	34 (15-310)	42 (10-920)	0.25
Median AST, IU/L (min-max)	28 (3-1,351)	28 (4-341)	27 (3-1,351)	0.96
Mean albumin, g/L (SD)	2.74 (0.6)	2.88 (0.6)	2.70 (0.6)	0.17
Hypoxia by arterial blood gas or pulse oxymeter	29 (19.9%)	15 (41.7%)	14 (12.7%)	< 0.01
Category of sepsis				
Sepsis	111 (76.0%)	25 (69.4%)	86 (78.2%)	0.53
Severe Sepsis	24 (16.5%)	8 (22.2%)	16 (14.5%)	
Septic Shock	11 (7.5%)	3 (8.3%)	8 (7.3%)	
Sepsis Related with pneumonia	146 (100%)	36 (100%)	110 (100%)	
Radiologic finding				
Extent of pneumonia				
Bronchopneumonia	78 (53.4%)	19 (52.8%)	59 (53.6%)	0.85
Multilobar	36 (24.7%)	8 (22.2%)	28 (25.5%)	
Lobar	32 (21.9%)	9 (25%)	23 (20.9%)	
Lung involvement				
Unilateral	112 (76.7%)	29 (80.6%)	83 (75.5%)	0.69
Bilateral	34 (23.3%)	7 (19.4%)	27 (24.5%)	
Presence of Pleural effusion	22 (15.0%)	5 (13.9%)	17 (15.5%)	0.97

Table 3. Microbiological results

	Total (n = 146)	HAP (n = 36)	VAP (n = 110)	p-value
Presence of bacteria from culture	140 (95.9%)	33 (91.7%)	107 (97.3%)	0.16
Source of microbiological culture				
Endotracheal aspirate	119 (85.0%)	18 (50.0%)	101 (91.8%)	<0.01
Expectorated sputum	15 (10.7%)	12 (33.3%)	3 (2.7%)	
Blood	6 (4.3%)	3 (8.3%)	3 (2.7%)	
Bacterial Isolation				
Monomicrobial	87 (62.1%)	19 (52.8%)	68 (61.8%)	0.28
Polymicrobial	53 (37.9%)	14 (38.9%)	39 (35.5%)	
A. baumannii	65 (46.4%)	9 (25.0%)	56 (50.9%)	0.01
MDR	8 (5.7%)	3 (8.3%)	5 (4.5%)	0.41
PDR	52 (37.1%)	5 (13.9%)	47 (42.7%)	<0.01
P. aeruginosa	42 (30.0%)	4 (11.1%)	38 (34.5%)	0.01
MDR	16 (11.4%)	3 (8.3%)	13 (11.8%)	0.76
PDR	3 (2.1%)	0	3 (2.7%)	1.0
S. aureus	22 (15.7%)	8 (22.2%)	14 (12.7%)	0.27
MRSA	11 (7.9%)	5 (13.9%)	6 (5.5%)	0.14
K. pneumoniae	44 (31.4%)	17 (47.2%)	27 (24.5%)	0.02
ESBL-producing	29 (20.7%)	8 (22.2%)	21 (19.1%)	0.87
E. coli	12 (8.6%)	5 (13.9%)	7 (6.4%)	0.17
ESBL-producing	7 (5.0%)	4 (11.1%)	3 (2.7%)	0.06
S. maltophilia	5 (3.6%)	4 (11.1%)	1 (0.9%)	0.01
C. koseri	1 (0.7%)	0	1 (0.9%)	1.00
E. aerogenes	1 (0.7%)	0	1 (0.9%)	1.00
E. cloacae	1 (0.7%)	0	1 (0.9%)	1.00
H. influenzae	1 (0.7%)	1 (2.8%)	0	0.25
S. marcescens	1 (0.7%)	1 (2.8%)	0	0.25
S. pneumoniae	1 (0.7%)	0	1 (0.9%)	1.00

ESBL = Extended-Spectrum-Beta-Lactamase
MRSA = Methicillin-Resistant *Staphylococcus aureus*

(10.3%) and blood samples (4.1%). A single type of bacteria was found in 59.6% of the patients. The major bacteria isolated from the patients were *A. baumannii* (46.4%), *P. aeruginosa* (30.0%), *K. pneumoniae* (31.4%) and *S. aureus* (15.7%). Antibiotic resistance was observed in $\geq$ 50% of the aforementioned isolated bacteria. *A. baumannii* and *P. aeruginosa* were significantly more common in the VAP patients whereas *K. pneumoniae* was significantly more common in the HAP patients. Antibiotic resistant *A. baumannii* and *P. aeruginosa* were also significantly more common in the VAP patients.

