RISK FACTORS OF MULTIDRUG - RESISTANT ACINETOBACTER BAUMANNII INFECTION IN INTUBATED PATIENTS IN NAKHON PATHOM HOSPITAL

PATTHANA LERSAKSOMBAT

A THESIS SUBMITTED IN PARTIAL FULFILLMENT
OF THE REQUIREMENTS FOR
THE DEGREE OF MASTER OF SCIENCE (PUBLIC HEALTH)
MAJOR IN INFECTIOUS DISEASES AND EPIDEMIOLOGY
FACULTY OF GRADUATE STUDIES
MAHIDOL UNIVERSITY
2008

Thesis
Entitled

RISK FACTORS OF MULTIDRUG-RESISTANT ACINETOBACTER BAUMANNII INFECTION IN INTUBATED PATIENTS IN NAKHON PATHOM HOSPITAL

……

Mrs. Patthana Lersaksombat

Candidate

……

Assoc. Prof. Dusit Sujirarat,

M.Sc. (Biostatistics)

Major – Advisor

……

Assoc. Prof. Dr. Kulaya Narksawat,

D.D.S., M.P.H., M.Sc

Co-Advisor

……..

Assoc. Prof. Dr. Kanokrat Siripanichgon

M.D., M.P.H.

Co-Advisor

……

Prof. Banchong Mahaisavariya

M.D.

Dean

Faculty of Graduate Studies

……

Assoc. Prof. Chakrit Hirunpetcharat

Ph.D. (Tropical Health)

Chair

Master of Science (Public Health)

Major in Infectious Diseases and Epidemiology

Faculty of Public Health

Thesis

Entitled

RISK FACTORS OF MULTIDRUG-RESISTANT ACINETOBACTER BAUMANNII INFECTION IN INTUBATED PATIENTS IN NAKHON PATHOM HOSPITAL

was submitted to the Faculty of Graduate Studies, Mahidol University.
For the degree of Master of Science (Public Health)
Major in Infectious Diseases and Epidemiology
On

August 25, 2008

……..
Mrs. Patthana Lersaksombat
Candidate

……	……..
Assoc. Prof. Dr. Kulaya Narksawat,	Assoc. Prof. Dusit Sujirarat,
D.D.S., M.P.H., M.Sc	M.Sc. (Biostatistics)
Member	Chair
……..	…….
Assoc. Prof. Dr. Amornrath Podhipak	Assoc. Prof. Dr. Kanokrat Siripanichgon
Ph.D.(Epidemiology)	M.D., M.P.H.
Member	Member
…….	……
Prof. Banchong Mahaisavariya	Assoc. Prof. Dr. Phitaya Charupoonphol,
M.D.	M.D., Dip.Thai Board of Epidemiology
Dean	Dean
Faculty of Graduate Studies	Faculty of Public Health
Mahidol University	Mahidol University

ACKNOWLEDGEMENTS

I wish to express my sincere gratitude and deep appreciation to my major advisor, Associate Professor Dusit Sujirarat, for his invaluable advice, supervision, guidance, kindness, construction criticism, and tremendous assistance throughout my study. I also want to thank my co-advisors, Associate Professor Dr. Kulaya Narksawat for her invaluable advice, and improving this thesis ; and Associate Professor Dr. Kanokrat Siripanichgon , my co-advisors, for her helpful guidance, assistance and kindness.

My special thank is Associate Professor Dr. AmornrathPodhipak. Dr. Amornrath, the external examiner of the thesis defense, was kind enough to provide suggestions for the research for improvement.

It was impossible to mention all the kindness and assistance of lectures, and the staff of the Epidemiology Department, Faculty of Public Health, Mahidol University.

Finally, I am grateful to my family to their encouragement, support and love. The merit of this thesis is dedicated to my mother, my father and all the teachers who had taught and inspired me to reach this goal.

Patthana Lersaksombat

RISK FACTORS OF MULTIDRUG - RESISTANT ACINETOBACTER BAUMANNII INFECTION IN INTUBATED PATIENTS IN NAKHON PATHOM HOSPITAL

PATTHANA LERSAKSOMBAT 4737293 PHPH/M

M.Sc. (PUBLIC HEALTH) MAJOR IN INFECTIOUS DISEASES AND EPIDEMIOLOGY

THESIS ADVISORS : DUSIT SUJIRARAT, M.Sc. (BIOSTAT), KULAYA NARKSAWAT, D.D.S., M.P.H., M.Sc., KANOKRAT SIRIPANICHGON, M.D., M.P.H., SUTHANYA BANCHONGPAK, M.D.

ABSTRACT

This cohort study was designed to determine the incidence and risk factors of multidrug-resistant (MDR) *Acinetobacter baumannii* infection among intubated patients in Nakhon Pathom Hospital during December 2005 to October 2006. The data were collected from the medical records using a data collection form. Among 507 patients with a diagnosis of Ventilator Associated Pneumonia (VAP), there were 89 cases of infection with multidrug-resistant *A. baumannii*. The incidence of VAP caused by multidrug-resistant *A. baumannii* was 17.55%, and incidence density was 21.75 per 1,000 person-days or 15.27 per 1,000 ventilator-days. The median survival time was 46 days. Multivariate analysis showed that the following factors were associated with MDR *A. baumannii* infection : male gender (HR = 2.26, 95%CI, 1.209-4.237), treatment with cephalosporin (HR = 1.49, 95%CI, 1.318 – 1.701), treatment with meronem (HR = 4.51, 95%CI, 4.076 – 4.999), treatment with vancomycin (HR = 4.19, 95%CI, 3.349 – 5.245), patients in surgical wards (HR 4.32, 95%CI, 0.197 – 15.616), and patients admitted to general wards (HR = 2.10, 95%CI, 0.811– 1.187) were associated with MDR *A. baumannii* infection. Protective factors among ventilated patients included patients with a tracheostomy and those who received aminoglycosides ($p < 0.001$).

This study supported the importance of initial antibiotic choices for treatment of VAP patients, and compliance with nosocomial infection control guidelines in general wards to the same standard as the intensive care units.

KEY WORDS : MULTIDRUG - RESISTANT ACINETOBACTER BAUMANNII / SURVIVAL RATE / RISK FACTOR

118 pp.

ปัจจัยเสี่ยงของการติดเชื้อดื้อยา *Acinetobacter baumannii* ในผู้ป่วยที่ใส่ท่อช่วยหายใจและใช้เครื่องช่วยหายใจ โรงพยาบาลนครปฐม (RISK FACTORS OF MULTIDRUG-RESISTANT ACINETOBACTER BAUMANNII INFECTION IN INTUBATED PATIENTS IN NAKHON PATHOM HOSPITAL)

พัฒนา เลอศักดิ์สมบัติ 4737293 PHPH/M

วท.ม.(สาธารณสุขศาสตร์) สาขาวิชาเอกโรคติดเชื้อและวิทยาการระบาด

คณะกรรมการควบคุมวิทยานิพนธ์ : ดุสิต สุจิรารัตน์, M.Sc. (BIOSTAT), กุลยา นาคสวัสดิ์, D.D.S., M.P.H., M.Sc., กนกรัตน์ ศิริพานิชกร, M.D., M.P.H., สุธัญญา บรรจงภาค, M.D.

บทคัดย่อ

การศึกษานี้เป็นการศึกษาอุบัติการณ์และปัจจัยพยากรณ์การติดเชื้อดื้อยา *Acinetobacter baumannii* ในผู้ป่วยที่ใส่ท่อช่วยหายใจ โรงพยาบาลนครปฐม ตั้งแต่วันที่ 1 ธันวาคม 2548 ถึงวันที่ 30 ตุลาคม 2549 โดยติดตามและเก็บข้อมูลผู้ป่วยจากเวชระเบียนด้วยแบบบันทึกข้อมูล ผู้ป่วยที่ใช้เครื่องช่วยหายใจจำนวน 507 ราย พบว่า 89 ราย เกิดภาวะปอดอักเสบที่สัมพันธ์กับการใช้เครื่องช่วยหายใจด้วยเชื้อดื้อยา *Acinetobacter baumannii* ซึ่งอุบัติการณ์การติดเชื้อเท่ากับร้อยละ 17.55 หรือ 21.75 ต่อ 1,000 วันนอนและ15.27 ต่อ 1,000 วันใส่เครื่องช่วยหายใจ โดยมีค่ามัธยฐานของจำนวนวันของการติดเชื้อ *Acinetobacter baumannii* ที่ดื้อยา เท่ากับ 46 วัน

เมื่อวิเคราะห์ความสัมพันธ์เชิงซ้อน พบว่าปัจจัยที่มีความสัมพันธ์กับการติดเชื้อดื้อยา *Acinetobacter baumannii* ได้แก่ เพศชาย (HR = 2.26, 95%CI, 1.209-4.237), การได้รับยาปฏิชีวนะกลุ่มเซฟาโลสปอริน (HR = 1.49, 95%CI, 1.318–1.701), เมโรเนม (HR = 4.51,95%CI, 4.076–4.999), แวนโคมัยซิน (HR = 4.19, 95%CI, 3.349–5.245), ผู้ป่วยแผนกศัลยกรรม (HR 4.32, 95%CI, 0.197 – 15.616), และผู้ป่วยหอสามัญ (HR = 2.10, 95%CI,0.811– 1.187) ทั้งนี้พบว่าการเจาะคอและการได้รับยากลุ่มอะมิโนไกลโคไซด์ เป็นปัจจัยป้องกันการติดเชื้อดื้อยาชนิดนี้ในผู้ป่วยที่ใช้เครื่องช่วยหายใจอย่างมีนัยสำคัญ ($p < 0.001$)

จากผลการวิจัยนี้ เสนอแนะว่าควรให้ความสำคัญและเพิ่มความระมัดระวังในการใช้ยาปฏิชีวนะอย่างเหมาะสมสำหรับผู้ป่วยที่ใช้เครื่องช่วยหายใจ รวมถึงการเข้มงวดในการปฏิบัติตามมาตรการการป้องกันและควบคุมการติดเชื้อในผู้ป่วยหอสามัญเช่นเดียวกับผู้ป่วยที่นอนรักษาในหน่วยอภิบาล.

118 หน้า

CONTENTS

CONTENTS (continued)

CONTENTS (continued)

CONTENTS (continued)

LIST OF TABLES

LIST OF FIGURES

CHAPTER I
INTRODUCTION

Pneumonia is currently the second most common nosocomial infection and has been named as the leading cause of death among hospital acquired infections. Accompanying with the underlying diseases, co-morbidity, and therapeutic interventions, the incidence of pneumonia patients has ranged from 5 to 10 cases per 1000 hospital admission among patients who has no major risk factor, but may increase by 6 to 20 folds in intensive care unit for the patients who require mechanical ventilation(1).

Ventilator Associated Pneumonia (VAP) is usually defined as an nosocomial infection that is occurring after 48 hours of admission in the hospital for the patient who needs ventilator support. The incidence of VAP ranges from 10% to 65% among intubated patients and varies as the risk factors(2). In the 1992 – 1998 data from the National Nosocomial Infections Surveillance (NNIS) system demonstrated that there was 31% of intensive care unit acquired infections were pneumonias, and 83% of these pneumonias were mechanical ventilation associated. The mortality rates among VAP patients were 20% - 50 %(3). The cost of care for nosocomial pneumonia was estimated as US$ 3,000 to US$ 6,000, averagely for each episode, and the length of hospital stay for the patient who developed VAP was 13 days averagely(4).

In Thailand , Danchaivijitr and Chokloikaew (1998) reported that nosocomial Infection, which originated from the respiratory tract were 20.1%, 28.4%, and 30.3% in 1994, 1998, and 2000 respectively, which was associated with the increased mortality, prolonged hospital stay and increase cost of treatment by 5,683 US$ or 238,689 baht averagely(5).

The most common microorganisms responsible for Ventilator Associated Pneumonia are gram negative enteric bacilli, *Staphylococcus aureus* and *Pseudomonas aeruginosa*(3). However, in early onset VAP, common pathogens include community

organisms such as methicillin sensitive *Staphylococcus aureus, Streptococcus pnuemoniae,* and *Haemophilus influenzae*, while, in late onset VAP more virulent pathogens are common such as methicillin resistant *Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*(6).

In the recent decade, *Acinetobacter baumannii* is primarily a healthcare-associated pathogen which is characterized by rapid development of resistance to the major antimicrobial drugs. It has been reported increasingly as the cause of outbreak and nosocomial infections such as blood stream infections, ventilator – associated pneumonia, urinary tract infections and wound infections(7, 8). These infections are especially common in critically ill patients. Outbreaks are frequently occurred in the intensive care and burn unit, involving the use of mechanical ventilators(9).

Acinetobacter baumannii has emerged as a pathogen frequently found in respiratory samples of patients who were suffering with VAP. This increasing problem had been reported worldwide(10,11). An outbreak in New York City in 2002, 53% of *Acinetobacter baumannii* were resisted to cabapenems while 12% resisted to all standard antimicrobial agents(12). Multidrug-resistant *Acinetobacter baumannii* has been reported worldwide and recognized as one of the healthcare-associated infections that are the most difficult to control and to treat(7). The Center for Disease Control and Prevention (CDC) has promulgated the guidelines for controlling of *Acinetobacter baumannii* infection, nevertheless, *Acinetobacter baumannii* infection remains a significant problem, with high morbidity and mortality and lengthened hospital stays(13).

Between 1998 – 2004, The National Antimicrobial Resistance Surveillance of Thailand (NARST) reported the top ten multidrug- resistant found in 32 hospitals in Thailand, *Acinetobacter baumannii* was one of the top ten which was accounted for 4% - 6%, while *E.coli was* 16%, *Pseudomonas aeruginosa* 11% and *Klebsiella pnuemoniae* 10%. In 2003, The Annual Epidemiological Surveillance reported a surveillance of multidrug-resistance isolates, *Acinetobacter calcoaceticus - baumannii complex* isolates were susceptible to aztreonam 1%, less than 35% to ceftazidime,

piperacillin/tazobactam and quinolone, 65% to imipenam, 34% to gentamycin, 60% to netilmycin, and 82% to amikacin, only 29% were susceptible to cotrimazole(14).

Nakhon Pathom Hospital is a tertiary care hospital with the 552 beds capacity. The report of nosocomial infection during the year of 2000 – 2004 was found in lower respiratory tract infection 47.4 %. In 2002 – 2004, the incidence of VAP rate were 14.55, 12.71, and 16.62 per 1000 ventilator-days in 2002, 2003, and 2004, respectively. Gram negative bacilli was the most causative microbiologic agent of VAP in 2004, which was categorized as *Pseudomonas aeruginosa* 30.79%, *Acinetobacter baumannii* 24.29%, and multidrug-resistant *Acinetobacter baumannii* 23.16%. Among VAP which is caused by multidrug-resistant pathogens, multidrug-resistant *Acinetobacter baumannii* was the most predominant pathogen, 81.18%, followed by multidrug-resistant *Psuedomonas aeruginosa* 2.54%, and methicillin resistant *Staphylococcus aureus* 2.54%. The multidrug-resistant *Acinetobacter baumannii* (MDRAB) infection rate was 10.30 % in the past(15).

In the past 2 – 3 years, the incidence of MDRAB infection has increased and associated with mechanical ventilation. The Infectious Control Committee of Nakhorn Pathom Hospital reported that nosocomial infection caused by multidrug-resistant *Acinetobacter baumannii* infection was the major concern with the highest incident rate (81.18%) among all multi-resistant infections in 2004. The majority of them were associated with mechanical ventilation dependent. A surveillance of multidrug-resistant *Acinetobacter baumannii* isolates were susceptible to imipenem 63% in 2003 and only 29% in 2004.

Even though the hospital has set the Infection Control Program and working actively on this, but incidence of MDRAB infection is increasing in the patients who were mechanical ventilator dependent. There were many studies about the risk factors for colonization or infection with multidrug-resistant *Acinetobacter baumannii* including length of in the hospital stayed, surgical course, wounds treatment, antibiotics treatment, parenteral nutrition, indwelling catheter, mechanical ventilator, and intensive care course(16).

The aim of this study is to determine the risk factors associated with multidrug-resistant *Acinetobacter baumannii* colonization or infection of VAP at Nakhon Pathom Hospital, in Nakhon Pathom Province. The result from this study is expected to be implied in nosocomial prevention program of Nakhon Pathom Hospital.

General objectives

To determine incidence and risk factors associated with multidrug resistant *Acinetobacter baumannii* infection in mechanical ventilator dependent patients who were admitted at Nakhon Pathom Hospital during December 2005 to August 2006.

Specific objectives

1. To determine the incidence of ventilator – associated pneumonia caused by multidrug resistant *Acinetobacter baumannii* in Nakhon Pathom Hospital
2. To determine the risk factors associated with multidrug resistant *Acinetobacter baumannii* ventilator – associated pneumonia among the ventilator dependent patients at Nakhon Pathom Hospital.

Hypothesis

There was an association between multidrug resistant *Acinetobacter baumannii* infection, in mechanical ventilator dependent patients, and the following risk factors :

- age
- sex
- ward of admission
- prior antibiotic usage
- underlying disease
- severity of illness
- wounds
- tracheostomy
- aerosol nebulizer

- central venous line
- inter-costal drainage
- stress ulcer prophylaxis
- antibiotic therapy

Definition of Variables

Ventilator – Associated Pneumonia (VAP): refers to nosocomial pneumonia in the patients who were dependent on mechanical ventilation support (by endotracheal tube or tracheostomy tube) for more than 48 hours, and had been diagnosed of pneumonia by the appearance of a new or progressive pulmonary infiltrate, fever, leukocytosis, and purulent tracheobronchial secretion.

Multidrug resistant *Acinetobacter baumannii*: refers to *Acinetobacter baumannii* agent which was resisted to the third generation of cephalosporin more than 3 drugs including ceftazidime, cefotaxime, ceftriaxone and gentamycin.

Incidence of VAP caused by multidrug resistant *Acinetobacter baumannii*: refers to number of the patient, who had developed VAP after 48 hours of mechanical ventilation assisted caused by multidrug resistant *Acinetobacter baumannii*, divided by 1000 ventilator days.

Colonization to multidrug resistant *Acinetobacter baumannii*: refers to agent of multidrug resistant *Acinetobacter baumannii* which was isolated from respiratory secretion of patients and had no clinical, radiographic or laboratory evidence of pneumonia.

Intubation: refers to the insertion of an endotracheal tube and tracheostomy tube into a body canal or hollow organ, e.g. trachea.

Tracheostomy: refers to creation of an opening in the anterior trachea by insertion of a tube to relieve upper airway obstruction and to facilitate ventilation.