Antibiotic Therapy for Pneumonia

Antibiotics were given to all patients as shown in Table 4. Sixty-five percent of the patients received monotherapy. The commonly used initial antibiotics were carbapenems (45.9%), colistin (21.9%), cephalosporins (21.2%), penicillins and derivatives (19.2%) and vancomycin (11.6%). The initial antibiotics were concordant with the isolated bacteria in 58.9% of the patients. Modification of initial antibiotics was made in 43.8% of the patients. The commonly modified antibiotics were colistin (50%), carbapenems (32.8%), cephalosporins (17.2%) and fluoroquinolones (17.2%). The concordance of modified antibiotics was 98.4%. The patterns of antibiotic therapy of the patients with HAP and VAP were not significantly different.

Supportive Treatments and Treatment Outcomes

The supportive treatments and treatment outcomes of the patients with pneumonia are shown in Table 5. Mechanical ventilation was required in 81.5% of the patients. Corticosteroids and vasoactive agents

Table 4. Antibiotic therapy of HAP and VAP

	Total (n = 146)	HAP (n = 36)	VAP (n = 110)	p-value
Initial Antibiotics				
Monotherapy	95 (65.1%)	21 (58.3%)	74 (62.3%)	0.44
Combination	51 (34.9%)	15 (41.7%)	36 (32.7%)	
Initial Antibiotics				
Carbapenems	67 (45.9%)	18 (50%)	49 (44.5%)	0.71
Colistin	32 (21.9%)	5 (13.9%)	27 (24.5%)	0.97
Cephalosporins	31 (21.2%)	7 (19.4%)	24 (21.8%)	0.95
Penicillin and derivatives	28 (19.2%)	6 (16.7%)	22 (20%)	0.84
Vancomycin	17 (11.6%)	7 (19.4%)	10 (9.1%)	0.13
Aminoglycosides	10 (6.8%)	5 (13.9%)	5 (4.5%)	0.07
Quinolones	7 (4.8%)	0	7 (6.4%)	0.19
Clindamycin	3 (2.1%)	1 (2.8%)	2 (1.8%)	1.00
Fosfomycin	2 (1.4%)	2 (5.6%)	0	0.06
Tigecycline	2 (1.4%)	1 (2.8%)	1 (0.9%)	0.43
Trimethoprim-Sulfamethoxazole	1 (0.7%)	1 (2.8%)	0	0.25
Concordance initial antibiotics	86 (58.9%)	22 (61.1%)	64 (58.2%)	0.91
Modification of initial antibiotics	64 (43.8%)	16 (44.4%)	48 (43.6%)	0.91
Modified Antibiotics				
Colistin	32 (50.0%)	5 (31.3%)	27 (56.3%)	0.27
Carbapenems	21 (32.8%)	3 (18.8%)	18 (37.5%)	0.36
Cephalosporins	11 (17.2%)	2 (12.5%)	9 (18.8%)	1.00
Quinolones	11 (17.2%)	5 (31.3%)	6 (12.5%)	0.14
Penicillin and derivatives	5 (7.8%)	4 (25.0%)	1 (2.1%)	0.01
Vancomycin	4 (6.3%)	2 (12.5%)	2 (4.2%)	0.25
Clindamycin	2 (3.1%)	1 (6.25%)	1 (2.1%)	0.43
Trimethoprim-Sulfamethoxazole	2 (3.1%)	1 (6.25%)	1 (2.1%)	0.43
Concordance of modified antibiotics with bacterial isolate	63 (98.4%)	16 (100%)	47 (97.9%)	0.99

were given to 3.4% and 16.4% of the patients respectively. The patients were transferred to ICU in 13.7% with the median length of ICU stay of 19.0 days. An improvement of pneumonia at 72 hours after treatment was observed in 56.8% whereas mortality due to pneumonia was observed in 14.4% of the patients. The cure and improvement rate was 53.4% at the end of treatment, whereas the mortality due to pneumonia increased to 42.5%. The mortality due to pneumonia at 30 days was similar to that at the end of treatment. The median length of hospital stay was 16 days. The isolated bacteria were eradicated, presumably eradicated and persistent in 28.7%, 23.3% and 9.6% of cases respectively. Superinfections were observed in 9.6% of the patients. The VAP patients were more likely to be transferred to ICUs and received mechanical ventilation, and had persistence of the isolated bacteria than the HAP patients.

Factors associated with antibiotic resistant A. baumannii or P. aeroginosa pneumonia

The factors that were significantly associated with pneumonia from PDR *A. baumannii* or *P. aeroginosa* were late onset pneumonia (OR 4.2, 95% CI 1.1-13.6, $p < 0.01$) and previous use of carbapenems within 72 hours prior to developing pneumonia (OR 3.5, 95% CI 1.4-9.2, $p < 0.01$).

Factors associated with outcomes of pneumonia

The factors significantly associated with unfavorable outcomes of pneumonia (failure and death) at 72 hours after treatment (analyzed by univariate analysis) were late onset of pneumonia, septic shock, severe sepsis, multilobar pneumonia, bilateral lung involvement, previous use of carbapenems within 72 hours prior to having pneumonia, pneumonia caused by PDR *A. baumannii*, and pneumonia caused by PDR *A.*

Table 5. Supportive treatments and treatment outcomes of the patients with HAP and VAP

	Total (n = 146)	HAP (n = 36)	VAP (n = 110)	p-value
Use of mechanical ventilator	119 (81.5%)	21 (58.3%)	98 (89.1%)	<0.01
Median ventilator day (range)	10 (1-136)	10 (1-136)	10.5 (1-112)	0.78
Use of steroid during treatment of pneumonia	5 (3.4%)	2 (5.6%)	3 (2.7%)	0.60
Use of vasoactive agents during treatment of pneumonia	24 (16.4%)	7 (19.4%)	17 (15.5%)	0.76
Transfer to ICU	20 (13.7%)	2 (5.6%)	18 (17.3%)	<0.01
Median length of ICU stay, days (range)	19.0 (1-91)	47.5 (25-70)	14.0 (1-91)	0.13
Initial response at 72 hours				
Improvement	83 (56.8%)	25 (69.4%)	58 (52.7%)	0.33
Failure	41 (28.1%)	8 (22.2%)	33 (30%)	
Death due to pneumonia	21 (14.4%)	3 (8.3%)	18 (17.3%)	
Death due to others	1 (0.7%)	0	1 (0.9%)	
End-of-treatment response				
Cure and Improvement	78 (53.4%)	21 (58.3%)	57 (51.8%)	0.69
Failure	3 (2.1%)	1 (2.8%)	2 (1.8%)	
Death due to pneumonia	62 (42.5%)	14 (38.9%)	48 (43.6%)	
Death due to others	3 (2.1%)	0	3 (2.7%)	
30-day mortality				
Survive	55 (37.7%)	12 (33.3%)	43 (39.1%)	0.25
Death due to pneumonia	67 (45.9%)	16 (44.4%)	51 (46.4%)	
Death due to others	4 (2.7%)	0	4 (3.6%)	
Unknown	20 (13.7%)	8 (22.2%)	12 (10.9%)	
Median length of hospital stay, days (range)	16 (1-136)	16 (1-136)	15 (1-123)	0.64
Microbiological outcome at the end of treatment				
Eradication	41 (28.1%)	6 (16.7%)	35 (31.8%)	0.12
Presumed eradication	41 (28.1%)	13 (36.1%)	28 (25.5%)	0.31
Persistence	14 (9.6%)	0	14 (12.7%)	0.02
Presumed persistence	34 (23.3%)	11 (30.6%)	23 (20.9%)	0.34
Super-infection	14 (9.6%)	4 (11.1%)	10 (9.1%)	0.75
Unable to evaluate	2 (1.4%)	2 (5.6%)	0	

baumannii or *P. aeruginosa*, as shown in Table 6. However, the factors significantly associated with unfavorable outcomes at 72 hours analyzed by multivariate analysis were septic shock (OR 3.7, 95% CI 1.1-6.9, $p < 0.01$) and bilateral lung involvement (OR 8.6, 95% CI 2.1-68.4, $p = 0.02$).

The factors significantly associated with mortality at the end of treatment analyzed by univariate analysis were septic shock, severe sepsis, multilobar involvement, bilateral lung involvement, previous carbapenem usage within 72 hours, BUN > 20 mg/dL, pneumonia caused by PDR *A. baumannii*, and pneumonia caused by PDR *A. baumannii* or *P. aeruginosa* as shown in Table 7. However the factors significantly associated with mortality at the end of treatment analyzed by multivariate analysis were only septic shock, severe sepsis, and previous carbapenem usage within 72 hours, as shown in Table 8.

The factors significantly associated with 30-day mortality from pneumonia were absence of tracheostomy at diagnosis of pneumonia, severe sepsis, multilobar pneumonia, and previous carbapenem usage within 72 hours as shown in Table 9. The multivariate analysis revealed that severe sepsis, septic shock, and previous carbapenem usage within 72 hours were associated with 30-day mortality from pneumonia, as shown in Table 10.