Mechanical ventilation: refers to the method with mechanically assistant for spontaneous breathing of the patient and must be done after intubation with an endotracheal or tracheostomy tube.

Underlying disease: refers to disease diagnosed of having chronic diseases and past history of sickness which had an impact to respiratory failure such as chronic obstructive pulmonary diseases, respiratory failure, cancer, diabetes mellitus(DM).

Severity of illness: refers to severity of illness which was categorized, by the infection control department at the time of intubation on the basis of functional capacity of the patient, into 5 categories, such as:

SIC 1: No significant disease present, healthy.
SIC 2: Mild to moderate systemic disease present, fairly well controlled, no life-threatening upon hospital admission.
SIC 3: Severe systemic disease present, not well controlled but not life-threatening upon hospital admission.
SIC 4: Severe life-threatening upon this hospital admission.
SIC 5: Death expected upon this hospital admission

Ward of admission: refers to hospital ward where the intubated patient was admitted including medical ward, surgical ward, private ward, and intensive care units.

Wounds: refers to post operation wounds or pressure sores or any wounds that results in a skin break down or opening in the skin.

Stress ulcer prophylaxis: refers to protocol to prevent the development of stress ulcer by giving H_2 blocker antagonists or antacid or sucralfate.

Prior antibiotic usage: refers to the use of antibiotics within 4 weeks before having multidrug resistant *Acinetobacter baumannii* ventilator – associated pneumonia.

Antibiotic therapy: refers to a type, number, and duration of antimicrobial drugs that the patient received between the time of admission to before having multidrug resistant *Acinetobacter baumannii* infection.

Operational Definition of Survival Analysis

Survival analysis: A class of statistical procedure for estimating the survival function, and for making inferences about the effects of infection, prognostic factors, exposures, and other covariates.

Survival function (Syn: survival distribution): A function of time, usually denoted by *S(t)*, that starts with a population 100% well at a particular time and provides the percentage of the population still well at later time. Survival function may be applied to any disease events, for example, incidence of infection or relapsed or recovery after the onset of infection.

Event: The event that is defined as a Ventilator Associated Pneumonia caused by multidrug-resistant *Acinetobacter baumannii* in patients after intubations.

Survival time: The time that was measured since the initiation of intubation with mechanical ventilator to the event of Ventilator Associated Pneumonia by MDR-AB nosocomial infection until taking off mechanical ventilator.

Median survival time: The value of which 50% of the intubated patients with mechanical ventilator have longer survival times and 50% had shorter survival times.

Survival rate (Syn: cumulative survival rate): The proportion of patients after intubation and had no Ventilator Associated Pneumonia caused by multidrug-resistant *Acinetobacter baumannii* (e.g., a 7 day period) who survive to the end of the interval.

Proportional hazard models: Represent an adaptation of multiple logistic regression which used a conventional technique for investigation the relationship between survival time and possible prognosis variables.

CHAPTER II
LITERATURE REVIEW

Review of literature included the following topic:

1. Ventilator associated pneumonia
    - 1.1 Epidemiology
    - 1.2 Diagnosis and microbiology
    - 1.3 Pathogenesis

2. Multiply antibiotic-resistant Gram- negative bacilli
    - 2.1 Definition and Mechanisms of multiple resistance
    - 2.2 Diagnostic criteria of multidrug-resistant *Acinetobacter* infection
    - 2.3 The Epidemiology of Multidrug-resistant *Acinetobacter baumannii*
    - 2.4 Emergence of selected multidrug-resistant bacteria in VAP
    - 2.5 Source of resistance strains
    - 2.6 Modes of transmission

3. Risk factors related VAP caused by multidrug resistant *Acinetobacter baumannii*(MDRAB) infection
    - 3.1 Demographic Factors
        - 3.1.1 Age
        - 3.1.2 Disease and basic factors
        - 3.1.3 Severity of illness
        - 3.1.4 Wound
        - 3.1.5 Prior antibiotic usage
    - 3.2 Risk factors from treatments.
        - 3.2.1 Antibiotic therapy
        - 3.2.2 Intubation

3.2.3 Tracheostomy

3.2.4 Stress Ulcer Prophylaxis

3.3 Environment Factors

3.3.1 Ward of admission

3.3.2 Department

Ventilator-associated pneumonia (VAP)

Ventilator associated pneumonia is a frequent complication of mechanical ventilation and causes increased mortality, morbidity, and costs(17). There are several clearly defined risk factors for VAP, and awareness of these can facilitate early diagnosis and hence treatment.

Epidemiology

VAP is usually caused by bacteria, is currently the second most common nosocomial infection in the United States, and is associated with high mortality and morbidity (2). The presence of VAP increases hospital stay by an average of 7 to 9 days per patient and has been reported to produce an excess cost of more than $40,000 per patient (18). Although VAP is not a reportable illness, available data suggest that it occurs at a rate of between 5 and 10 cases per 1,000 hospital admissions, with the incidence increasing by as much as 6- to 20-fold in mechanically ventilated patients (7, 9).

HAP accounts for up to 25% of all ICU infections and for more than 50% of the antibiotics prescribed (19). VAP occurs in 9–27% of all intubated patients(4). In ICU patients, nearly 90% of episodes of HAP occur during mechanical ventilation.
In mechanically ventilated patients, the incidence increases with duration of ventilation.

The risk of VAP is highest early in the course of hospital stay, and is estimated to be 3%/day during the first 5 days of ventilation, 2%/day during Days 5 to 10 of

ventilation, and 1%/day after this (10). Because most mechanical ventilation is short term, approximately half of all episodes of VAP occur within the first 4 days of mechanical ventilation. The intubation process itself contributes to the risk of infection, and when patients with acute respiratory failure are managed with noninvasive ventilation, nosocomial pneumonia is less common (17).

Time of onset of pneumonia is an important epidemiologic variable and risk factor for specific pathogens and outcomes in patients with HAP and VAP . Early-onset HAP and VAP, defined as occurring within the first 4 days of hospitalization, usually carry a better prognosis, and are more likely to be caused by antibiotic sensitive bacteria. Late-onset HAP and VAP (5 days or more) are more likely to be caused by multidrug-resistant (MDR) pathogens, and are associated with increased patient mortality and morbidity(20). However, patients with early-onset HAP who have received prior antibiotics or who have had prior hospitalization within the past 90 days are at greater risk for colonization and infection with MDR pathogens and should be treated similar to patients with late-onset HAP or VAP .

The crude mortality rate for VAP may be as high as 30 to 70%, but many of these critically ill patients with VAP die of their underlying disease rather than pneumonia. The mortality related to the HAP or "attributable mortality" has been estimated to be between 33% and 50% in several case-matching studies of VAP. Increased mortality rates were associated with bacteremia, especially with *Pseudomonas aeruginosa* or *Acinetobacter* species, medical rather than surgical illness, and treatment with ineffective antibiotic therapy (21). Other studies using similar methodology failed to identify any attributable mortality due to VAP, suggesting a variable outcome impact, according to the severity of underlying medical conditions .

Diagnosis and Microbiology

Clinical diagnosis relies on the patient having received mechanical ventilation for a prolonged period (generally longer than 48 h, and sometimes 72 h), and various

signs of pneumonia, including new or changing pulmonary infiltrates on X-ray, fever, leukocytosis, raised C-reactive protein, purulent tracheal secretions, etc.

Diagnosis in pneumonia case in the hospital adapted from CDC Surveillance definition of nosocomial infection that is considered by signs and symptoms on daily including data from laboratory, X-ray and any of the following :

Criteroin 1. Patient has rales or dullness to percussion on physical examination of the chest. And at least one of the following :

New onset of purulent sputum or change in characteristic of sputum.

Organism cultured for blood.

Isolation of an etiologic agent from a specimen obtained by transtracheal aspirate, bronchial brushing, biopsy.

Criteroin 2. Patient has a chest radiographic examination that shows new or progressive infiltrate, consolidation, cavitation, or pleural effusion plus at least two of the following : (3,5)

2.1 Body temperature > 38.5 °C or < 35 °C

2.2 A leukocyte count of more than 10,000 per cubic millimeter or less than 5,000 per cubic millimeter.

2.3 New onset of purulent sputum or change in characteristic of sputum.

2.4 Isolation of an etiologic agent from a specimen obtained by transtracheal aspirate, bronchial brushing, biopsy.

Pathogenesis of VAP

For VAP to occur, the delicate balance between host defenses and microbial propensity for colonization and invasion must shift in favor of the ability of the pathogens to persist and invade the lower respiratory tract. Sources of infection for VAP include healthcare devices or the environment (air, water, and equipment) and

can occur with transfer of microorganisms between staff and patients (22). A number of host- and treatment-related colonization factors, such as the severity of the patient's underlying disease, prior surgery, exposure to antibiotics, other medications, and exposure to invasive respiratory devices and equipment, are important in the pathogenesis of VAP(21) .

VAP requires the entry of microbial pathogens into the lower respiratory tract, followed by colonization, which can then overwhelm the host's mechanical (ciliated epithelium and mucus), humoral (antibody and complement), and cellular (polymorphonuclear leukocytes, macrophages, and lymphocytes and their respective cytokines) defenses to establish infection (23). Aspiration of oropharyngeal pathogens or leakage of bacteria around the endotracheal tube cuff is the primary route of bacterial entry into the trachea . The stomach and sinuses have been suggested as potential reservoirs for certain bacteria colonizing the oropharynx and trachea, but their importance remains controversial . Some investigators postulate that colonization of the endotracheal tube with bacteria encased in biofilm may result in embolization into the alveoli during suctioning or bronchoscopy(20). Inhalation of pathogens from contaminated aerosols, and direct inoculation, are less common . Hematogenous spread from infected intravascular catheters or bacterial translocation from the gastrointestinal tract lumen are quite rare.

Multiply antibiotic-resistant Gram- negative bacilli

Since the 1960s reports of antibiotic-resistant bacteria in hospitals have appeared with increasing frequency. For example, before 1965 no hospital outbreaks involving multiply antibiotic-resistant gram negative bacilli were investigated by the Centers of Disease Control. Bacteria resistant has become a fact of hospital life . One of the major side effects of broad spectrum antibiotic usage and advanced invasive medical techniques is the emergences and spread of multiply antibiotic-resistant Gram- negative bacilli(MRGN)(24). These organisms may be intrinsically resistant to the more commonly used ß-lactam antibiotics or, more usually, carry antibiotic-

resistance plasmids, which can spread not only between the same species, but also to other species. MRGNs are now endemic in most hospital environments.

Definition and Mechanisms of multiple resistance

Although there is no standard definition for multiple resistance in bacteria, one definition commonly used is resistance to two or more unrelated antibiotics to which the bacteria are normally considered susceptible. Alternatively, resistance to certain key or first line drugs may be used as a marker for problems, such as aminoglycoside resistance in gram negative bacilli. In this study, multidrug resistant *Acinetobacter baumannii* refers to *Acinetobacter baumannii* become resistant to the third generation of cephalosporin more than 3 drugs including ceftazidime, cefotaxime, ceftriaxone and gentamycin(25).

The most common mechanisms of resistance include production by bacteria of antibiotic- inactivating enzymes, such as penicillinases or aminoglycoside-modifying enzymes; changes in cell wall permeability or take up of antibiotics ; alteration in target sites, such as ribosome; changes in susceptible metabolic pathways; or changes in cell wall binding sites that prevent antibiotic attachment.

Diagnostic criteria of multidrug-resistant *Acinetobacter* infection

Determinating whether resistant bacteria are hospital acquired is often problematic since patients may be colonized asymptomatically when they enter the hospital. In addition to the difficulties in defining hospital acquisition , we considered colonization an important epidemiologic problem since is increases the reservoir of resistant bacteria and is often a precursor to clinical disease.

From a microbiologic standpoint, defining resistance may have pitfalls. Infection or colonization with *Acinetobacter* is usually diagnosed by clinical culture of blood, sputum, urine, wound, sterile body fluid, etc. Microbiologic cultures can be processed by standard methods on routine media. Antimicrobial susceptibility can be determined by various means, with the agar-dilution method being the gold-standard.

Definitions for "multidrug-resistance" vary widely in the published literature. At our institution, multidrug-resistant *Acinetobacter* is defined as *Acinetobacter baumannii* become resistant to the third generation of cephalosporin more than 3 drugs including ceftazidime, cefotaxime, ceftriaxone and gentamycin(26).

The Epidemiology of Multidrug-resistant *Acinetobacter baumannii*

Acinetobacter is a group of bacteria commonly found in soil and water. It can also be found on the skin of healthy people, especially healthcare personnel. While there are many types or "species" of *Acinetobacter* and all can cause human disease, *Acinetobacter baumannii* accounts for about 80% of reported infections(27). Outbreaks of *Acinetobacter* infections typically occur in intensive care units and healthcare settings housing very ill patients(28). *Acinetobacter* infections rarely occur outside of healthcare settings. *Acinetobacter* causes a variety of diseases, ranging from pneumonia to serious blood or wound infections and the symptoms vary depending on the disease(29). Typical symptoms of pneumonia could include fever, chills, or cough. *Acinetobacter* may also "colonize" or live in a patient without causing infection or symptoms,especially in tracheostomy sites or open wounds. *Acinetobacter* poses very little risk to healthy people. However, people who have weakened immune systems, chronic lung disease, or diabetes may be more susceptible to infections with *Acinetobacter*.

Hospitalized patients, especially very ill patients on a ventilator, those with a prolonged hospital stay, or those who have open wounds, are also at greater risk for *Acinetobacter* infection(30, 31). *Acinetobacte* can be spread to susceptible persons by person-to-person contact, contact with contaminated surfaces, or exposure in the environment(32). *Acinetobacter* can live on the skin and may survive in the environment for several days. Careful attention to infection control procedures such as hand hygiene and environmental cleaning can reduce the risk of transmission.

For more information on infection control practices and hand hygiene. *Acinetobacter baumannii* is primarily a healthcare-associated pathogen(33). It is increasingly reported as the cause of outbreaks and nosocomial infections such as blood-stream infections, ventilator-associated pneumonia, urinary tract infections and wound infections. *Acinetobacter* isolates demonstrate increasing resistance to commonly prescribed antimicrobials(34). Multidrug-resistant Acinetobacter baumannii has been reported worldwide and is now recognized as one of the most difficult healthcare-associated infections to control and treat. In a report of a citywide clonal outbreak in New York City, 53% of *A. baumannii* were resistant to carbapenems while 12% were resistant to all standard antimicrobial agents(35).

In the 1998 – 2004 , National Antimicrobial Resistance Surveillance, Thailand (NARST), reported top ten multidrug- resistant isolated from all region of 32 hospitals in Thailand(36). *Acinetobacter baumannii* was one among the top ten isolates accounted for 4% - 6%. The first one was *E.coli* 16%, and followed by *Pseudomonas aeruginosa* 11% and *Klebsiella pnuemoniae* 10% . From the Annual Epidemiological Surveillance report in 2003, a surveillance of multidrug-resistance isolates, *Acinetobacter calcoaceticus - baumannii complex* isolates were susceptible to aztreonam 1%, less than 35% to ceftazidime , piperacillin/tazobactam and quinolone, 65% to imipenam, 34% to gentamycin, 60% to netilmcin, and 82% to amikacin, only 29% were susceptible to cotrimazole.

Multidrug-resistant *Acinetobacter* rarely causes serious infection in otherwise healthy people, and therefore poses minimal threat to healthcare workers or patients' family members(12). Pregnant healthcare workers are not at increased risk from this organism, and can therefore care for patients infected or colonized with the organism. Outbreaks are frequently located in intensive-care units and burn units involving patients on mechanical ventilation(37, 38, 39). An outbreak of MDR Acinetobacter at our institution was linked to the use of a pulsatile lavage with suction device for wound care(40, 41). Widespread environmental contamination and healthcare-associated transmission of the organism occurred during this outbreak. As a result, The Hospital Epidemiology and Infection Control Department at The Johns Hopkins

Hospital has implemented new infection control precautions that are followed for all pulsatile lavage with suction treatments

Emergence of selected multidrug-resistant bacteria in VAP

VAP may be caused by a wide spectrum of bacterial pathogens, may be polymicrobial, and are rarely due to viral or fungal pathogens in immunocompetent hosts(39). Common pathogens include aerobic gram-negative bacilli, such as *P. aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Acinetobacter* species. Infections due to gram-positive cocci, such as *Staphylococcus aureus*, particularly methicillinresistant *S. aureus* (MRSA), have been rapidly emerging in the United States(42).

The frequency of specific MDR pathogens causing VAP may vary by hospital, patient population, exposure to antibiotics, type of ICU patient, and changes over time, emphasizing the need for timely, local surveillance data(35, 43). VAP involving anaerobic organisms may follow aspiration in non intubated patients, but is rare in patients with VAP. In fact, MRSA and *K. pneumoniae* were more common in nonventilated than ventilated patients, whereas certain resistant gram-negative bacilli were more common in patients with VAP (*P. aeruginosa, Stenotrophomonas maltophilia*, and *Acinetobacter* species).

Rates of VAP due to MDR pathogens have increased dramatically in hospitalized patients, especially in intensive care and transplant patients(44). Data on mechanisms of antibiotic resistance for specific bacterial pathogens have provided new insight into the adaptability of these pathogens. Acinetobacter species, Stenotrophomonas maltophilia, and Burkholderia cepacia although generally less virulent than *P. aeruginosa, Acinetobacter* species have nonetheless become problem pathogens because of increasing resistance to commonly used antimicrobial agents.

Source of resistance strains

The source of most resistance strains in hospitals appears to be patients who are colonized or infected(25). Because the normal pharyngeal and intestinal flora of hospitalized patients may be displaced by multiply resistant bacteria, there are often many colonized patients for each patients with recognized infection-the ice-berg effect. Personnel occasionally have been documented to disseminated resistant gram positive strains, such as MRSA. However, personnel carriage of resistant gram negative bacilli appears to be very unusual. *Acinetobacter*, one of the few gram negative bacilli that may be among normal skin flora, was noted in one outbreak to recur periodically despite disinfection of the environment reservoirs.

Reservoirs of MRGN include of hand of staff, stool of patients on broad spectrum antibiotic, drains and sinks, poorly disinfected clinical equipment, and bars of soap lying in pool of water(12, 24). Routes of spread MRGNs are spread via hand and non compliance with hand disinfection procedures, bedpans and urinals, bed clothes that become contaminated with urine or faeces, staff sitting on the beds of colonized patients, use of antibiotics that further select or plasmids conferring antibiotic resistance , and open containers of contaminated disinfectants and other fluid on the ward.

Modes of transmission

The most important way that resistant bacteria are spread in the hospital is from an infected patient to a susceptible patient via transient carriage on hands of personnel. Common source spread of resistant strains has been noted primary in out break setting(24). Sources of transmission identified of MDRAB in the outbreak setting include predominately respiratory equipment such as resuscitator bags, valves, ventilator circuits, spirometers, peak flow meters, suction catheters, etc. Other sources include humidifiers, warming baths, multidose vials, distilled water, pillows, mattresses, bedpans, showers and water faucet aerators. No source was identified in approximately 50% of reported outbreaks(12). Airborne spread of resistant bacteria has been documented rarely.

Risk factors related VAP caused by multidrug resistant *Acinetobacter baumannii* infection

The patient who were intubation have defense mechanism to reject the ventilation which could be another risk factors to VAP. In several study, the risk factors for colonization or infection with multidrug-resistant *Acinetobacter* include length of hospital stay, surgery, wounds, treatment with broad-spectrum antibiotics, parenteral nutrition, indwelling catheters, mechanical ventilation, and admission to an intensive care unit(37, 38, 45). as follows :

1. Demographic Factors

- Age : Facon et al (20) show that incidence rate of VAP in patients average age 65 years but age factors were not directly risk factors to may be increasing of another medical underlying disease and cause of illness which admission in hospitals while the studies of Torres et al, show that age was not statistics significantly associated with VAP.

- Disease and basic factors such as coma, hypertension, metabolic acidosis, chronic alcoholism, diabetic mellitus, neutropenia, neutrophillia, chronic obstructive pulmonary disease (COPD) , human immunodeficiency, cardiovascular disease and malnutrition. Torres et al, show that the patient who were underlying disease not severity would be VAP at 10 % but the patient who were underlying disease severity would be VAP at 24%.

- Severity of illness : The patient who used ventilations were severity signs and symptoms because of underlying disease and complications. The critical ill patients had be risk factors for colonization in respiratory tract by Enteric Gram Negative Bacilli (EGNB) and were be VAP. Johnanson et al, show that EGNB was colonization in oral cavity and pharynx of patients would be associated with level of severity disease although seldom finding EGNB in oral cavity and pharynx of

normal persons but finding that the most critical ill patients would be these EGNB at 75 %. The study of Jose Ganacho-Montero et al, show that the severity of illness measurement by Acute Physiology and Chronic Health Evaluation (APACHE) to prognosed of VAP caused by *Acinetobacter baumannii* did not differ from that with other virulent pathogens(46), but the SOFA score on the day of diagnosis was the only independent predictor of in hospital mortality. In further study , Lorthalary et al, (13)show that the severity of illness on admission was an independent risk factors for nosocomial acquisition of multi- resistant *Acinetobacter baumannii.*

- Wounds : In Division of Health care Quality Promotions, Centers of Disease Control and Prevention, 2004, suggest about general information of *Acinetobacter* infection that hospitalized patients, especially very ill patients on a ventilator, those with a prolonged hospital stay, or those who have open wounds, are also at great risk for *Acinetobacter* infection. Aharon Abbo et al, 2001, study on a matched case control study to identify the individual risk factors for having multi-resistant *Acinetobacter baumannii*, show that the case patients have wound site infection were 19.5% in the study(47). Maragakis LL et al, show that an outbreak of MDR *Acinetobacter* in a 1000 bed tertiary care hospital in Baltimore in 2003 was linked to the use of a pulsatile lavage with suction device for wound care(41). In a well-design(45), of all intubated patients who have *A. baumannii* bacteremia infection with nosocomial pneumonia, received surgery more than the patient who was not surgery 2.8 times(Zhou P, Chen EG, 2004).

- Prior antibiotic usage : Prior antibiotic use can be associated with an increased risk of late onset pneumonia. Trouillet et al , have show that patients having and ICU stay of more than 7 days and having received antibiotics within the past 2 weeks are at high risk of having infection with potential drug resistant organism (20)such as *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, Stenotrophomonas spp., and MRSA. Prior use of broad spectrum drugs were the most important risk factors associated with antibiotic resistant bacteria. Rello, J E et al, show that prior antibiotic therapy, particularly third generation cephalosporin agents, increased the likelihood of VAP due to oxacillin- resistant staphylococci and highly resistant gram-

negative bacilli(10). Jose Garnacho-Montero, et al, study on a prospectively study of *Acinetobacter baumannii* isolation imipenem resistant in VAP in ICU, Spain 2004 shown that prior imipenem exposure was associated with the isolation of imipenem resistant strains more than the patient who was not prior imipenem exposure 4 times(46).

2. Risk factors from treatments.

- Antibiotic therapy : American Thoracic Society Documents, 2004, suggestion to the combination antibiotic therapy and dosage of antibiotics for empirical antibiotic therapy of VAP in patient with risk factor for multidrug resistance *Acinetobacter baumannii* as antipsuedomonal cephalosporin (cefepime,ceftazidime) or antipsuedomonal carbapenem (immipenem or meropenem) or ß-Lactam(piperacillin-tazobactam) plus antipsuedomonal fluoroquinolone (ciprofloxacin or levofloxacin) or aminoglycoside(amikacin,gentamicin, or tobramycin(17).

Antibiotic therapy especially cephalosporins and the routine of combination antibiotic therapy had been advocated as a means of reducing the subsequent emergence of bacterial resistance and was be risk factors of VAP by increasing of colonization and incidence rate of VAP from gram negative bacterial in gastrointestinal tract. *Pseudomonas aeruginosa, Acinetobacter baumannii* and MRSA were several bacterial resistant. Jose Garnacho-Montero, et al, study on a prospectively study of *Acinetobacter baumannii* isolation imipenem resistant in VAP in ICU, Spain 2004 shown that adequacy of empirical antibiotic therapy was a protective factor(46). Gruoon D et al, show a program of antibiotic strategy control to restricted use of ceftazidime and ciprofloxacin in patients who admitted in ICU can minimize the incidence of VAP caused by potential antibiotic resistant microorganisms significantly.

- Intubation : Intubation shows that risk of VAP was increasing post intubation and used ventilation by increasing amount days until the second day of intubation or increasing risk at 1 % every one day(39, 45). Torres et al, show that intubation more than one time was risk factors which associated with VAP. Siham Mahgoub, et al., study on a retrospectively review in 2002 of all *A.baumannii* isolates from miscellaneous site in 2 community teaching hospital, Queens, New York , factors associated significantly with *A.baumannii* isolates from non sterile respiratory were mechanical ventilator , prior antibiotic use and ICU stay(48, 49). Same of study of Vincent JL, 2004, mechanical ventilation was associated with multidrug resistant *Acinetobacter baumannii* colonization or infection(3).

- Tracheostomy tube : Celis et al, show that the patient who was tracheostomy would be risk of VAP more than the patient who was not tracheostomy 3.5 times and the patient who was tracheostomy and used ventilators for a long time would be risk of VAP more than the patient who was not intubation at 20.9 times(50). Mah et al, show the outbreak in patients who have *Acinetobacter baumannii* acquisition was independently associated with presence of a tracheostomy, presence of a central venous catheter, and duration of mechanical ventilation(51).

- Stress ulcer prophylaxis such as sucralfate, antacid and H2 receptor antagonists finding that lowering gastric pH was increasing incidence of VAP. Torres et al, show that incidence of VAP in patient who was used antacid or H2 receptor antagonists more than two times of patients who was not used antacid. A gastro pulmonary route of colonization can be demonstrated in at least 30-40 % of intubated patients(21, 52) (Tryba, et al). In a randomized study of 244 mechanically-ventilated patients, the potential benefit of using sucralfate was confirmed. Prod-hom et al, show that late onset VAP was observed in only 5% of the patients who had received sucralfate, compared with 16 and 21% of the patients who had receive antacids or ranitidine, respectively.

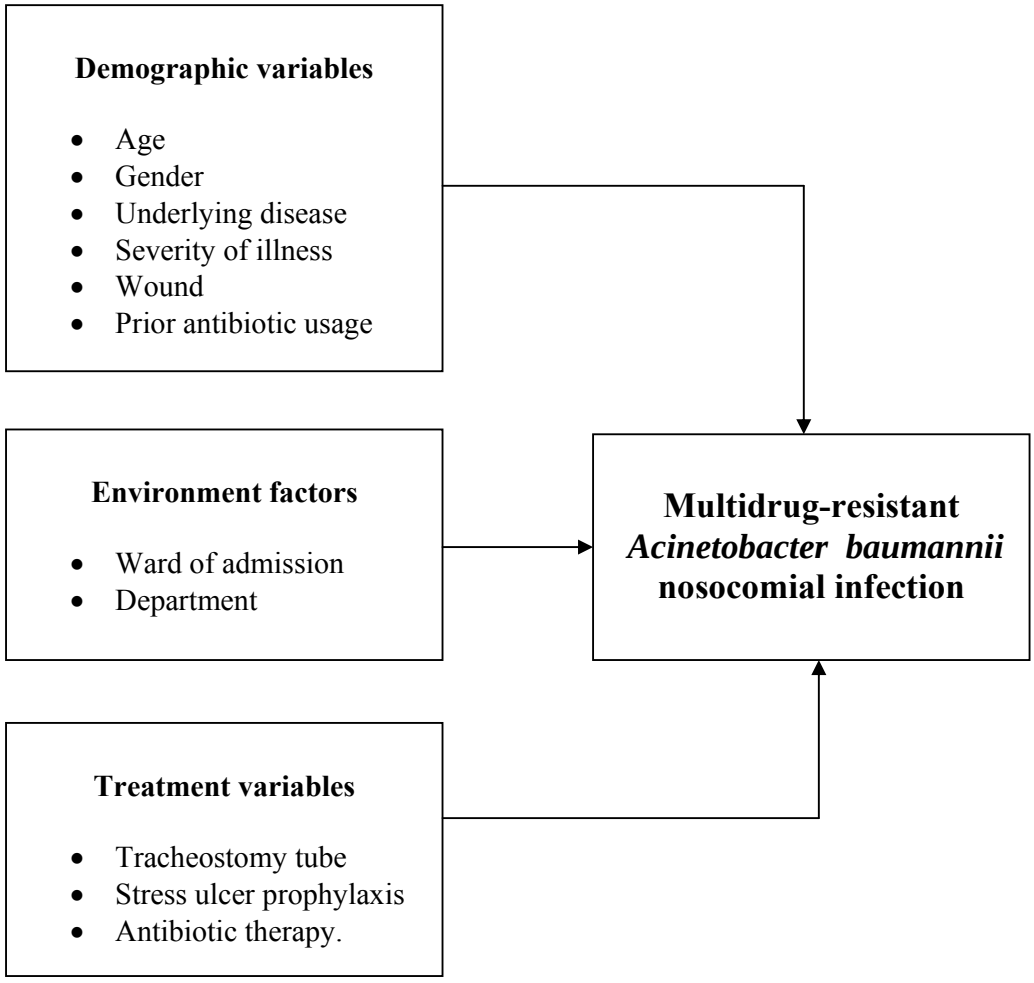
3. Environment Factors

- Ward of admission : Intensive care unit (ICU) -acquired lower respiratory tract infection include acute tracheobronchitis and hospital-acquired and ventilator associated pneumonia (VAP). ICU ventilated patients with VAP have a 2 to 10 fold higher risk of death than patients without it. The Greece study(11, 28), 68 % of the isolates of multi-resistant *Acinetobacter baumannii* recovered from the intensive care units. Rodrigues-Bano J et al, study in a prospective multi center cohort, of 25 Spain hospitals , all cases of *Acinetobacter baumannii* colonization and infection were highest in intensive care units(53).

The study of nosocomial infection by multi-resistant pathogens of Jover Saenz A et al, have show that *Acinetobacter baumannii* showed the highest individual rate of incidence particularly, at the intensive care units significantly(26). In Taiwan, 2002, The out break of pan-drug resistant *Acinetobacter baumannii* (PDRAB) infection occurred in SICU of the National Taiwan University Hospital , report by S. H. Wang, et al(48). A study of Vincent JL et al, show that patients who admission to an intensive care unit were associated with multidrug resistant *Acinetobacter baumannii* colonization or infection. However, in China 2004, Zhou P et al, have studied prospective on patients who have trauma of head would be higher risk of *A. baumannii* bacteremia infection in intubated patients with nosocomial pneumonia more than the patient who was not have trauma of head at 4.2 times(45).

- Crowed people : Numerous outbreaks of hospital infection with *Acinetobacter* have been reported, and they are often associated with the spread of multi-resistant strains. The routes of spread of multiply antibiotic-resistant Gram-negative bacilli were the hand and non compliance with hand disinfection procedure, bedpans and urinals, bed clothes, staff sitting on the beds of colonized patients, use of antibiotics, and contaminated disinfectants(24). In study of Scott k et al, have show that several factors unique to intensive care units contribute to cross transmission of antimicrobial resistant pathogens(54).

Figure 1 Conceptual framework of multidrug resistant *Acinetobacter baumannii* nosocomial infection



CHAPTER III
MATERIAL AND METHOD

Research Design

Prospective cohort study was conducted to assess incidence of Ventilator Associated Pneumonia with multidrug resistant *Acinetobacter baumannii* (MDR-AB) nosocomial infection and the factors related to Ventilator Associated Pneumonia with multidrug resistant *Acinetobacter baumannii* infection in Nakhon Pathom Hospital, Nakhon Pathom Province, Thailand, during December 2005 to August 2006.

All patients with mechanical ventilator were follow up everyday for the episodes of Ventilator Associated Pneumonia by MDR-AB nosocomial infection and Ventilator Associated Pneumonia caused by other organisms until Ventilator Associated Pneumonia was found, the data were mainly retrieved from medical record and surveillance form.

Study population

This study was conducted in the in-patient units of Nakhorn Pathom Hospital, a 552-bed capacity tertiary care hospital, during December 2005 to August 2006. The study population were all mechanical ventilator dependent patients who were admitted in 14 wards consisted of 2 intensive care units, 2 surgical wards, 3 medical wards, and 7 private wards.

Inclusion Criteria

All mechanical ventilator dependent patients, in the same age group and older than 15 year-old, who were during the study period and agreed to participate in this study.

Exclusion Criteria

The patients with the following criteria were excluded from the study :

1. The mechanical ventilator dependent patients who have non-infectious origin such as:
   - atelectasis
   - pulmonary edema
   - postoperative changes
   - congestive heart failure
   - pulmonary hemorrhage
   - Acute Respiratory Distress Syndrome(ARDS)
   - pulmonary embolism
   - chemical aspiration
   - drug reaction
2. The mechanical ventilator dependent patients who had incomplete data for the analysis

Sample Size

The proportion was used to estimate the sample size of Ventilator Associated Pneumonia among mechanical ventilator dependent patients by the following formula.

$$n = \frac{Z^2_{\alpha/2}\, p\,(1-p)\, N}{Z^2_{\alpha/2}\, p\,(1-p) + (N-1)\, d^2}$$

p = proportion of Ventilator Associated Pneumonia by multidrug resistant *Acinetobacter baumannii* infection among mechanical ventilator dependent patients = 0.10 (European Prevalence of Infection in Intensive Care Study, 2005)

N = Number of target population = 3,385 patients (Jan – Dec, 2004)

α = Significant level = 0.05

d = Precision of estimation of 3 % = 0.025

$Z_{\alpha/2}$ = statistic value under standard normal curve = 1.96

n = minimum sample size = 483.4

There for, the minimum number of sample size of mechanical ventilator dependent patients was 484. The total sample size was 507 patients included in analysis for this study.

Material and Method

Material : The data collection was performed as follows:

1. Data collection form was constructed by the researcher, consisted of 2 following sections.

   Part1: General characteristics of the patient, included age, sex, hospital number, admission number, admission date, diagnosis, and ward of admission.

   Part 2: Multidrug-resistant *Acinetobacter baumannii* infection risk factors data which included underlying diseases, severity of illness, wounds, prior antibiotic usage, prior infection and co-infection. Treatment received was included such as: tracheostomy, neubulizer, intercostal drainage, central venous line, stress ulcer prophylaxis drugs, and antibiotic therapy.
2. The target surveillance for Ventilator Associated Pneumonia form (include the risk factors for multidrug resistant infection) were used for the data collection form retrieved the data form by the researcher and nurses.
3. The environment factors data, such as ward and department was collected from medical records by the researcher.
4. Severity of the illness of patients by classification for Ventilator Associated Pneumonia was measured at the time of diagnosis of intubation by infection control department. The functional capacity of the patient during hospitalization were classified in 5 levels:

   SIC 1: No significant disease present, healthy.

   SIC 2: Mild to moderate systemic disease present, fairly well controlled, no life–threatening on hospital admission.

   SIC 3: Severe systemic disease present, not well controlled but not Life-threatening on hospital admission.

   SIC 4: Severe life–threatening on this hospital admission.

   SIC 5: Death expected on this hospital admission

Method of Data Collection

1. The mechanical ventilator dependent patients were assessed by the researcher and nurses. The duration of event was starting since patients were intubated before acquiring Ventilator Associated Pneumonia to multidrug-resistant *Acinetobacter baumannii* nosocomial infection and Ventilator Associated Pneumonia in the patients was recorded.

2. Diagnosis of pneumonia cases in the hospital was adapted from CDC Surveillance definition of nosocomial infection which has been considered by signs and symptoms on daily basis. The *Acinetobacter* infection was diagnosed by laboratory culture of sputum.

3. Microbiological examination for MDR-AB nosocomial infection and Ventilator Associated Pneumonia was performed by the agar-dilution method for antimicrobial susceptibility, from laboratory culture of sputum. Definition for "multidrug-resistance" was defined as *Acinetobacter baumannii* becomes resistant to the third generation of cephalosporin more than 3 drugs including ceftazidime, cefotaxime, ceftriaxone and gentamycin.

4. Numbers of Ventilator Associated Pneumonia episode by MDR-AB nosocomial infection in one patients occurred more than one time during time of study.

5. The data of factors related to Ventilator Associated Pneumonia by MDR-AB nosocomial infection has been retrieved from medical records of the patients who were intubated during time of study and recorded in the data collection form.

6. The following variables were recorded as predisposing factors for the development of Ventilator Associated Pneumonia by MDR-AB nosocomial infection and infected by other microorganisms in intubated patients such as age, sex, ward of admission, underlying diseases, severity of illness, wounds, prior antibiotic usage, previous infection, co-infection, tracheostomy, neubulizer, inter-costal drainage, central venous line, stress ulcer prophylaxis, and antibiotic therapy. The follow-up assessment started from the beginning of intubations until taking off the mechanical ventilator.

Statistical Analysis

Descriptive statistics:

1. Descriptive statistics such as frequencies, percentages were used to describe the demographic data of the study population.