Discussion

Our prospective active surveillance on HAP and VAP in hospitalized adults at Siriraj Hospital was conducted in order to accomplish the locally relevant information to be used for proper management, control and prevention of NP in Siriraj Hospital. Many patients

Table 6. Univariate analysis of the factors associated with unfavorable outcomes at 72 hours

	Odds Ratio	95% CI	p-value
Late onset of HAP/VAP	3.62	1.18-11.85	0.02
Diabetes mellitus	1.57	0.79-3.13	0.27
COPD	1.59	0.59-4.39	0.52
No Tracheostomy at diagnosis of pneumonia	0.89	0.40-1.99	0.94
Category of sepsis : Septic shock	8.53	1.59-60.43	<0.01
Severe sepsis	3.16	1.16-8.71	<0.01
Extent of pneumonia : multilobar	4.16	1.66-10.57	<0.01
Bilateral lung involvement	3.86	1.59-9.50	<0.01
Previous carbapenem usage within 72 hours	5.17	1.87-14.79	<0.01
Previous colistin usage within 72 hours	4.17	0.37-106.72	0.31
Hypotension, Systolic BP < 90 mmHg	2.06	0.27-18.27	0.65
Tachycardia, Pulse Rate > 90 BPM	3.91	0.44-34.35	0.24
Tachypnea, Respiratory Rate > 24/ min.	1.34	0.33-4.78	0.76
BUN > 20 mg/dL	2.17	0.99-4.81	0.05
Non-concordance of initial antibiotics	1.57	0.74-3.32	0.27
Positive blood culture of pathogen	2.63	0.40-21.47	0.41
Pneumonia caused by PDR *A. baumannii*	2.43	1.13-5.27	0.02
Pneumonia caused by PDR *P. aeruginosa*	2.73	0.19-78.04	0.58
Pneumonia caused by MRSA	0.32	0.0.1-3.20	0.39
Pneumonia caused by ESBL-producing pathogens	1.22	0.40-3.73	0.90
Pneumonia caused by PDR *A. baumannii* or *P. aeruginosa*	2.34	1.09-5.06	<0.01

developed NP and were treated for NP in the general medical wards because the capacity of ICUs was limited and the ICUs were unable to accommodate all patients who needed intensive care. Most of the patients were elderly males with chronic and serious co-morbidities. The factors associated with HAP and VAP at Siriraj Hospital were similar to those reported in the literature such as receiving proton-pump inhibitor, having nasogastric intubation[5,6,13-17]. Almost all NP patients in our series had bacteria isolated from respiratory secretions but the bacteria could be isolated from their blood samples in only 4.2% of them. Therefore, blood culture had very low sensitivity in determining the causative bacteria of NP, as previously reported[18,19]. Since 37.9% of the cases had more than one bacteria isolated from their respiratory secretions, the definite causative bacteria of NP could not be made with certainty. Our series also observed that aerobic gram negative bacteria were the most common pathogens for NP, similar to other centers[4]. The most common gram negative bacteria of NP at Siriraj Hospital was *A. baumannii* (46.4%) and such prevalence was comparable to the retrospective data of NP at Siriraj Hospital in 2007 and in other series[4,20,21]. The most worrisome observation on the isolated bacteria from the patients was that the prevalence of antibiotic-resistant *A. baumannii* was dramatically increased to 92.3% in our series. The second and the third most common pathogens were *K. pneumoniae* and *P. aeruginosa* in which most of *K. pneumoniae* isolates were ESBL-producing strains. The factors associated with NP caused by PDR bacteria were late-onset hospital-acquired pneumonia and previous carbapenem usage within 72 hours. This observation was logical since these two factors were the predisposing factors for acquiring MDR or PDR bacterial infections. The study from Maharaj Nakorn Chiang Mai Hospital also found that one of the risk factors for PDR-*A. bamannii* infection was previous use of imipenem[22].

A delay in the administration of appropriate antibiotic or inappropriate empirical initial antibiotic treatment among the patients with sepsis and microbiologically documented infections was associated with excess hospital mortality[8-10,21,23]. Therefore, the appropriate initial antibiotics and early administration of appropriate antibiotics are crucial for therapy of serious infections including NP. The empirical initial antibiotics given to our patients with NP were concordant with the isolated bacteria in only 58.9%. We observed only a trend toward a significant difference in mortality

Table 7. Univariate analysis of the factors associated with mortality at the end of treatment

	Odds Ratio	95% CI	p value
Late onset of HAP/VAP	2.37	0.92-6.08	0.11
DM	1.40	0.70-2.78	0.43
COPD	1.92	0.69-5.37	0.32
Having tracheostomy at diagnosis of pneumonia	1.72	0.71-4.22	0.27
Septic shock	7.68	1.44-54.33	<0.01
Severe sepsis	2.85	1.05-7.82	<0.01
Multilobar involvement	3.78	1.52-9.52	<0.01
Bilateral lung involvement	2.94	1.32-6.55	<0.01
Previous carbapenem usage within 72 hours	4.06	1.65-9.98	<0.01
Previous Colistin usage within 72 hours	3.87	0.39-38.12	0.32
Hypotension (Systolic BP < 90 mmHg)	5.25	0.53-126.46	0.17
Tachycardia (Pulse Rate > 90 BPM)	1.64	0.29-9.22	0.69
Tachypnea (Respiratory Rate > 24/min)	1.44	0.43-5.16	0.76
BUN > 20 mg/dL	2.50	1.19-5.24	0.02
Non-concordance of initial antibiotics	1.63	0.76-3.50	0.23
Positive blood culture of pathogen	0.56	0.07-3.72	0.81
PDR *A. baumanni* pneumonia	3.39	1.57-7.40	<0.01
PDR *P. aeruginosa* pneumonia	0.62	0.02-8.95	1.00
MRSA pneumonia	0.44	0.09-1.94	0.35
ESBL-producing bacterial pneumonia	1.00	0.44-2.27	0.86
PDR *A. baumannii* or PDR *P. aeruginosa*	2.79	1.38-5.63	<0.01

Table 8. Multivariate analysis of the factors associated with mortality at the end of treatment

	Odds Ratio	95% CI	p value
Category of sepsis: Septic Shock	12.82	2.26-72.72	<0.01
Severe sepsis	2.83	1.04-7.69	0.04
Previous carbapenem usage within 72 hours	3.54	1.33-9.45	0.01

Table 9. Univariate analysis of the factors associated with 30-day mortality

	Odds Ratio	95% CI	p-value
Absence of tracheostomy at diagnosis of pneumonia	2.77	1.07-7.32	0.04
Category of sepsis : Severe sepsis	3.25	1.07-10.27	0.04
Septic Shock	5.16	1.53-2.15	<0.01
Multilobar involvement	2.9	1.08-7.78	0.03
Previous carbapenem usage within 72 hours	3.23	1.09-9.98	0.03
PDR *A. baumannii* or *P. aeruginosa*	2.46	1.46-2.01	0.03

Table 10. Multivariate analysis of the factors associated with 30-day mortality

	Odds Ratio	95% CI	p-value
Severe sepsis	2.976	1.05-8.41	0.04
Septic shock	5.172	1.04-25.75	0.05
Previous Carbapenem usage within 72 hours	3.668	1.21-9.29	0.02

between the patients who received concordant initial antibiotics and those who did not receive concordant initial antibiotics (OR 1.57, 95%CI 0.74-3.32) in a univariate analysis. This could be due to a sample size and/or most of our patients had serious and severe pneumonia *i.e.* septic shock (OR 3.7, 95% CI 1.1-6.9, $p < 0.01$) and bilateral lung involvement (OR 8.6, 95% CI 2.1-68.4, $p = 0.02$) that were found to be associated with mortality from pneumonia. Nearly half of initial antibiotics given to the patients were modified and half of modifications were switching to colistin according to the susceptibility profiles of the isolated bacteria. The decision analysis of including polymyxin in the initial empirical antibiotic regimen for treating serious infections revealed that polymyxin was justified in a healthcare setting where the prevalence of gram negative pathogens were susceptible only to polymyxins was found to be approximately 50%[24]. The prevalence of PDR *A. baumanni* and *P. aeruginosa* in our patients was 31.8%. Therefore, colistin may not be necessary to be included in empiric antibiotic regimen for all patients with NP at Siriraj Hospital. However, if the patient was likely to have NP due to *A. baumanni* such as the patient who had recently received carbapenem or the patient who had *A. baumanni* colonization in the respiratory tract prior to developing NP, or if gram stain of the respiratory secretion revealed gram negative bacteria suggestive of being *A. baumanni*, colistin should be included in empiric antibiotic therapy regimen.

Clinical improvement of NP usually becomes apparent after 48 to 72 hours of therapy and is associated with the outcomes of treatment[25,26]. Clinical improvement at 72 hours after treatment was observed in 56.8% of the patients in our series. The concordance of initial antibiotic was not significantly associated with the initial improvement at 72 hours as mentioned earlier. The mortality from NP observed in the patients at the end of treatment and at 30 days after treatment was approximately 40% that was comparable to the retrospective data of NP at Siriraj Hospital in 2007 and other large series[4,11,15,20,21,27-29]. The factors associated with unfavorable outcomes at 72 hours, at the end of treatment, and at 30 days after treatment were septic shock, sever sepsis, multilobar pneumonia, and bilateral lung involvement. Pneumonia caused by PDR-pathogens was associated with unfavorable outcomes in univariate analysis but not present in the multivariate analysis. This might be explained by the fact that NP caused by PDR pathogens usually led to septic shock, severe sepsis, multilobar pneumonia, and bilateral pneumonia. Carbapenem usage within 72 hours was significantly associated with mortality at end of treatment and at 30 days. Therefore the clinician should avoid inappropriate use of carbapenem in order to minimize the risk of acquiring severe infections caused by PDR bacteria.