2. Description cumulative rate of Ventilator Associated Pneumonia caused by multidrug-resistant *Acinetobacter baumannii* was calculated.

Causal analytic statistics:

1. Univariate analysis: Survival analysis with Kaplan-Meier was used to estimate survival function, median survival time and survival rate by independent factors. The log-rank test was used for crude comparing of survival rate between or among variables.

2. Multivariate analysis: Cox' s proportional hazard model was used to explore the factors associated with Ventilator Associated Pneumonia caused by multidrug-resistant *Acinetobacter baumannii*. The Incidence density by adjusted hazard ratio and 95%confident interval to measure the strength of the association.

CHAPTER IV
RESULTS

The study was carried out at Nakhon Pathom Hospital, Nakhon Pathom Province to determine the association of some risk factors with multidrug-resistant *Acinetobacter baumannii* infection among intubated patients who on mechanical ventilator. The site of study included two intensive care units, two surgical wards, three medical wards, and seven private wards. Total 507 patients with mechanical ventilator admitted during December 2005 to August 2006 were followed up and included in the analysis.

Results were presented as follow:

1. Characteristics of study population.
2. Cumulative Incidence and Incidence Density rate of Ventilator Associated Pneumonia rate, Ventilator Associated Pneumonia by multidrug resistant *Acinetobacter baumannii*.
3. To analyze comparative differences of survival time of Ventilator Associated Pneumonia by multidrug resistant *Acinetobacter baumannii* patients with personal factors , treatment factors and environment factors by using the Kaplan-Meier and the log-rank test .
4. To analyze relationship between independent factors and survival time by Cox's Proportional Hazard Model(unadjusted).
5. Multivariate Analyses of the relationships between independent factors and survival time by Cox's Proportional Hazard Model.

Part 1 Characteristics of the study population

The general characteristics of study population

The majority of the cases were male (57.40%) , and proportion of female was 42.60%. The patient's age ranged from 15 to 98 years with mean age of 57.85 years. There was 32.93 % of the patients was in the age group 55-74 years followed by age group more than or equal to 75 years old (26.83 %). The time on mechanical ventilator in study population ranged from 2 days to 273 days. The mean of ventilator days was 18.52 days (SD ± 28.72 days). About 45.37% of cases was on mechanical ventilator more than 48 hours to 7 days, the less were on mechanical ventilator more than 8 days to 14 days (18.73 %), more than 28 days (18.34 %), 15 days to 21 days (10.05 %), and 7.51 % was on mechanical ventilator 22 days to 28 days, respectively. (Table 1)

Table 1 General characteristics of the study population

General Characteristics	Number (n)	Percent (%)
Total	507	
Gender		
Male	291	57.40
Female	216	42.60
Age (years)		
15-34	101	19.92
35-54	103	20.32
55-74	167	32.93
More than 75	136	26.83
Time on mechanical ventilator		
More than 48 hours – 7 days	230	45.37
8 – 14 days	95	18.73
15 – 21 days	51	10.05
22 – 28 days	38	7.51
More than 28 days	93	18.34

The medical characteristics of study population

Level 3 of severity of illness was commonly found in this study (67.65 %), followed by severity of illness level 4 and level 5 found in 17.35%, and 7.70 %. Most of patients had underlying disease (77.72 %), and 22.28 % had no underlying disease. Underlying disease among study population were hypertension (40.43 %), followed by Diabetes mellitus (22.48%), Head injury (18.14 %), Respiratory failure (17.35 %), and Renal failure (14.0 %).

Most of cases had not received prior antibiotic before admission (83.44 %). Prior blood stream infection were found in patient with mechanical ventilator 11.04 %, followed by prior urinary tract infection 6.90% . About 36.68 % and 7.32 % of study population received surgery and had decubitus ulcer. There were co-infection by urinary tract infection 11.43 %, and 79.68% had not co-infection. (Table 2)

Table 2 Medical characteristics of study population

Medical Characteristics	Number (n)	Percent (%)
Total	507	
Severity of illness at the time of admission		
SIC 2	37	7.30
SIC 3	343	67.65
SIC 4	88	17.35
SIC 5	39	7.70
Known Underlying disease of the patients		
No underlying disease	113	22.28
Had underlying disease	394	77.72
Hypertension	205	40.43
Diabetes mellitus	114	22.48
Head injury	92	18.14
Respiratory failure	88	17.35
Renal failure	71	14.00
IHD*	43	8.48
COPD*	30	5.91
Cancer	19	3.74
Chest injury	14	2.76
TB*	13	2.56
Prior antibiotic treatment	84	16.56

* IHD = Ischaemic or ischemic heart disease , COPD = Chronic Obstructive Pulmonary Disease , TB = Tuberculosis

Table 2 Medical characteristics of study population (continued)

Medical Characteristics	Number (n)	Percent (%)
Presence of wound		
None	258	50.88
Surgical wound	186	36.68
Decubitus ulcer	37	7.32
Lacerated wound	26	5.12
Co- infection		
None	404	79.68
Having co- infection	103	20.32
Urinary tract infection	58	11.43
Blood stream infection	13	2.56
Skin and Soft tissue infection	16	3.15
Surgical Site infection	10	1.97
Urinary tract infection with Blood stream infection	6	1.18
Prior-infection		
None	398	78.50
Having prior - infection	109	21.50
Blood stream infection	56	11.04
Urinary tract infection	35	6.90
Skin and Soft tissue infection	7	1.38
Urinary tract infection with Blood stream infection	7	1.38
Surgical Site infection	2	0.44

The treatment factor of study population

Total 59.96 % of the cases received neubulizer. More than half of the patients (73.37 %) received tracheotomy tube. Most of cases had not received Inter costal drainage (96.45 %). Stress ulcer prophylaxis used in Ranitidine found more often (38.65 %) among patients with mechanical ventilator followed by Losec (16.56 %) , used Ranitidine and Losec (7.49 %) and Sulcralfate (0.6 %). Almost of study population was received single antimicrobial drug use (32.42%) and the less were in double antimicrobial drug use (25.88%), triple antimicrobial drug use (20.35 %), and multiple antimicrobial drug use (17.20%).

The most common used antimicrobial agents before Ventilator Associated Pneumonia by multidrug resistant *Acinetobacter baumannii* infection were Sulperazole (26.82 %), followed by Ceftriaxone (26.25 %), Rocephin (20.91 %), Amikin (18.15 %), and Tienem (16.8 0%), respectively. (Table 3)

The Hospital environment factor of study population

Almost of the patients were in medical department (60.15 %), and the less were in surgical department (36.10 %)and orthopedic department (3.15 %) . Regarding ward admitted, 71.79 % and 15.00 % were admitted in general ward and private ward respectively, followed by intensive care unit with the proportions of 13.21 %, respectively. (Table 4)

Table 3 Treatment factors of the study population

Treatment factors	Number (n)	Percent (%)
Tracheostomy	372	73.37
Nebulizer	304	59.96
Central venous line	57	11.24
Inter costal drainage	18	3.55
Stress ulcer prophylaxis		
None	186	36.68
Yes	321	63.32
Ranitidine	196	38.65
Losec	84	16.56
Ranitidine + Losec	38	7.49
Sulcralfate	3	0.60
Antibiotic therapy		
None	21	4.15
Single	164	32.42
Double	131	25.88
Triple	103	20.35
Multiple	87	17.20

Table 4 Environment factors of the study population

Environment factors	Number (n)	Percent (%)
Hospital Department		
Medical	305	60.15
Surgical	183	36.10
Orthopedic	16	3.15
Other	3	0.60
Ward		
General ward	364	71.79
Private ward	76	15.00
Intensive care unit	67	13.21

Part 2 Cumulative Incidence and Incidence Density rate of Ventilator Associated Pneumonia rate, Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii*.

Total person-days of the samples was 14,506 days and total ventilator days was 5,828 days. Of 507 patients, Ventilator Associated Pneumonia was found in 204 cases with total cumulative incidence of 40.23% (Table 5). Top five of pathogens of VAP were *Acinetobacter baumannii* (46.56%), followed by *Pseudomonas aeruginosa* (36.76%), *Klebsiella pnuemoniae* (10.29 %), *Methicillin Resistant Staphylococcus Aureus* (2.50 %) and *Escherichia Coli* (2.00 %) (Table 6). Ventilator Associated Pneumonia by multidrug resistant *Acinetobacter baumannii* was found in 89 cases. 88.8 % of cases were first episode of infection, second episode of infection, third episode of infection and forth episode of infection found in 7.9 % , 2.1 %, and 1.1 % , respectively (Table 5).

Overall incidence density of Ventilator Associated Pneumonia was 35.00 per 1000 ventilator days. Incidence of Ventilator Associated Pneumonia by multidrug resistant *Acinetobacter baumannii* was 17.55% and Incidence density of Ventilator Associated Pneumonia by multidrug resistant *Acinetobacter baumannii* was 21.75 per 1000 person-days and 30.62 per 1000 ventilator days. About Ventilator Associated Pneumonia by other organisms was found in 115 cases. The incidence of Ventilator Associated Pneumonia by other organisms was 22.68% and incidence density of Ventilator Associated Pneumonia by other organisms was 19.5 per 1000 person-days and 29.10 per 1000 ventilator days.

Table 5 Cumulative Incidence of Ventilator Associated Pneumonia by Multidrug-resistant *Acinetobacter baumannii* (MDRAB) and other organisms (n = 507)

Variable	Number of episode (n)	Incidence (%)
Total of all VAP	204	40.23
VAP by other organisms	115	22.68
VAP by MDRAB	89	17.55
First episode	79	88.80
Second episode	7	7.90
Third episode	2	2.20
Forth episode	1	1.10

Table 6 Cumulative Incidence by etiologic microorganisms of Ventilator Associated Pneumonia (n = 204)

Micro-organisms	Number (n)	Percent (%)
Acinetobacter baumannii	95	46.56
Multidrug Resistant *Acinetobacter baumannii* (MDRAB)	89	93.68
Pseudomonas aruginosa	75	36.76
Multidrug Resistant *Pseudomonas aruginosa*	19	25.33
Klebsiella pneumoniae	21	10.29
ESBL-Producing *Klebsiella pneumoniae* *	6	28.57
Methicillin Resistant *Staphylococcus aureus*	5	2.50
Escherichia coli	4	2.00

* ESBL Producing = Emerging Extended-Spectrum Beta-Lactamase Producing

Table 7 Incidence Density rate of Ventilator Associated Pneumonia by Multidrug-resistant *Acinetobacter baumannii* and by other organisms (n = 507)

Variable	Number VAP	Person-Time (ventilator-days)	Incidence density rate (per1000ventilator-days)
Overall	204	5,828	35.00
VAP by MDRAB	89	2,906	30.62
VAP by other organisms	115	3,951	29.10

Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* among male was slightly higher in those of female (23.45 vs 20.23 per 1000 person-days). Incidence density rate by age groups was higher 26.05 per 1000 person-days in the age groups 35-54 years. It was found that patients without underlying disease develop to Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumanni* (34.48 per 1000 person-days) higher than those having underlying disease. Incidence density rate by severity of illness was highest 24.05 per 1000 person-days in severity of illness level 3 (Table 8).

It was found that patients who had surgery wound develop Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumanni* (30.51 per 1000 person-days) higher than those patients who had lacerated wound or decubitus ulcer (29.41, 5.62 per 1000 person-days), respectively. Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* also found patients who had co-blood stream infection (23.38 per 1000 person-days) and prior urinary tract infection (29.85 per 1000 person-days)(Table 8).

Incidence density rate of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumanni* among the patients admitted in surgical department

(31.83 per 1000 person-days) was higher than those of orthopedic department and medical department (20.20 and 19.42 per 1000 person-days). Intensive care unit, the highest incidence of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumanni* 29.94 per 1000 person-days, followed by general ward and private ward (23.35 and 16.90 per 1000 person-days) (Table 8).

Incidence density of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumanni* in the patients who on inter-costal drainage, nebulizer, central venous line and tracheostomy were 26.08, 19.60, 18.86 and 16.60 per 1000 person-days, respectively. It was found incidence density of patients who had prior antibiotic therapy was 17.61 per 1000 person-days. Incidence density of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumanni* wad comparable between the patients who received ranitidine and losec were 21.63 and 10.04 per 1000 person-days(Table 8).

Incidence density of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumanni* among patients who received single antimicrobial drug use and the less were in triple antimicrobial drug use, multiple antimicrobial drug use, and double antimicrobial drug use were 53.63, 34.55, 28.22 and 24.82 per 1000 person-days, respectively(Table 8).

Table 8 Incidence Density of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* (n = 89)

Variable	Number VAP by MDRAB	Person-Time (person-days)	Incidence density rate (per 1000 person-days)
Total	89	4,093	21.75
Gender			
Female	45	2,224	20.23
Male	44	1,869	23.54
Age (year)			
15-34	14	1,009	13.87
35-54	16	614	26.05
55-74	33	1,223	26.98
75-94	26	1,247	20.85
Underlying disease			
None	12	348	34.48
Had underlying disease	77	3,745	20.56
Hypertension	50	2,717	18.40
Respiratory failure	28	1,406	19.91
Diabetes mellitus	22	1,320	16.66
Renal failure	18	1,064	16.91
Head injury	15	436	34.40
IHD	10	493	20.28
COPD	3	138	21.74
Chest injury	3	84	35.71
Cancer	1	29	34.48
TB	1	43	23.25

Table 8 Incidence Density of Ventilator Associated Pneumonia by multidrug resistant *Acinetobacter baumannii* (n = 89) (continued)

Variable	Number VAP by MDRAB	Person-Time (person-days)	Incidence density rate per 1000 person-days)
Severity of illness			
SIC 2	9	670	13.43
SIC 3	67	2,785	24.05
SIC 4	13	638	20.37
Prior antibiotic	36	2,044	17.61
Wound			
None	44	5,898	7.63
Surgical wound	22	721	30.51
Decubitus ulcer	18	3,202	5.62
Lacerated wound	5	170	29.41
Co- infection			
None	57	5,898	9.66
Urinary tract infection	19	970	19.58
Blood stream infection	6	268	22.38
Skin infection	4	335	11.94
Urinary tract infection with Blood stream infection	3	125	24.00
Prior-infection			
None	78	5,898	13.22
Urinary tract infection	6	201	29.85
Blood stream infection	4	3,818	1.05
Urinary tract infection with Blood stream infection	1	74	13.51

Table 8 Incidence Density of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* (n = 89) (continued)

Variable	Number VAP by MDRAB	Person-Time (person-days)	Incidence density rate (per 1000 person-days)
Department			
Medical	61	3,141	19.42
Surgical	24	754	31.83
Orthopedic	4	198	20.20
Ward			
General ward	56	2,398	23.35
Private ward	23	1,361	16.90
Intensive care unit	10	334	29.94
Tracheostomy	48	2,880	16.66
Nebulizer	69	3,519	19.60
Central venous line	8	424	18.86
Inter Costal Drainage (ICD)	3	115	26.08
Stress ulcer prophylaxis			
None	25	5,898	4.23
Ranitidine	36	1,664	21.63
Losec	17	1,693	10.04
Ranitidine + Losec	9	88	102.27
Sulcralfate	2	648	3.08
Antibiotic therapy			
None	1	68	14.70
Single	17	317	53.63
Double	24	966	24.84
Triple	17	492	34.55
Multiple	30	1,063	28.22

Table 8 Incidence Density of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* (n = 89) (continued)

Variable	Number VAP by MDRAB	Person-Time (person-days)	Incidence density rate (per 1000 person-days)
Antibiotic kinds			
Single	17	317	53.63
Double	24	966	24.84
Triple	17	492	34.55
Multiple	30	1,063	28.22
Group of antibiotic			
Penicillin			
None	69	3,258	21.17
Yes	20	835	23.95
Anti-psuedomonal penicillins			
None	45	1,465	30.71
Yes	44	2,628	16.74
Cephalosporin			
None	15	634	23.60
Yes	74	3,450	21.45
Aminoglycoside			
None	61	2,311	26.40
Yes	28	1,782	15.71
Meropenem			
None	60	2,576	23.30
Yes	29	1,514	19.15

Table 8 Incidence Density of Ventilator Associated Pneumonia by multidrug resistant *Acinetobacter baumannii* (n = 89) (continued)

Variable	Number VAP by MDRAB	Person-Time (person-days)	Incidence density rate (per 1000 person-days)
Group of antibiotic			
Vancomycin(Polypeptide)			
None	85	3,901	21.78
Yes	4	192	20.83
Sulfonamide			
None	73	2,846	25.65
Yes	16	1,247	12.83
Macrolides			
None	85	3,872	21.95
Yes	4	221	18.09

Part 3 To analyze comparative differences of survival time of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* patients with personal factors , treatment factors and environment factors by using the Kaplan-Meier and the log-rank test

Univariate Analysis

Log rank test was used to demonstrate :

1. Survival rates for 7, 14, 21 and 28-days of follow up after on mechanical ventilator.
2. Median survival time (time starting from on mechanical ventilator until having Ventilator Associated Pneumonia by multidrug resistant *Acinetobacter baumannii*).
3. Risk to develop Ventilator Associated Pneumonia by multidrug resistant *Acinetobacter baumannii* with 95%CI among various study factors.

Overall

Of two hundred and four cases, eighty nine cases had Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* (17.55%). The incidence density was 15.27 per 1000ventilator-days and median survival time was about 46 days. The over all 7, 14, 21 and 28-days survival rates were about 98.92%, 96.16%, 89.13%, and 74.87%, respectively. (Table 9)

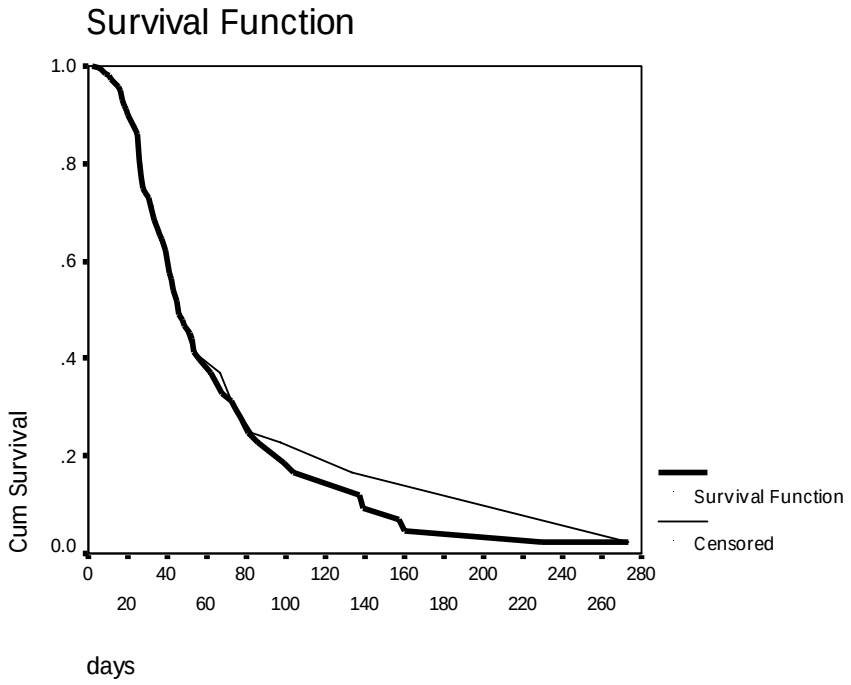


Figure 2 The over all survival curves of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* patients

The factors such as gender, age, diabetes mellitus, head injury, tracheostomy, antibiotic anti-psuedomonal penicillins drug group and antibiotic sulfonamide drug group were significantly different with the survival time. (Table 9)

Gender

Male and female had incidence density of 23.54 and 20.23 per 1000 persons-day, respectively. The median survival times for male and female were 41 and 56 days respectively with significant.