Conclusion

Nosocomial pneumonia remains the important problem in hospitalized patients at Siriraj Hospital because of its' high morbidity and high mortality rate. This infection mainly affected elderly with co-morbidity who had prolonged hospitalization, particularly in medical wards and ICUs. The common isolated pathogens were MDR or PDR-organisms, especially *A. baumannii*, *P. aeruginosa*, *K. pneumoniae* and MRSA. Most episodes of inadequate antimicrobial treatment were attributed to potentially antibiotic-resistant gram-negative bacteria. The responsible healthcare personnel should be aware of drug-resistant pathogens in causing nosocomial pneumonia and they should provide antimicrobial agents that are active against such common drug-resistant bacteria.

Acknowledgements

The authors thank Jansen-Cilag and Asian Network Surveillance of Resistant Pathogens (ANSORP) for supporting the study, and Mr. Suthipol Udompanturak for statistical analyses.

References

1. Hospital-acquired pneumonia in adults: diagnosis, assessment of severity, initial antimicrobial therapy, and preventive strategies. A consensus statement, American Thoracic Society, November 1995. Am J Respir Crit Care Med 1996; 153: 1711-25.
2. Porzecanski I, Bowton DL. Diagnosis and treatment of ventilator-associated pneumonia. Chest 2006; 130: 597-604.
3. Alcon A, Fabregas N, Torres A. Hospital-acquired pneumonia: etiologic considerations. Infect Dis Clin North Am 2003; 17: 679-95.
4. Chawla R. Epidemiology, etiology, and diagnosis of hospital-acquired pneumonia and ventilator-associated pneumonia in Asian countries. Am J Infect Control 2008; 36 (4 Suppl): S93-100.
5. American Thoracic Society; Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care Med 2005; 171: 388-416.
6. McEachern R, Campbell GD Jr. Hospital-acquired