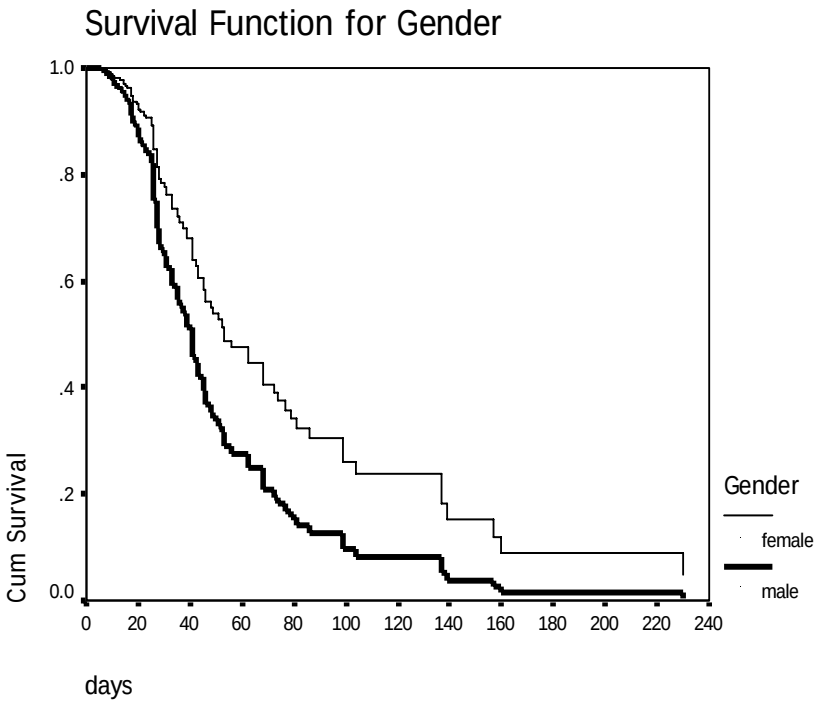


Figure 3 Comparison of survival curves of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* patients by gender (p=0.011)

Age

Patients with age group 55-74 years had the highest incidence density, 26.98 per 1000 persons-day and the median survival times of 56 days. The other age group 35-54 years, 75-94 years, and 15-34 years had lower amounts of incidence density were 26.05, 20.85 and 13.87 per 1000 persons-day, respectively, and the median survival times were 28, 62 and 41 days, respectively.

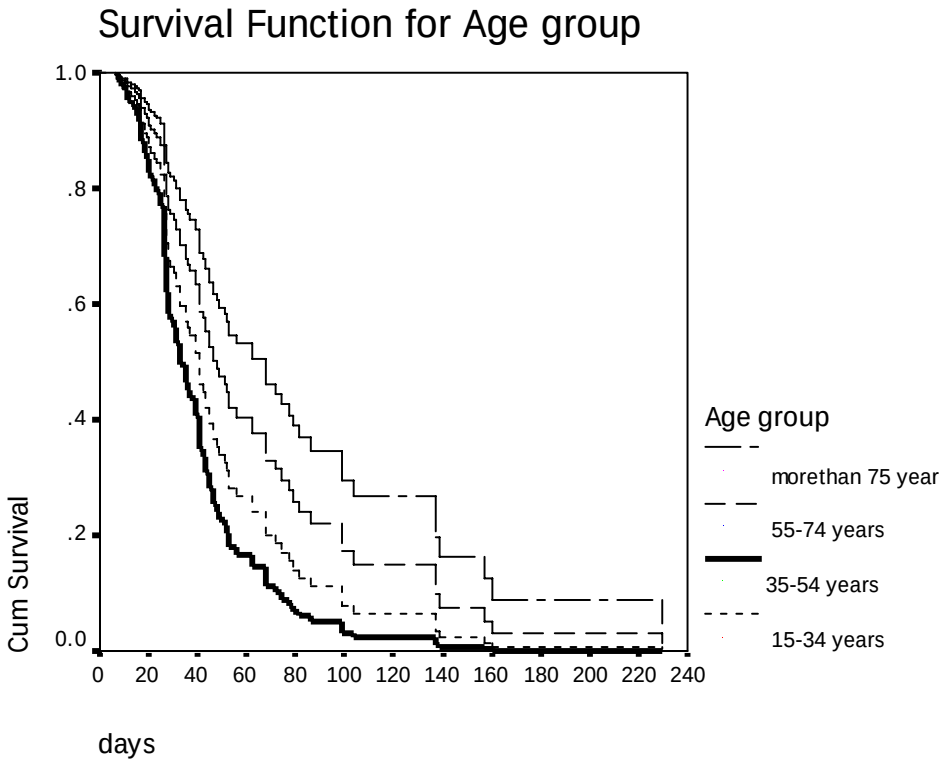


Figure 4 Comparison of survival curves of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* patients by age group (p=0.009)

Diabetes mellitus

Patients with diabetes mellitus had the incidence density 16.66 per 1000 persons-day and the median survival times of 68 days. The incidence density of patients without diabetes mellitus was 24.16 per 1000 persons-day and the median survival times of 41 days, respectively with significant.

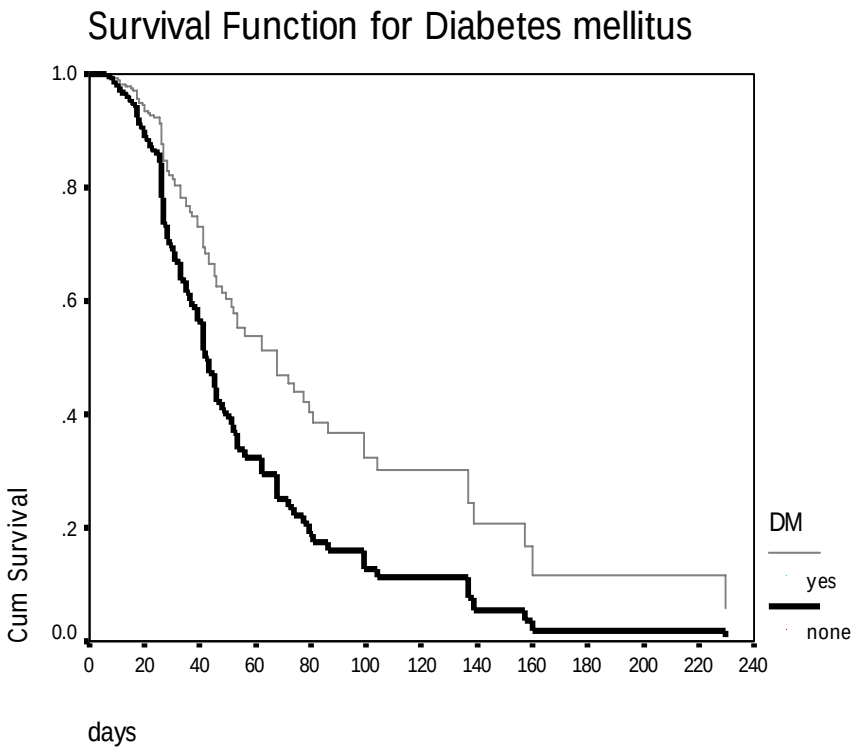


Figure 5 Comparison of survival curves of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* in patients with diabetes mellitus (p=0.016)

Head Injury

Patients with head injury had the incidence density 34.40 per 1000 persons-day and the median survival times of 35 days. The incidence density of patients without head injury was 20.23 per 1000 persons-day and the median survival times was about 49 days, respectively with significant.

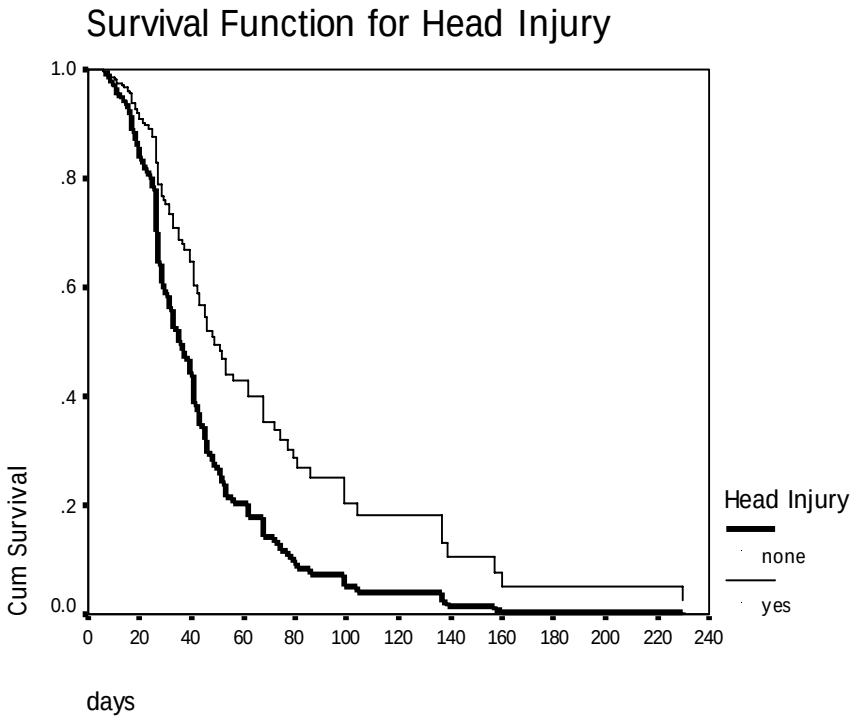


Figure 6 Comparison of survival curves of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* in patients with head injury (p=0.045)

Tracheostomy

Patients who on tracheostomy tube had the incidence density 16.66 per 1000 persons-day and the median survival times of 49 days. The incidence density of patients who on tracheostomy tube was 36.27 per 1000 persons-day and the median survival times of 43 days, respectively.

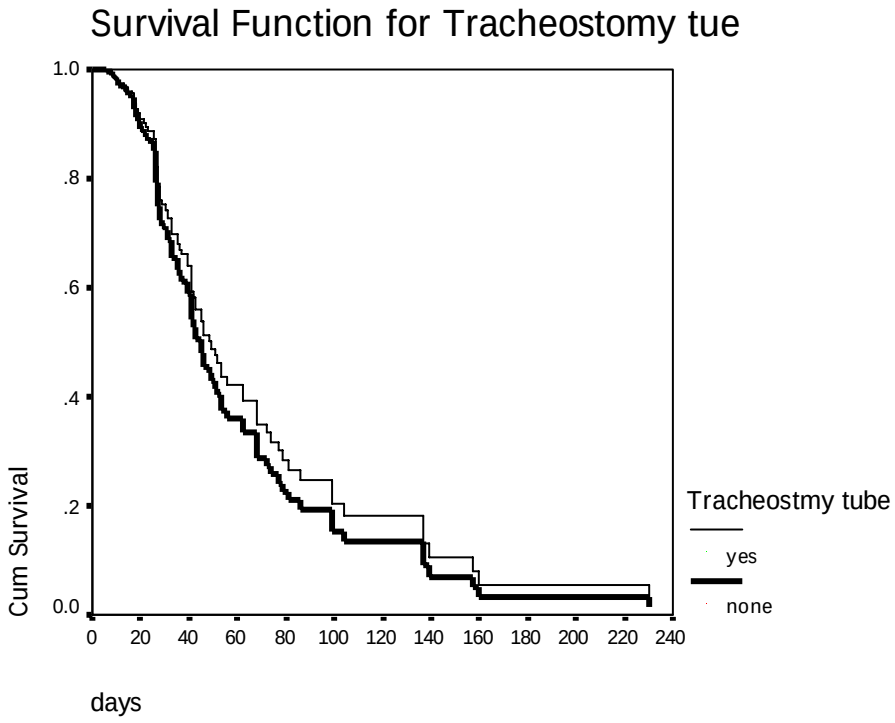


Figure 7 Comparison of survival curves of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* in patients with tracheostomy tube (p=0.038)

Antibiotic therapy

Anti -psuedomonal penicillins drug group

Patients who received anti-psuedomonal penicillin drug group had the incidence density of 16.74 per 1000 persons-day and the median survival times of 46 days. The incidence density of patients who had not received anti-psuedomonal penicillin drug group was 30.71 per 1000 persons-day and the median survival times of 27 days, respectively.

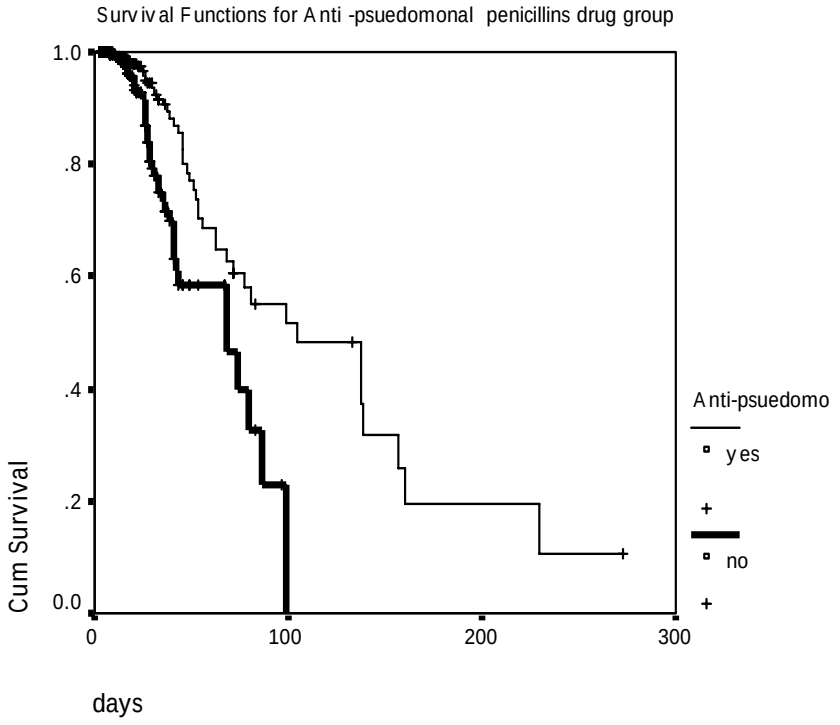


Figure 8 Comparison of survival curves of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* in patients who received anti-psuedomonal penicillin drug group (p=0.001)

Antibiotic therapy

Sulfonamide drug group

Patients who received antibiotic sulfonamide drug group had the incidence density of 12.83 per 1000 persons-day and the median survival times of 53 days . The incidence density of patients who had not received antibiotic sulfonamide drug group was 25.65 per 1000 persons-day and the median survival times of 31 days, respectively.

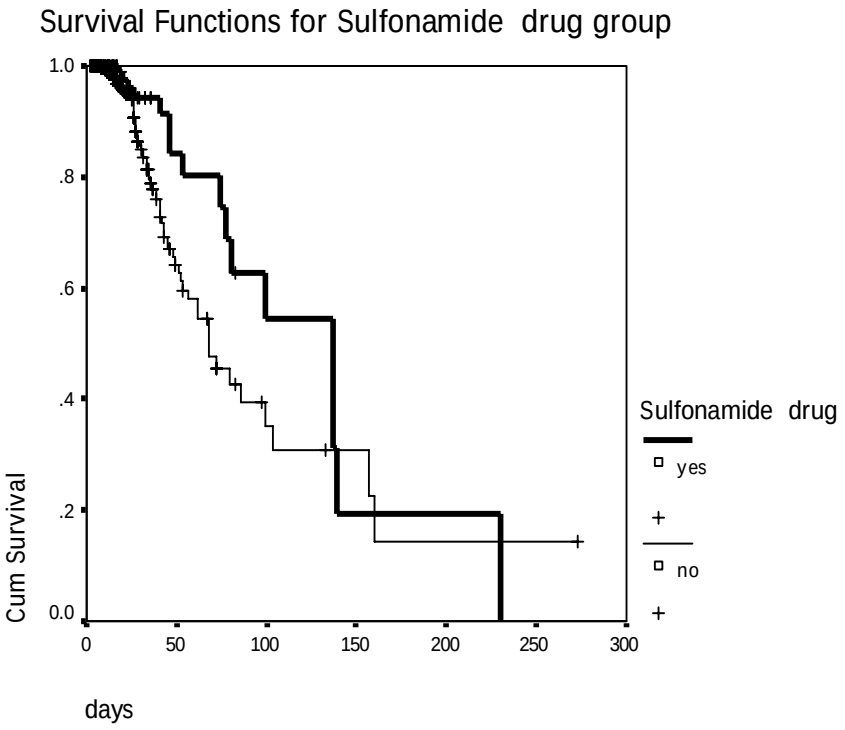


Figure 9 Comparison of survival curves of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* in patients who received antibiotic sulfonamide drug group (p=0.003)

The survival rate of Ventilator Associated Pneumonia by multidrug resistant *Acinetobacter baumannii* (Detail is shown in Table 9)

The 7-day survival rates (7D-SR)

Gender

The 7-day survival rates of male patients were 99.32 % and female patients were 99.26 %, respectively.

Age

The 7-day survival rates of patients age group 15-34 years and 75-94 years were 100 %. The 7-day survival rates of patients age group 35-54 years and 55-74 years were 97.96 % and 98.97 %, respectively.

Diabetes mellitus

The 7-day survival rates of patients with diabetes mellitus were 98.57 % and patients without diabetes mellitus were 99.52 %, respectively.

Head Injury

The 7-day survival rates of patients with head injury were 96.43 % and patients without head injury were 98.70 %, respectively.