pneumonia: epidemiology, etiology, and treatment. Infect Dis Clin North Am 1998; 12: 761-79, x.
7. Kollef MH. Inadequate antimicrobial treatment: an important determinant of outcome for hospitalized patients. Clin Infect Dis 2000; 31 (Suppl 4): S131-8.
8. Kollef MH, Sherman G, Ward S, Fraser VJ. Inadequate antimicrobial treatment of infections: a risk factor for hospital mortality among critically ill patients. Chest 1999; 115: 462-74.
9. Iregui M, Ward S, Sherman G, Fraser VJ, Kollef MH. Clinical importance of delays in the initiation of appropriate antibiotic treatment for ventilator-associated pneumonia. Chest 2002; 122: 262-8.
10. Ibrahim EH, Sherman G, Ward S, Fraser VJ, Kollef MH. The influence of inadequate antimicrobial treatment of bloodstream infections on patient outcomes in the ICU setting. Chest 2000; 118: 146-55.
11. Luna CM, Aruj P, Niederman MS, Garzon J, Violi D, Prignoni A, et al. Appropriateness and delay to initiate therapy in ventilator-associated pneumonia. Eur Respir J 2006; 27: 158-64.
12. Paterson DL. The epidemiological profile of infections with multidrug-resistant Pseudomonas aeruginosa and Acinetobacter species. Clin Infect Dis 2006; 43 (Suppl 2): S43-8.
13. Craven DE, Steger KA. Epidemiology of nosocomial pneumonia. New perspectives on an old disease. Chest 1995; 108 (2 Suppl): 1S-16S.
14. Hanson LC, Weber DJ, Rutala WA. Risk factors for nosocomial pneumonia in the elderly. Am J Med 1992; 92: 161-6.
15. Celis R, Torres A, Gatell JM, Almela M, Rodriguez-Roisin R, Agusti-Vidal A. Nosocomial pneumonia. A multivariate analysis of risk and prognosis. Chest 1988; 93: 318-24.
16. Herzig SJ, Howell MD, Ngo LH, Marcantonio ER. Acid-suppressive medication use and the risk for hospital-acquired pneumonia. JAMA 2009; 301: 2120-8.
17. Taylor GD, Buchanan-Chell M, Kirkland T, McKenzie M, Wiens R. Bacteremic nosocomial pneumonia. A 7-year experience in one institution. Chest 1995; 108: 786-8.
18. Luna CM, Videla A, Mattera J, Vay C, Famiglietti A, Vujacich P, et al. Blood cultures have limited value in predicting severity of illness and as a diagnostic tool in ventilator-associated pneumonia. Chest 1999; 116: 1075-84.
19. Malaporn M. Angkasakevinai N, Thamlikitkul V. Epidemiology of hospital-acquired pneumonia at Siriraj Hospital, 2007 [personal communication].
20. Pothirat C. Hospital-acquired pneumonia: insight and reality in Northern Thailand [Internet]. [cited 2009 Nov 6]. Available from: http://www.med.cmu.ac.th/etc/NT3C/HAP%20 North%20.pdf
21. Lee SC, Hua CC, Yu TJ, Shieh WB, See LC. Risk factors of mortality for nosocomial pneumonia: importance of initial anti-microbial therapy. Int J Clin Pract 2005; 59: 39-45.
22. Chaiwarith R, Mahatthanaphak S, Boonchoo M, Supparatpinyo K, Sirisanthana T. Pandrug-resistant *Acinetobacter baumannii* at Maharaj Nakorn Chiang Mai Hospital. J Infect Dis Antimicrob Agents 2005; 22: 1-8.
23. Shani V, Kariv G, Muchtar E, Leibovici L, Paul M. Appropriate vs. inappropriate empirical antibiotic treatment: systematic review and meta-analysis of effects and modifiers [abstract O210]. 19th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Helsinki, Finland; May 16-19, 2009.
24. Falagas ME, Rafailidis PI. When to include polymyxins in the empirical antibiotic regimen in critically ill patients with fever? A decision analysis approach. Shock 2007; 27: 605-9.
25. Luna CM, Blanzaco D, Niederman MS, Matarucco W, Baredes NC, Desmery P, et al. Resolution of ventilator-associated pneumonia: prospective evaluation of the clinical pulmonary infection score as an early clinical predictor of outcome. Crit Care Med 2003; 31: 676-82.
26. Luna CM, Niederman MS. What is the natural history of resolution of nosocomial pneumonia? Semin Respir Crit Care Med 2002; 23: 471-9.
27. Takano Y, Sakamoto O, Suga M, Muranaka H, Ando M. Prognostic factors of nosocomial pneumonia in general wards: a prospective multivariate analysis in Japan. Respir Med 2002; 96: 18-23.
28. Kim JM, Park ES, Jeong JS, Kim KM, Kim JM, Oh HS, et al. Multicenter surveillance study for nosocomial infections in major hospitals in Korea. Nosocomial Infection Surveillance Committee of the Korean Society for Nosocomial Infection Control. Am J Infect Control 2000; 28: 454-8.
29. Connelly SM, Trinh JV, Johnson MD, Dodds-Ashley ES, Stout J, Engemann JJ, et al. Mortality and time to extubation in severe hospital-acquired pneumonia. Am J Infect Control 2009; 37: 143-9.

ปอดอักเสบติดเชื้อที่เกิดในโรงพยาบาลและปอดอักเสบติดเชื้อที่สัมพันธ์กับเครื่องช่วยหายใจในผู้ป่วยผู้ใหญ่ที่โรงพยาบาลศิริราช: สาเหตุ ผลการรักษา และผลกระทบจากเชื้อดื้อยาต้านจุลชีพ

พีระวงษ์ วีรารักษ์, ภัทรชัย กีรติสิน, วิษณุ ธรรมลิขิตกุล

บทนำ: *ปอดอักเสบติดเชื้อที่เกิดในโรงพยาบาล และปอดอักเสบติดเชื้อที่สัมพันธ์กับเครื่องช่วยหายใจเป็นสาเหตุของการป่วย และการตายที่สำคัญในผู้ป่วยที่รับไว้รักษาในโรงพยาบาล ปัจจัยหนึ่งที่มีส่วนทำให้อัตราตายสูง คือ เชื้อก่อโรคดื้อยาต้านจุลชีพ*

วัตถุประสงค์: *เพื่อทราบความชุกของแบคทีเรียที่เป็นสาเหตุ ลักษณะทางคลินิก ปัจจัยเสี่ยง การดื้อของเชื้อก่อโรค การรักษา และผลการรักษาของผู้ป่วยปอดอักเสบติดเชื้อที่เกิดในโรงพยาบาลและปอดอักเสบติดเชื้อที่สัมพันธ์กับเครื่องช่วยหายใจ*

วัสดุและวิธีการ: *การศึกษานี้เป็นการเฝ้าระวัง และติดตามผู้ป่วยผู้ใหญ่ที่รับไว้รักษาที่โรงพยาบาลศิริราชที่เป็นปอดอักเสบติดเชื้อที่เกิดในโรงพยาบาล และปอดอักเสบติดเชื้อที่สัมพันธ์กับเครื่องช่วยหายใจตั้งแต่เดือนธันวาคม พ.ศ. 2550 ถึง มีนาคม พ.ศ. 2552 โดยเก็บข้อมูลของผู้ป่วยตั้งแต่ได้รับการวินิจฉัยโรค จนผู้ป่วยออกจากโรงพยาบาลหรือถึงแก่กรรม*

ผลการศึกษา: *มีผู้ป่วยจำนวน 146 ราย ร้อยละ 70 ของผู้ป่วยเป็นชาย อายุเฉลี่ย 70.8 ปี เป็นผู้ป่วยปอดอักเสบติดเชื้อที่เกิดในโรงพยาบาลร้อยละ 24.7 และปอดอักเสบติดเชื้อที่สัมพันธ์กับเครื่องช่วยหายใจร้อยละ 75.3% ผู้ป่วยร้อยละ 82.9 เป็นปอดอักเสบที่เกิดหลัง 4 วัน โดยมีค่ามัธยฐาน 11 วัน ผู้ป่วยร้อยละ 67 อยู่หอผู้ป่วยสามัญอายุศาสตร์ พบปอดอักเสบชนิด Bronchopneumonia ร้อยละ 53.4 และปอดอักเสบที่มีรอยโรคในปอดมากกว่าหนึ่งกลีบร้อยละ 24.7 เชื้อก่อโรคที่พบบ่อยที่สุดคือ A. baumanni โดยร้อยละ 92.3 ของเชื้อดังกล่าว เป็นเชื้อดื้อยาหลายขนาน เชื้ออื่นที่พบบ่อย ได้แก่ K. pneumoniae, P. aeruginosa และ methicillin-resistant S. aureus (MRSA) ยาที่ใช้รักษาระยะแรก ได้แก่ Carbapenem (ร้อยละ 45.9), colistin (ร้อยละ 21.9) และ cephalosporins (ร้อยละ 21.1) ยาที่ผู้ป่วยได้รับตรงกับความไวของเชื้อร้อยละ 58.9 ผู้ป่วยร้อยละ 43.8 มีการ ปรับเปลี่ยนยาด้านจุลชีพที่สำคัญ คือ colistin และ carbapenem โดยยาที่ปรับนี้ สอดคล้องกับความไวของเชื้อ ร้อยละ 98.4 ผู้ป่วยได้รับเครื่องช่วยหายใจร้อยละ 81.5 โดยมีระยะเวลาที่ใช้เครื่อง ช่วยหายใจประมาณ 10 วัน ผู้ป่วยตอบสนองต่อการรักษาในวันที่ 3 ร้อยละ 56.8 โดยมีอัตราตายจากปอดอักเสบร้อยละ 14.4 ในวันที่สาม และร้อยละ 42.5 และร้อยละ 45.9 เมื่อสิ้นสุดการรักษาและเมื่อ 30 วัน หลังการรักษาตามลำดับ ปัจจัยที่สัมพันธ์กับการติดเชื้อดื้อยาคือปอดอักเสบที่เกิดหลังอยู่โรงพยาบาลนาน และได้รับยากลุ่ม carbapenem ภายในสามวันก่อนเกิดปอดอักเสบ ปัจจัยที่สัมพันธ์กับผลการรักษาในวันที่สาม ได้แก่ septic shock และปอดอักเสบ ทั้งสองข้าง ส่วนปัจจัยที่สัมพันธ์กับผลการรักษาในวันที่หยุดการรักษา และวันที่ 30 ได้แก่ septic shock, severe sepsis และได้รับยากลุ่ม carbapenem ภายในสามวันก่อนเกิดปอดอักเสบ*

สรุป: *ปอดอักเสบติดเชื้อที่เกิดในโรงพยาบาล และปอดอักเสบติดเชื้อที่สัมพันธ์กับเครื่องช่วยหายใจยังคงเป็นการติดเชื้อที่เกิดในโรงพยาบาลที่สำคัญของโรงพยาบาลศิริราช เชื้อก่อโรคมักดื้อยาหลายขนาน อัตราตายสูง ข้อมูลจากการศึกษานี้น่าจะมีประโยชน์ในการพิจารณาเลือกใช้ยาต้านจุลชีพที่เหมาะสมสำหรับรักษาผู้ป่วยซึ่งน่าจะลดอัตราตาย และลดโอกาสเกิดเชื้อดื้อยาได้*