Tracheostomy

The 7-day survival rates of patients with tracheostomy were 98.59 % and patients without tracheostomy were 98.54 %, respectively.

Anti - psuedomonal penicillin drug group

The 7-day survival rates of patients who received antibiotic-psuedomonal penicillin drug group were 97.73 % and patients who not received antibiotic-psuedomonal penicillin drug group were 97.78 %, respectively.

Sulfonamide drug group

The 7-day survival rates of patients who received antibiotic sulfonamide drug group were 100 % and patients who not received antibiotic sulfonamide drug group were 98.63 %, respectively.

The 14-day survival rates (14D-SR)

Gender

The 14-day survival rates of male patients were 93.81 % and female patients were 98.44 %, respectively.

Age

The 14-day survival rates of patients' age group 15-34, 35-54, 55-74, and 75-94 years were 96.67 %, 92.10 % , 93.86 % and 100 %, respectively.

Diabetes mellitus

The 14-day survival rates of patients with diabetes mellitus were 96.90 % and patients without diabetes mellitus were 95.91 %, respectively.

Head Injury

The 14-day survival rates of patients with head injury were 92.72 % and patients without head injury were 96.17 %, respectively.

Tracheostomy

The 14-day survival rates of patients with tracheostomy were 95.56 % and patients without tracheostomy were 95.01 %, respectively.

Antibiotic Therapy

Anti-psuedomonal penicillin drug group

The 14-day survival rates of patients who received antibiotic anti-psuedomonal penicillin drug group were 90.91 % and patients who not received antibiotic-psuedomonal penicillin drug group were 86.67 %, respectively.

Sulfonamide drug group

The 14-day survival rates of patients who received antibiotic sulfonamide drug group were 100 % and patients who not received antibiotic sulfonamide drug group were 89.41 %, respectively.

The 21-day survival rates (21D-SR)

Gender

The 21-day survival rates of male patients were 83.56 % and female patients were 93.90 %, respectively.

Age

The 21-day survival rates of patients' age group 15-34, 35-54, 55-74, and 75-94 years were 90.02 %, 79.62 % , 88.01 % and 98.31 %, respectively.

Diabetes mellitus

The 21-day survival rates of patients with diabetes mellitus were 93.96 % and patients without diabetes mellitus were 86.57 %, respectively.

Head Injury

The 21-day survival rates of patients with head injury were 84.99 % and patients without head injury were 86.76 %, respectively.

Tracheostomy

The 21-day survival rates of patients with tracheostomy were 93.99 % and patients without tracheostomy were 84.86 %, respectively.

Anti - psuedomonal penicillin drug group

The 21-day survival rates of patients who received antibiotic-psuedomonal penicillin drug group were 84.09 % and patients who not received antibiotic-psuedomonal penicillin drug group were 68.89 %, respectively.

Sulfonamide drug group

The 21-day survival rates of patients who received antibiotic sulfonamide drug group were 75.00 % and patients who not received antibiotic sulfonamide drug group were 78.82 %, respectively.

The 28-day survival rates (28D-SR)

Gender

The 28-day survival rates of male patients were 64.01 % and female patients were 83.20 %, respectively.

Age

The 28-day survival rates of patients' age group 15-34, 35-54, 55-74, and 75-94 years were 71.07 %, 60.66 % , 85.91 % and 84.43 %, respectively.

Diabetes mellitus

The 28-day survival rates of patients with diabetes mellitus were 90.83 % and patients without diabetes mellitus were 68.08 %, respectively.

Head Injury

The 28-day survival rates of patients with head injury were 61.66 % and patients without head injury were 77.43 %, respectively.

Tracheostomy

The 28-day survival rates of patients with tracheostomy were 79.46 % and patients without tracheostomy were 70.28 %, respectively.

Anti - psuedomonal penicillin drug group

The 28-day survival rates of patients who received antibiotic-psuedomonal penicillin drug group were 72.73 % and patients who not received antibiotic-psuedomonal penicillin drug group were 40.00 %, respectively.

Sulfonamide drug group

The 28-day survival rates of patients who received antibiotic sulfonamide drug group were 50.00 % and patients who not received antibiotic sulfonamide drug group were 58.82 %, respectively.

Table 9 Univariate analysis of survival time of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* patients by using the Kaplan-Meier and the log-rank test

Variables	n	Survival rate at 7 day	14 day	21 day	28 day	Median Survival (days)	*p***
Baseline Characteristics							
Gender							**0.011****
male	44	99.32	93.81	83.56	64.01	41	
female	45	99.26	98.44	93.90	83.20	56	
Age group (Years)							**0.009****
15-34	14	100	96.97	90.02	71.07	41	
35-54	16	97.96	92.10	79.62	60.66	28	
55-74	33	98.97	93.89	88.01	85.91	56	
75-94	26	100	100	98.31	84.43	62	

Incidence density* = infection rate per 1000 persons-day
p =** log-rang test (p-value)

Table 9 Univariate analysis of survival time of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* patients by using the Kaplan-Meier and the log-rank test (continued)

Variables	n	Survival rate at 7 day	14 day	21 day	28 day	Median Survival (days)	*p***
Medial Characteristics							
Severity of illness							0.171
SIC 2	9	100	100	100	94.74	74	
SIC 3	67	99.54	97.02	90.31	72.98	43	
SIC 4	13	95.24	89.19	72.32	66.29	35	
Underlying disease							0.280
None	12	97.96	94.19	90.42	71.59	42	
Yes	77	99.56	95.70	88.86	75.53	51	
DM							**0.016****
None	67	99.52	95.91	86.57	68.08	41	
Yes	22	98.57	96.90	93.96	90.83	68	
HT							0.921
None	39	99.26	97.34	88.96	70.65	41	
Yes	50	99.17	94.31	84.04	82.39	49	

Incidence density* = infection rate per 1000 persons-day
p = log-rang test (p-value)

Table 9 Univariate analysis of survival time of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* patients by using the Kaplan-Meier and the log-rank test (continued)

Variables	n	Survival rate at 7 day	14 day	21 day	28 day	Median Survival (days)	*p***
Head Injury							**0.045****
None	74	98.70	96.17	86.76	77.43	49	
Yes	15	96.43	92.72	84.99	61.66	35	
COPD							0.824
None	86	99.25	96.32	88.89	74.88	46	
Yes	3	100	93.33	93.33	74.67	104	
Chest injury							0.593
None	86	99.65	96.03	88.72	75.37	46	
Yes	3	100	100	100	83.33	33	
Respiratory failure							0.234
None	61	99.59	96.77	89.26	76.59	48	
Yes	28	97.96	90.83	88.08	69.29	46	
Renal failure							0.693
None	71	99.61	96.57	89.85	75.65	46	
Yes	18	93.55	89.30	75.41	70.38	43	

Incidence density* = infection rate per 1000 persons-day
p = log-rang test (p-value)

Table 9 Univariate analysis of survival time of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* patients by using the Kaplan-Meier and the log-rank test (continued)

Variables	n	Survival rate at 7 day	14 day	21 day	28 day	Median Survival (days)	*p***
Wound							0.053
None	44	99.30	93.93	83.11	70.87	43	
surgical wound	22	100	98.63	95.36	76.63	45	
decubitus ulcer	18	100	95.45	90.43	90.43	81	
lacerated wound	5	100	100	83.33	66.67	25	
Prior antibiotic							0.622
None	53	99.59	96.83	88.50	75.85	48	
Yes	36	100	92.34	90.29	73.54	43	
Prior infection							0.512
None	78	96.04	84.26	77.20	67.37	27	
Yes	11	97.14	93.79	88.28	81.97	56	

Incidence density* = infection rate per 1000 persons-day
p = log-rang test (p-value)**

Table 9 Univariate analysis of survival time of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* patients by using the Kaplan-Meier and the log-rank test (continued)

Variables	n	Survival rate at 7 day	14 day	21 day	28 day	Median Survival (day)	*p***
Treatment factors							
Tracheostomy							**0.038****
None	44	98.54	95.01	84.86	70.28	43	
Yes	48	98.59	95.56	93.99	79.46	49	
Nebulizer							0.471
None	20	99.07	97.47	87.81	71.28	45	
Yes	69	98.82	94.50	88.27	76.06	48	
ICD							0.575
None	86	98.89	96.02	88.76	74.71	46	
Yes	3	80.00	80.00	80.00	40.00	45	
Stress ulcer prophylaxis							0.536
Ranitidine	36	98.08	91.73	88.05	69.38	46	
Losec	17	97.78	91.11	87.31	69.45	45	
Sucrulfate	2	93.33	93.33	84.85	84.85	53	

Incidence density* = infection rate per 1000 persons-day
p =** log-rang test (p-value)

Table 9 Univariate analysis of survival time of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* patients by using the Kaplan-Meier and the log-rank test (continued)

Variables	n	Survival rate at 7 day	14 day	21 day	28 day	Median Survival (day)	*p***
Antibiotic group							
Penicillin							0.441
None	69	100	89.86	79.71	57.97	37	
Yes	20	95.00	90.00	70.00	55.00	31	
Anti-psuedomonal penicillins							**0.002****
None	45	97.78	86.67	68.89	40.00	27	
Yes	44	97.73	90.91	84.09	72.73	46	
Cephalosporin							0.647
None	15	93.33	73.33	60.00	53.33	28	
Yes	74	98.65	91.89	79.73	60.81	36	
Aminoglycoside							
None	61	95.08	88.52	70.49	49.18	28	0.006
Yes	28	96.43	92.83	85.71	75.00	45	

Incidence density* = infection rate per 1000 persons-day
p = log-rang test (p-value)

Table 9 Univariate analysis of survival time of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* patients by using the Kaplan-Meier and the log-rank test (continued)

Variables	n	Survival rate at 7 day	14 day	21 day	28 day	Median Survival (day)	*p***
Antibiotic group							
Meropenem							
None	60	98.33	91.67	75.00	51.67	29	0.232
Yes	29	96.55	93.10.	86.21	68.97	43	
Vancomycin(Polypeptide)							0.792
None	85	98.82	89.41	76.47	55.29	33	
Yes	4	100	100	100	75.00	39	
Sulfonamide							**0.003****
None	73	98.63	89.67	75.34	53.42	31	
Yes	16	100	100	87.50	75.00	53	
Macrolides							.844
None	85	98.82	89.41	78.82	58.82	35	
Yes	4	100	100	75.00	50.00	20	

Incidence density* = infection rate per 1000 persons-day
p = log-rang test (p-value)

Table 9 Univariate analysis of survival time of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* patients by using the Kaplan-Meier and the log-rank test (continue)

Variables	n	Survival rate at 7 day	14 day	21 day	28 day	Median Survival (day)	*p***
Department							0.519
Medical	61	98.23	94.66	86.83	78.48	49	
Surgical	24	98.31	96.52	86.96	66.79	35	
Orthopedic	4	100	100	85.71	35.71	72	
Ward							0.419
General ward	56	96.93	84.84	69.19	41.93	33	
Intensive care unit	10	96.15	82.42	61.81	46.36	29	
Private ward	23	97.56	94.08	81.53	54.35	25	

Incidence density* = infection rate per 1000 persons-day
p =** log-rang test (p-value)

Part 4 Univariate analysis for relationship between risk factors and Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* by Cox's Proportional Hazard Model(unadjusted).

Personal factors

Gender

The gender was significantly associated with survival time. The risk of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* in male was 1.59 times (HR = 1.59, 95 % CI, 1.040 - 2.450, p = 0.032). (Table 10)

Age

The risk of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* at the age group of 35-54 years and 55-74 years were 1.96 times(HR = 1.96, 95%CI, 0.931- 4.163, p = 0.076), 0.86 times(HR = 0.86 95%CI, 0.458 - 1.617, p = 0.641). But, there were not significantly different. Patients who had 75-94 years was significantly associated with survival time 0.50 times (HR = 0.50, 95%CI, 0.258 - 0.968, p = 0.040).

Medical factors

Severity of illness at the time of admission

The risk of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* of patients who had severity of illness level 3 was 1.27 times(HR = 1.27, 95%CI, 0.630 - 2.591, p = 0.498) of patients who had severity of illness level 2. In the other level of severity of illness were not significantly different. However, severity of illness did not significantly affect survival time (p = 0.924).

Known Underlying disease of the patients

Diabetes mellitus

Patient who had underlying disease did not significantly affect survival time (p = 0.941). In addition, the risk of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* of patients who had diabetes mellitus was 0.54 times of patients who had not diabetes mellitus. There was significantly different (p = 0.016).

Chest injury

Patient who had chest injury was significantly associated with survival time. The risk of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* in patient who had chest injury was 4.08 times (HR = 4.08, 95%CI, 1.252 -13.310, p = 0.020).

Head injury

Head injury was significantly associated with survival time. The risk of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* in patient who had head injury was 1.75 times (HR = 1.75, 95%CI, 1.001 – 3.067, p = 0.050).

Prior antibiotic treatment

The prior antibiotic treatment was not significantly associated with survival time (p = 0.325).

Having wound during admission

Patient who having wound during admission was not significantly associated with survival time of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii*.). In addition, the risk of Ventilator Associated Pneumonia by multidrug resistant *Acinetobacter baumannii* of patients who had surgical wound, decubitus ulcer and lacerated wound were 0.96, 0.75 and 1.41 times.

Prior-infection

The risk of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* of patients who had prior-infection was 0.41 times of patients who had not prior-infection.There was not significantly different (p = 0.245).

Treatment Factor

Tracheostomy, Nebulizer, Inter costal drainage

The Tracheostomy, Nebulizer, and Inter costal drainage were not significantly affect survival time of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* (p = 0.875, 0.145 and 0.553).

Stress ulcer prophylaxis

The risk of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* of patients who received ranitidine was 1.07 times(HR = 1.07, 95%CI, 0.255 - 4.498, p = 0.926) of patients who were not received stress ulcer prophylaxis. In the other stress ulcer prophylaxis were not significantly different. However, stress ulcer prophylaxis did not significantly affect survival time (p = 0.947).

Antibiotic drug group therapy

Penicillin

Patient who received antibiotic penicillin drug group were significantly associated with survival time of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* . The risk of Ventilator Associated Pneumonia by multidrug resistant *Acinetobacter baumannii* of patients who received penicillin drug group was 1.87 times(HR = 1.87, 95%CI, 1.038 – 3.399, p = 0.037).

Anti-psuedomonal penicillins

Patient who received anti-psuedomonal penicillins drug group were significantly associated with survival time of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii*. And the risk of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* of patients who received antibiotic-psuedomonal penicillin drug group was 0.46 times (HR = 0.46, 95%CI, 0.274 – 0.794, p = 0.005).

Cephalosporin

Patient who received cephalosporin drug group were not significantly associated with survival time of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* (p = 0.661).

Aminoglycoside

The risk of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* of patients who received aminoglycoside drug group was 0.91 times (HR = 0.91, 95%CI, 0.875 – 0.991, p = 0.025) of patients who did not received aminoglycoside drug group.

Meropenem

Patient who received meropenem drug group were significantly associated with survival time of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii*. And the risk of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* of patients who received meropenem drug group was 1.78 times (HR = 1.78, 95%CI, 1.667 – 1.906, p = < 0.001).

Vancomycin(Polypeptide)

The risk of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* of patients who received vancomycin drug group was 2.66

times (HR = 2.66, 95%CI, 2.297 – 3.084, p = < 0.001) of patients who did not received vancomycin drug group.

Sulfonamide

Patient who received sulfonamide drug group were significantly associated with survival time of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii*. And the risk of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* of patients who received sulfonamide drug group was 0.80 times (HR = 0.80, 95%CI, 0.755 – 0.864, p = < 0.001).

Macrolides

Patient who received macrolides drug group were not significantly associated with survival time of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* (p = 0.200).

Hospital Environment Factor

Study sites (Department)

The surgical department of patient was significantly associated with survival time. The risk of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* in patient who admitted in surgical department was 1.90 times of patient who admitted in medical department (HR = 1.90, 95%CI, 1.153 – 3.112 , p = 0.012). And patient who admitted in orthopedic department was not significantly different.

Ward

Ward sector were significantly associated with survival time (p < 0.001). In addition, the risk of Ventilator Associated Pneumonia by multidrug-resistant *Acinetobacter baumannii* of patients who admitted in general ward and intensive care unit were 1.30 times and 0.48 times of patients who admitted in private ward. There were significantly different.

Table 10 The relationship between other factors and survival time by Cox's Proportion Hazard Model (unadjusted).

Variables	n	HR	95%CI of HR	*P-value*
Gender				
female	45	1		
male	44	1.59	1.040 - 2.450	**0.032***
Age group (Years)				
15-34	14	1		
35-54	16	1.96	0.931- 4.163	0.076
55-74	33	0.86	0.458 - 1.617	0.641
75-94	26	0.50	0.258 - 0.968	**0.040***
Severity of illness				
SIC 2	9	1		
SIC 3	67	1.27	0.630 - 2.591	0.498
SIC 4	13	1.19	0.505 - 2.843	0.682
Underlying disease				
None	12	1		
Yes	77	0.97	0.525 - 1.810	0.941
DM				
None	67	1		
Yes	22	0.55	0.334 - 0.894	**0.016***

HR = Hazard ratio

* Statistical significant at $\alpha < 0.05$

Table 10 The relationship between other factors and survival time by Cox's Proportion Hazard Model (unadjusted) (continued).

Variables	n	HR	95%CI of HR	*P-value*
HT				
None	39	1		
Yes	50	1.05	0.691 - 1.614	0.802
Head Injury				
None	74	1		
Yes	15	1.75	0.999 -3.067	**0.050***
COPD				
None	86	1		
Yes	3	0.81	0.253 - 2.597	0.725
Chest injury				
None	86	1		
Yes	3	4.08	1.252 - 13.310	**0.020***
Respiratory failure				
None	61	1		
Yes	28	1.17	0.744 - 1.841	0.495
Renal failure				
None	71	1		
Yes	18	1.20	0.715 -2.026	0.485

HR = Hazard ratio

* Statistical significant at $\alpha < 0.05$

Table 10 The relationship between other factors and survival time by Cox's Proportion Hazard Model (unadjusted) (continued).

Variables	n	HR	95%CI of HR	*P-value*
Wound				
None	44	1		
surgical wound	22	0.96	0.456 - 1.272	0.865
decubitus ulcer	18	0.75	0.320 – 1.236	0.221
lacerated wound	5	1.41	0.719 - 4.628	0.416
Prior antibiotic				
None	53	1		
Yes	36	1.24	0.808 - 1.905	0.325
Prior infection				
None	78	1		
Yes	11	0.41	0.219 - 1.776	0.245
Tracheostomy				
None	44	1		
Yes	48	0.96	0.629 - 1.484	0.875
Nebulizer				
None	20	1		
Yes	69	0.67	0.400 -1.144	0.145

HR = Hazard ratio

***** Statistical significant at $\alpha < 0.05$

Table 10 The relationship between other factors and survival time by Cox's Proportion Hazard Model (unadjusted) (continued).

Variables	n	HR	95%CI of HR	*P-value*
Stress ulcer prophylaxis				
Ranitidine	36	1		
Losec	17	1.09	0.651 - 1.823	0.740
Sucralfate	2	0.96	0.513 - 1.804	0.916
ICD				
None	86	1		
Yes	3	1.42	0.447 - 4.515	0.553
Group of antibiotic				
Penicillin				
None	69	1		
Yes	20	1.87	1.038 – 3.399	**0.037 ***
Anti-psuedomonal penicillins				
None	45	1		
Yes	44	0.46	0.274 – 0.794	**0.005***
Cephalosporin				
None	15	1		
Yes	74	0.86	0.439 – 1.687	0.661

HR = Hazard ratio

***** Statistical significant at $\alpha < 0.05$

Table 10 The relationship between other factors and survival time by Cox's Proportion Hazard Model (unadjusted) (continued).

Variables	n	HR	95%CI of HR	*P-value*
Group of antibiotic				
Aminoglycoside				
None	61	1		
Yes	28	0.91	0.875– 0.991	**0.025***
Meropenem				
None	60	1		
Yes	29	1.78	1.667 – 1.906	**< 0.001***
Vancomycin(Polypeptide)				
None	85	1		
Yes	4	2.66	2.297 – 3.084	**< 0.001***
Sulfonamide				
None	73	1		
Yes	16	0.80	0.755 – 0.864	**< 0.001***
Macrolides				
None	85	1		
Yes	4	0.44	0.131– 1.532	0.200

HR = Hazard ratio

***** Statistical significant at $\alpha < 0.05$

Table 10 The relationship between other factors and survival time by Cox's Proportion Hazard Model (unadjusted) (continued).

Variables	n	HR	95%CI of HR	*P-value*
Department				
Medical	61	1		
Surgical	24	1.90	1.153 - 3.112	**0.012***
Orthopedic	4	0.85	0.306 – 2.360	0.755
Ward				
Private ward	23	1		
General ward	56	1.30	1.222 – 1.398	**< 0.001***
Intensive care unit	10	0.48	0.430 – 0.546	**< 0.001***

HR = Hazard ratio

* Statistical significant at $\alpha < 0.05$

Part 5 Multivariate Analyses of the relationships between independent factors and survival time by Cox's Proportional Hazard Model.(Detail is shown in Table 11)

Cox proportional hazard regression analysis was used to demonstrate adjusted risk to develop Ventilator Associated Pneumonia by multidrug resistant *Acinetobacter baumannii* among significant factors from univariate analysis which were gender, age, diabetes mellitus, head injury, chest injury, antibiotic drug group : penicillin, anti-psuedomonal penicillin , aminoglycoside, meropenem, vancomycin(Polypeptide), sulfonamide, ward and department.

The factors were significantly associated with survival time ($p < 0.05$) base on multivariate analysis of gender, tracheostomy, antibiotic drug group : cephalosporin , aminoglycoside , meronem , vancomycin(polypeptide), ward and department.
(Table 11)

Gender

The risk of Ventilator Associated Pneumonia by multidrug resistant *Acinetobacter baumannii* in male was significantly different when compared to female (HR = 2.26, 95%CI, 1.209 - 4.237, p = 0.011).

Tracheostomy

The risk to develop Ventilator Associated Pneumonia by multidrug resistant *Acinetobacter baumannii* of patients who on tracheostomy tube was significantly different when compared with patients who did not receive tracheostomy tube (HR = 0.20, 95%CI, 0.091 - 0.459, p < 0.001).

Antibiotic drug group therapy

Cephalosporin

Risk to develop Ventilator Associated Pneumonia by multidrug resistant *Acinetobacter baumannii* in patients who received cephalosporin drug group were significantly when compared with patients who did not received cephalosporin drug group (HR = 1.49, 95%CI, 1.318 – 1.701, p < 0.001).

Aminoglycoside

The risk of Ventilator Associated Pneumonia by multidrug resistant *Acinetobacter baumannii* of patients who received aminoglycoside drug group was 0.91 times (HR = 0.23, 95%CI, 0.875 – 0.991, p < 0.001) of patients who did not received aminoglycoside drug group.

Meropenem

Patient who received meropenem drug group were significantly different.

And the risk of Ventilator Associated Pneumonia by multidrug resistant *Acinetobacter baumannii* of patients who received meropenem drug group was 4.51 times (HR = 4.51, 95%CI, 4.076 – 4.999, p < 0.001).

Vancomycin(Polypeptide)

The risk of Ventilator Associated Pneumonia by multidrug resistant *Acinetobacter baumannii* of patients who received vancomycin drug group was 2.66 times (HR = 4.19, 95%CI, 3.349 – 5.245, p = < 0.001) of patients who did not received vancomycin drug group.

Study sites (Department)

There was risk to develop Ventilator Associated Pneumonia by multidrug resistant *Acinetobacter baumannii* in patients who admission in surgical department when compared with patients who admission in medical department(HR 4.32, 95%CI,

0.197 – 15.616, p = 0.025), significantly. And patient who admitted in orthopedic department was not significantly different. .

Ward

The risk of Ventilator Associated Pneumonia by multidrug resistant *Acinetobacter baumannii* of patients who admitted in general ward was 2.10 times of patients who admitted in private ward. There were significantly different (HR = 2.10, 95%CI, 0.811 – 1.187, p = < 0.001). And patient who admitted in intensive care unit was not significantly different. .

Table 11 Multivariate analysis of the relationship between other factors and survival time by Cox's Proportion Hazard Model.

Variables	n	HR	95%CI of HR	*P-value*
Gender				
female	45	1.00		
male	44	2.26	1.209 - 4.237	**0.011**
Tracheostomy				
None	44	1.00		
Yes	48	0.20	0.091 - 0.459	**< 0.001**
Cephalosporin				
None	15	1		
Yes	74	1.49	1.318 – 1.701	**< 0.001***
Aminoglycoside				
None	61	1		
Yes	28	0.23	0.208 – 0.259	**< 0.001***
Meronem				
None	60	1		
Yes	29	4.51	4.076 – 4.999	**< 0.001***
Vancomycin(Polypeptide)				
None	85	1		
Yes	4	4.19	3.349 – 5.245	**< 0.001***

HR = Hazard ratio, adjusted for all variables in Table 11

Statistical significant at $\alpha < 0.05$

Table 11 Multivariate analysis of the relationship between other factors and survival time by Cox's Proportion Hazard Model (continued)

Variable	Number	HR	95%CI	*P-value*
Department				
Medical	61	1.00		
Surgical	24	4.32	0.197 - 12.616	**0.025***
Orthopedic	4	2.28	0.025 – 1.282	0.452
Ward				
Private ward	23	1		
General ward	56	2.10	1.847 – 2.392	**< 0.001***
Intensive care unit	10	0.981	0.811 – 1.187	0.844

HR = Hazard ratio, adjusted for all variables in Table 11

Statistical significant at $\alpha < 0.05$

CHAPTER V
DISCUSSIONS

Ventilator associated pneumonia is a common complication of mechanical ventilation which increases risks of mortality, morbidity, and costly for medical management(17). *Acinetobacter baumannii* which has emerged as a causal pathogen was frequently found in the sputum collected from patients who were suffering with ventilator associated pneumonia(10,11). Multidrug-resistant *Acinetobacter baumannii* has been reported worldwide in recognition as one of the most difficult to control and treatment of healthcare-associated infections(7). *A. baumannii*, a clinically specific species has a tendency of cross-transmission, particularly in the intensive care units (ICUs), where numerous outbreaks are encountered (12, 13, 16).

This cohort study aimed to determine the incidence of ventilator–associated pneumonia (VAP) caused by multidrug-resistant *Acinetobacter baumannii* and risk factors of multidrug-resistant *Acinetobacter baumannii* infection among 507 intubated patients enrolled in Nakhon Pathom Hospital of Nakhon Pathom Province during December 2005 to October 2006.

The incidence of VAP ranges from 10%to 65% of intubated patients depending on the risk factors(2). In this study, the incidence of ventilator associated pneumonia by multidrug-resistant *Acinetobacter baumannii* was 17.55%, and the incidence density of ventilator associated pneumonia by multidrug-resistant *Acinetobacter baumannii* was 21.75 per 1,000 person-days and 30.62 per 1,000 ventilator days. Respiratory infections due to *Acinetobacter* in mechanically ventilated patients in ICU were also high at JIPMER hospital (44.7%) during 1996-1997 (Dutta TK, unpublished data). One of the most recent study revealed that *Acinetobacter* spp. was responsible for 35% of ventilator associated pneumonia (VAP).

About 57% of VAP caused by multidrug-resistant agents were found within 7 days after initiation of mechanical ventilation, and in 80% of late VAP. The median survival time of ventilator associated pneumonia, by multidrug-resistant *Acinetobacter*

baumannii, was 46 days. The over all 7, 14, 21 and 28-days survival rates were about 98.92%, 96.16%, 89.13%, and 74.87%, respectively. From The study of infectious control and prevention of Nakhon Pathom Hospital, there is a good structure of infectious control and prevention system. There is supportive from the administrator of the hospital, over decades, for the development of infectious control and prevention which is correspondent to the CDC recommendation, about infectious control of *Acinetobacter baumannii,* that emphasized on strict standard precaution especially a hand washing, environmental surface cleaning, will decrease spread of organisms dramatically(21)

This study included patient demographic factors such as gender, age, underlying disease, severity of illness, wounds, method of treatment such as invasive procedures, stress ulcer prophylaxis, antibiotic therapy and environment factors. The factors such as gender, age, diabetes mellitus, head injury, tracheostomy, antibiotic anti-psuedomonal penicillins drug group and antibiotic sulfonamide drug group were found significantly influence the survival rate($p < 0.05$).

The survival time of the patients who were suffering with ventilator associated pneumonia caused by multidrug-resistant *Acinetobacter baumannii* among age group 75- 94 years was significant different in comparison with the patients among age group 15-34 years. Another factor, the patient with underlying disease such as diabetes mellitus was found significant association with Ventilator Associated Pneumonia caused by multidrug-resistant *Acinetobacter baumannii* ($p < 0.05$). The elderly and those patients who were suffering with diabetes mellitus were at high risk for infection because of the susceptibility and low immune system.

In this study found that there were a group of patients who were complicated with diabetes mellitus had not had ventilator associated pneumonia caused by multidrug-resistant *Acinetobacter baumannii*. The data supported that those patients received 2 antibiotic drugs combination treatment, and almost every patient received aminoglycosides drug group. Therefore, this study could be concluded that the aminoglycosides drug group could be used for prevention of ventilator associated pneumonia caused by multidrug-resistant *Acinetobacter baumannii* significantly.

In this study, tracheostomy has been proven for prevention of ventilator associated pneumonia cause by multidrug-resistant *Acinetobacter baumannii* effectively. Contrary, the study of Siham Mahgoub et al concluded that tracheostomy was a risk factor for highly resistant *Acinetobacter baumannii* infection ($p < 0.01$). Another study of Manuel W, Mah et al. concluded that tracheostomy was a relatively strong risk factor for *Acinetobacter baumannii* acquisition; but in long term ventilator dependent, the effect of tracheostomy was less important because duration of ventilator dependent becomes an important factor itself.

The other factors which could predict the probabilities of survival time were head injury and chest injury. Zhou P et al, found injury was a risk of VAP due to *Acinetobacter baumannii* in patients with head trauma (OR=2.8, CI: 1.78 to 4.66). The study of an outbreak of pan-drug resistant *Acinetobacter baumannii* in surgical intensive care unit, and the patients who had injury(13) found that the risk of ventilator associated pneumonia by multidrug resistant *Acinetobacter baumannii* in surgical and orthopedic department were 1.30 times and 0.48 times of medical department, respectively, and there were significantly different of risk ($p < 0.001$). The previous study indicated that the majority of head injury patients are risky for aspiration due to loss of gag reflex and intrinsic aspiration prevention mechanisms, which are susceptible to pneumonia more than others, so they should be assessed and monitored closely to prevent multidrug resistant *Acinetobacter baumannii.*

Antimicrobial agents are the significant risk factor for multidrug resistant nosocomial infection. The risks are varied among different kinds of antibiotic as in some studies (11,14, 16, 29). Cox' s Proportional Hazard Model, of the risk of Ventilator Associated Pneumonia caused by multidrug-resistant *Acinetobacter baumannii* nosocomial infection, were antimicrobial used such as antibacterial penicillin drug group and anti-pseudomonal penicillin drug group(HR= 1.87 and 0.46).

The multivariate analysis indicated the association among antibiotic drug groups such as: cephalosporins, aminoglycosides, meronem and vancomycin (polypeptide). Some reports found the association between previous used of third

generation cephalosporins and the development of multidrug-resistant *Acinetobacter baumannii* nosocomial infection (14, 30, 31). Gruoon D. et al, concluded that a program of antibiotic strategic control, to restricted use of ceftazidime and ciprofloxacin in patients who admitted in ICU, was able to minimize the incidence of VAP caused by potential antibiotic resistant microorganisms significantly, which was corresponding to this study, resulted in correlation between cephalosporin used and the incidence of infection. There was a study concluded that the previous exposure of tienem was associated with the isolation of imipenem resistant strain organisms (OR= 4), which is corresponding to the finding of this study that the use of tienem was associated with the infection. In our study found that aminoglycosides therapy was effective for the treatment of multidrug-resistant *Acinetobacter baumannii* nosocomial infection (17).

The study of antibiotic used in the mechanical ventilator dependent patients, found that the most popular treatment strategy was the usage of only one antibiotic drug group or single antibiotic therapy (32.42%), and the second most popular strategy was the usage of the combination of two antibiotic drug groups therapy (25.88%). There are the recommendations from The American Thoracic Society Documents 2005 about the initial empirical therapy by the use of the combination antibiotic therapy of antipseudomonal cephalosporin, or antipseudomonal cabarpenem, or β-Lactamase inhibitor, and antipseudomonal fluoroquinolone, or the aminoglycosides drug group for ventilator associated pneumonia in patient with late onset disease or risk factors for multidrug resistant pathogens,

On the other hands, the intubated patients, who were admitted to the general in-patients wards, were high risks for infection rather than private room wards. According to increased length of stay of patients in the general wards (100 – 120%), averagely, and the unlimited patient admissions, and nursing understaffed, could be contributed factors to compromise the quality of care.

The minimization of the risk for pneumonia, caused by multidrug-resistant *Acinetobacter baumannii*, in mechanical ventilator dependent patients should be considered to increase the quality of life for those patients. The strategies to increase

efficacy in patient care, such as: providing sufficient nursing staff, training the caregivers, development of the project systematically to improve quality of care for mechanical ventilator dependent patients in the general wards, including other strategies to minimize infection, which needs attention from the hospital administrator.

CHAPTER VI
CONCLUSION AND RECOMMENDATIONS

This descriptive cohort study had been performed for the purpose of investigating the incidence of multidrug-esistant *Acinetobacter baumannii* infection among mechanical ventilator dependent patients in association with some risk factors to multidrug-esistant *Acinetobacter baumannii* infection. The study was performed at Nakhon Pathom Hospital, Nakhon Pathom Province, including two intensive care units, two surgical wards, three medical wards, and seven private wards.

The 507 mechanical ventilator dependent patients enrolled in the study during December 2005 to August 2006. The data collection had been performed by following-up the patients who were mechanical ventilator dependent. The event of Ventilator Associated Pneumonia was considered after the patients had been intubated, until the mechanical ventilator had been taken off, which has been collected from the medical records and surveillance forms. The survival analysis had been used to determine the incidence, survival rate, median survival times and risk for the development of multidrug-esistant *Acinetobacter baumannii* infection between the study factors.

Among 507 patients, Ventilator Associated Pneumonia caused by multidrug-resistant *Acinetobacter baumannii* was found in 89 cases. An incidence of Ventilator Associated Pneumonia caused by multidrugresistant *Acinetobacter baumannii* was 17.55% and incidence density was 21.75 per 1,000 person-days and 15.27 per 1,000 ventilator days with the median survival time 46 days. Male had slightly higher incidence rate than female (23.54 vs 20.23 per 1000 person-days). Most patients were in age groups 35-54 years (26.05 per 1000 person-days), the severity of illness was level 3 (24.05 per 1000 person-days). There were 30.51 per 1000 person-days of those who had surgery, 23.38 per 1000 person-days of co-blood stream infection and 29.85 per 1000 person-days prior urinary tract infection).

Most of the participants were admitted in surgical department (31.83 per 1000 person-days). The participants who were retained inter-costal drainage, nebulizer, central venous line, and tracheostomy were 26.08, 19.60, 18.86 and 16.60 per 1000 person-days, respectively. Prior antibiotic therapy was found 17.61 per 1000 person-days. The majority of the patients received ranitidine and losec, 21.63 and 10.04 per 1000 person-days, respectively. The incidence density of Ventilator Associated Pneumonia caused by multidrug-resistant *Acinetobacter baumanni* among the participants who received antibiotic such as: cloxacillin, cefrom, and unasyn were 37.38, 32.65, and 28.57 per 1000 person-days, respectively. The over all 7, 14, 21 and 28-days survival rates were about 98.92%, 96.16%, 89.13%, and 74.87%, respectively.

Kaplan-Meier's univariate analysis and the log-rank test indicated the significance of median survival time between genders, male was higher than female ($p = 0.032$). The age and the survival time was also different significantly($p < 0.001$). In general, the elderly patients had higher median survival time. The survival time of the severity of illness were not different significantly in level 2, 3,and 4 ($p = 0.498$). The patients who had severity of illness in the level 2 had higher median survival time than the other levels. Among patients with underlying disease such as diabetes mellitus patients demonstrated significant difference of median survival time ($p = 0.016$), and the patients with underlying disease had highier median survival time. Wound type was not significant different ($p = 0.460$). Patients who had previous treatment with antibiotic, had lower median survival time . However, the 21 days survival rate among patients who received prior antibiotic treatment were higher than those who were not (90.29% and 87.40%, respectively). There were no significant differences among patients who had previous infection and co-infection. Previous blood stream infection patients had highest median survival time than others. The median survival time of the Invasive procedure and Stress ulcer prophylaxis were not significant different. There were significant difference, between Gender, age, diabetes mellitus, head injury, tracheostomy, antibiotic anti-pseudomonal penicillin drug group and sulfonamide drug group with median survival time in Ventilator Associated Pneumonia by multidrug resistant *Acinetobacter baumanni*($p < 0.05$).

According to Cox proportional hazard regression analysis with unadjusted factors, the factors such as, gender, age, diabetes mellitus, head injury, chest injury, antibiotic drug group : penicillins , anti-psuedomonal penicillins ,aminoglycoside, meropenem, vancomycin (Polypeptide), sulfonamide, wards and department were significantly associated with survival time at 95 % CI.

Based on multivariate analysis, the factors which were significantly associated with survival time ($p < 0.05$) were gender, tracheostomy, antibiotic drug group: cephalosporin, aminoglycoside, meronem, vancomycin (polypeptide), wards and departments. The risk of Ventilator Associated Pneumonia caused by multidrug resistant *Acinetobacter baumannii* in male was significantly different in comparison to female ($p = 0.011$). Tracheostomy has been proven as the effective treatment for Ventilator Associated Pneumonia by multidrug resistant *Acinetobacter baumannii* ($p = 0.001$). The risk of Ventilator Associated Pneumonia caused by multidrug resistant *Acinetobacter baumannii* among patients who received therapy with antibiotic drug group: cephalosporin, meronem and vancomycin (polypeptide). While the aminoglycosides drug group was a protective factor for Ventilator Associated Pneumonia caused by multidrug resistant *Acinetobacter baumannii* ($p < 0.05$). There was a risk for the development of Ventilator Associated Pneumonia caused by multidrug resistant *Acinetobacter baumannii* in patients who were admitted in the surgical department in comparison to the patients who were admitted in the medical department ($p = 0.025$). There were significant different, of the risk for Ventilator Associated Pneumonia caused by multidrug resistant *Acinetobacter baumannii*, among the patients who were admitted in general wards.

Recommendation for implication of the results

1. The mechanical ventilator dependent patients, who are high risk for the development of Ventilator Associated Pneumonia caused by multidrug-resistant *Acinetobacter baumannii*, will present any of the following characteristic: Patients who were admitted in the surgical department and in the general wards should be considered for the prevention of infection carefully. Prior to the exposure of antimicrobials is a predictor group for the development of Ventilator Associated Pneumonia caused by multidrug-resistant *Acinetobacter baumannii* should follow the guidelines of American Thoracic Society Documents 2005, which focused on the initial empiric therapy for ventilator associated pneumonia in patients with late onset disease or risk factors for multidrug resistant pathogens.
2. Tracheostomy has been proven as the effective treatment for ventilator associated pneumonia caused by multidrug resistant *Acinetobacter baumannii*. But, in the long duration of ventilator dependent, the effectiveness of tracheostomy was minimized because of the duration of ventilator becomes a risk factor itself.
3. Infection control of MDRAB has been problematic because it can be survived on dry surfaces for extended periods of time and may also be spreaded by the airborne route. Thus, routine infection control measures such as hand washes and contact isolation techniques are mandated. In spite of those, it may not be adequately controlled the spread of MDRAB in hospitals. In addition to routine measures, many experts have successfully utilized special infection control measures to manage hospital epidemics and endemics of MDRAB.
4. These special infection control measures included cohorting of patients, equipment, and staff; vigorous cleaning and disinfection of the environment; control of antibiotic uses, especially third-generation cephalosporins and carbapenems
5. Surveillance behavior of patients, environmental surfaces, and staff, and continuous quality control and education should be implement.

Recommendation for the further studies

1. The further study design should be considered on the identification of the type of multidrug-resistant *Acinetobacter baumannii* isolates which is genetically characterized by pulse-field gel electrophoresis (PFGE). For a clear demonstration of the epidemiology and risk factors may varies in the different cloning.
2. The future study in mechanical ventilator dependent patients who are high risk for the development of Ventilator Associated Pneumonia caused by multidrug-resistant *Acinetobacter baumannii* should be emphasized in order.
3. Future hospital research projects about costs of patients can be demonstrated with, multidrug-resistant *Acinetobacter baumannii* should be studied, because of the longer and expensive antibiotic courses, more patient-days and/or other hospital complications.

REFERENCES

1. American Thoracic Society. Hospital-acquired pneumonia in adults: diagnosis assessment of severity, initial antimicrobial therapy and preventative strategies. Am J Respir Crit Care Med 1996(153):1711-1725
2. Mandakini P., Yatin M, Poonam K., Anshumali C., Vinay K., T. N. Ventilator - Associated Pnuemonia: Incidence, Risk Factor, Outcome, and Microbiology. Cardiothoracic and Vascular Anesthesia 2003;17(1):22-28.
3. J.L.Vincent. Ventilatior-Associated Pneumonia. Hospital Infection 2004;57(4):272-280.
4. Wenzel R. Hospital acquired pnuemonia: Overview of the current state of the art for prevention and control. Eur J Microbiology Infect Dis 1989;8:56-60.
5. Danchaivijitr S, Chokloikaew S. A national prevalence, Study on nosocomial infection. J Med Asso Thai 1988;72:1-5.
6. Rello J, Torres A. Microbial causes of ventilator-associated pneumonia. Semin Respir Infect 1996;11:24-31.
7. Urban C, Segal-Maurer S, Rahal J. Considerations in control and treatment of nosocomial infections due to multidrug-resistant Acinetobacter baumannii. Clin Infect Dis 2003;36(10):1268-1274.
8. Smolyakov R, Borer A, Riesenberg K, Schlaeffer F, Alkan M, Porath A, et al. Nosocomial multi-drug resistant Acinetobacter baumannii bloodstream infection: risk factors and outcome with ampicillin-sulbactam treatment. J Hosp Infect 2003;54(1):32-8.

9. Villegas M, Hartstein A. Acinetobacter outbreaks. Infect Control Hosp Epidemiol ,1977-2000 2003;24(4):284-295.

10. Rello J, Sa-Borges M, Correa H, Leal S, Baraibar J. Variations in etiology of ventilator-associated pneumonia across four treatment sites: implications for antimicrobial prescribing practices. Am J Respir Crit Care Med 1999;160:608-613.

11. Erbay H, Yalcin A, Serin S, Turgut H, Tomatir E, Cetin B, et al. Nosocomial infections in intensive care unit in a Turkish university hospital: a 2-year survey. Intensive Care Med 2003;29:1482-8.

12. Maragakis L. Multidrug-Resistant (MDR) Acinetobacter. *Infectious Diseaes: Preventon & Control Surviellance Reseach*; 2003.

13. Garcia-Garmendia J, Ortiz-Leyba C, Garnacho-Montero J: et al. Mortality and the increased length of stay attributable to the acquisition of *Acinetobacter* in critically ill patients. Crit Care Med 1999;27(9):1794-8.

14. NARST. Topten Isolates from al region of THailand. Thailand: National Institube of Health, Department of Medical Science; 1998-2004.

15. Report of Nosocomial Infection in Nakhon Pathom hospital during 2000-2004. Thailand: Nakhon Pathom Hospital; 2000-2004.

16. Allen DM, Hartman BJ. Acinetobacter species. *Principles and Practice of Infectious Diseases* (5th ed.). In: In: J.L. Mandell JEBaRD, Editors, editor. Churchill Livingstone, New York; 2000. p. 2339-2342.

17. American Thoracic Society Documents: Guideline for the Management of Adults with Hospital acquired, Ventilator-associated, and Healthcare-associated Pnuemonia. Am J Respir Crit Med 2005;171:388-416.

18. Combes A, C Figliolini, JL Trouillet: et al. Incidence and outcome of polymicrobial ventilator-associated pneumonia. Chest 2002(121):1618-1623.

19. Wisplinghoff H, Edmond M, Pfaller M, Jones R, Wenzel R, Seifert H. Nosocomial bloodstream infections caused by Acinetobacter species in United States hospitals: clinical features, molecular epidemiology, and antimicrobial susceptibility. Clin Infect Dis 2000;31(3):690-69.

20. Trouillet JT. CJ, Vuagnat A, et al. Ventilator associated pnuemonia caused by potential drug resistant bacteria. Am J Respir Crit Care Med 1998;157:531-539.

21. Manuela C, Mauricio V, Torres A. Respiratory nosocomial infections in the medical intensive care unit. Microbes and Infection 2005;7:292-301.

22. Kollef M, Schuster D. Ventilatior-associated pneumonia: clinical consideratins. AJR Am J Roentgenol 1994;163:1031-1035.

23. Chastre J. Conference Summery: Ventilator -Associated Pnuemonia. Respir Care 2005;50(7):975-983.

24. Mehtar S. Hospital Infection Contol: Setting up with minimal resources. United States: Oxford University Press; 1992.

25. John V. Bennett, Brachman PS. Hospital Infections. United States of America: Little, Brown and company Boston/ Toronto; 1986.

26. Jover Saenz A, Barcenila Gaite F, Barbe Illa E, Garcia Gonzalez M, Lopez Salcedo R, Castellana Perello D, et al. Nosocomial infection by multiresisyant pathogens during one year in a secondary hospital: clinical and epidemiological analysis. An Med Interna 2005;22(2):59-64.

27. Cisneros JM, Pachon J. [Acinetobacter baumannii: a nosocomial pathogen difficult to control]. Enferm Infecc Microbiol Clin 2003;21(5):221-3.

28. Chastre J. Infections due to Acinetobacter Baumannii in the ICU. Semin Respir Crit Care Med 2003;24(1):69-78.

29. Jain R, Danziger LH. Multidrug-resistant Acinetobacter infections: an emerging challenge to clinicians. Ann Pharmacother 2004;38(9):1449-59.

30. Levidiotou S, Galanakis E, Vrioni G, Papamichael D, Nakos G, Stefanou D. A multi-resistant Acinetobacter baumannii outbreak in a general intensive care unit. In Vivo 2002;16(2):117-22.

31. Ling ML, Ang A, Wee M, Wang GC. A nosocomial outbreak of multiresistant Acinetobacter baumannii originating from an intensive care unit. Infect Control Hosp Epidemiol 2001;22(1):48-9.

32. Levin AS, Gobara S, Mendes CM, Cursino MR, Sinto S. Environmental contamination by multidrug-resistant Acinetobacter baumannii in an intensive care unit. Infect Control Hosp Epidemiol 2001;22(11):717-20.

33. El Shafie SS, Alishaq M, Leni Garcia M. Investigation of an outbreak of multidrug-resistant Acinetobacter baumannii in trauma intensive care unit. J Hosp Infect 2004;56(2):101-5.

34. Garnacho-Montero J, Ortiz-Leyba C, Jimenez-Jimenez FJ, Barrero-Almodovar AE, Garcia-Garmendia JL, Bernabeu-Wittel IM, et al. Treatment of multidrug-resistant Acinetobacter baumannii ventilator-associated pneumonia (VAP) with intravenous colistin: a comparison with imipenem-susceptible VAP. Clin Infect Dis 2003;36(9):1111-8.

35. Kucukates E. Antimicrobial Resistance among Gram-Negative Bacteria Isolated from Intensive Care Units in a Cardiology Institute in Istanbul, Turkey. Jpn J Infect Dis 2005;58(4):228-31.

36. Report of topten Isolates from al region of THailand: NARST: National Institube of Health, Department of Medical Science; 1998-2004.

37. Wong TH, Tan BH, Ling ML, Song C. Multi-resistant Acinetobacter baumannii on a burns unit--clinical risk factors and prognosis. Burns 2002;28(4):349-57.

38. Simor AE, Lee M, Vearncombe M, Jones-Paul L, Barry C, Gomez M, et al. An outbreak due to multiresistant Acinetobacter baumannii in a burn unit: risk factors for acquisition and management. Infect Control Hosp Epidemiol 2002;23(5):261-7.

39. Salas Coronas J, Cabezas Fernandez T, Alvarez-Ossorio Garcia de Soria R, Rogado Gonzalez MC, Delgado Fernandez M, Diez Garcia F. [Nosocomial infection/colonization of the respiratory tract caused by Acinetobacter baumannii in an Internal Medicine ward]. An Med Interna 2002;19(10):511-4.

40. PT Scott, K Peterson D, J Fishbain. Acinetobacter baumannii Infections Among Patients at Military Medical Facilities Treatment Injured U.S.Service Members,2002-2004. MMWR Weekly 2004;53(45):1063-1066.

41. Maragakis LL, Cosgrove SE, Song X, Kim D, Rosenbaum P, Ciesla N, et al. An outbreak of multidrug-resistant Acinetobacter baumannii associated with pulsatile lavage wound treatment. Jama 2004;292(24):3006-11.

42. Webber DJR, W.A. Nosocomial Infection Associated with Respiratory Therapy. in Mayhall.CG. Hospital Epidemiology and Infection Control. Baltimore: Williams & Wilkins.pp.; 1996.

43. Maniatis AN, Pournaras S, Orkopoulou S, Tassios PT, Legakis NJ. Multiresistant Acinetobacter baumannii isolates in intensive care units in Greece. Clin Microbiol Infect 2003;9(6):547-53.

44. Zeana C, Larson E, Sahni J, Bayuga SJ, Wu F, Della-Latta P. The epidemiology of multidrug-resistant Acinetobacter baumannii: does the community represent a reservoir? Infect Control Hosp Epidemiol 2003;24(4):275-9.

45. Zhou P, EG C. A prospective study on the risk factors of Acinetobacter baumannii bacteremia infection in incubated patients with nosocomial puemonia. Zhonghua Liu Xing Bing Xue Za Zhi 2004;25(7):617-9.

46. Garnacho-Montero J, Ortiz-Leyba C, Jimenez-Jimenez FJ, Barrero-Almodovar AE, Garcia-Garmendia JL, Bernabeu-Wittel IM, et al. Risk factor for infection by Acinetobacter baumannii in patients with VAP: analysis of imipenem resistant episodes. In: Abstrac, 44 th Interscience Conference on Antimicrobial Agents and Chemotherapy; 2005; Washington pp; 2005. p. 351-352.

47. Abbo A, Navon-Venezia S, Hammer-Muntz O, Krichali T, Siegman-Igra Y, Carmeli Y. Multidrug-resistant Acinetobacter baumannii. Emerg Infect Dis 2005;11(1):22-9.

48. S.H. Wang, W.H.Sheng, Y.Y.Chang, L.H. Wang, H.C. Lin, M.L.Chen, et al. Healthcare associated outbreak due to pan-drug resistant Acinetobacter baumannii in a surgical intensive care unit. journal of Hospital Infection 2003;53:97-102.

49. Mahgoub S, Ahmed J, Glatt AE. Underlying characteristics of patients harboring highly resistant Acinetobacter baumannii. Am J Infect Control 2002;30(7):386-90.

50. C.Valero, J.D.Garcia Palomo, P.Martorras, C. Fermandez-Mazarrasa, C. Gonzalez Fernandez, M.C.Farinas, et al. Acinetobacter bacteraemia in a teaching hospital, 1989-1998. EUr J Inter Med 2001;12:425-429.

51. Manuel W, Zaid A, Gwendolyn C. Outbreak of Acinetobacter baumannii in an intensive care unit associated with tracheostomy. Am J Infect Control 2001;29:284-8.

52. Agusti C, Pujol M, Argerich MJ, Ayats J, Badia M, Dominguez MA, et al. Short-term effect of the application of selective decontamination of the digestive tract on different body site reservoir ICU patients colonized by multi-resistant Acinetobacter baumannii. J Antimicrob Chemother 2002;49(1):205-8.

53. Rodriguez-Bano J, Cisneros JM, Fernandez-Cuenea F, Ribera A, Vila J, Pascual A, et al. Clinical features and epidemilogy of Acinetobacter baumannii colonization and infection in Spanish hospitals. Infect Control Hosp Epidemiol 2004;25(10):819-24.

54. Scott K. Fridki, Robert P. Gaynes. Antimicrobial Resistance in Intensive Care Unit. Clinic in Chest Medicine 1999;20(2).

55. Stephen J. Wilson MD, MPH, Cynthia J. Knipe RN, Madeline J. Zieger PA,

Direct costs of multidrug-resistant *Acinetobacter baumannii* in the burn unit of a public teaching hospital, American Journal of Infection Control ,Volume 32, Issue 6 , October 2004, Pages 342-344

56. Husni, Rola N. MD; Goldstein, Lawrence S. MD; Arroliga, Alejandro C. MD. Risk Factors for an Outbreak of Multi-Drug-Resistant Acinetobacter Nosocomial Pneumonia Among Intubated Patients.CHEST 1999; 115:1378-1382)
57. Piazza O, Iasiello A, PapaIanni C, Incidence of antimicrobial-resistant ventilator associated pneumonia: an eighteen-month survey.Panminerva Med. 2005 Dec;47(4):265-7.

APPENDIX

เอกสาร จธ 4.1

เอกสารชี้แจงการวิจัยแก่ผู้ยินยอมตนให้ทำการวิจัย

(Information sheet)

การวิจัยเรื่อง

ปัจจัยที่มีผลต่อการติดเชื้ออะซินิโตเบาแมนนิไอที่ดื้อต่อยาปฏิชีวนะหลายชนิดในผู้ป่วยที่ใส่ท่อช่วยหายใจ ในโรงพยาบาลนครปฐม จังหวัดนครปฐม

สถานที่ทำการวิจัย

หอผู้ป่วยอายุรกรรม, หอผู้ป่วยศัลยกรรม, หน่วยอภิบาลอายุรกรรม, หน่วยอภิบาลศัลยกรรมและ หอผู้ป่วยพิเศษ โรงพยาบาลนครปฐม จังหวัดนครปฐม

หัวหน้าโครงการและผู้ร่วมโครงการ ตามรายละเอียด ดังนี้

ชื่อผู้วิจัยหลัก นางพัฒนา เลอศักดิ์สมบัติ

นักศึกษาหลักสูตรวิทยาศาสตรมหาบัณฑิต สาขาเอกโรคติดเชื้อและวิทยาการระบาด

ภาควิชาระบาดวิทยา เลขประจำตัวนักศึกษา 4737293 PHPH/M

สถานที่ปฏิบัติงาน กลุ่มการพยาบาล โรงพยาบาลนครปฐม จังหวัดนครปฐม

ประธานกรรมการผู้ควบคุมวิทยานิพนธ์

รศ. ดุสิต สุจิรารัตน์

คุณวุฒิ B.Sc. (Sanitary Science), M.Sc. (Biostatistics)

ตำแหน่งทางวิชาการ รองศาสตราจารย์

ภาควิชาระบาดวิทยา คณะสาธารณสุขศาสตร์ มหาวิทยาลัยมหิดล

กรรมการผู้ควบคุมวิทยานิพนธ์

รศ. กุลยา นาคสวัสดิ์

คุณวุฒิ D.D.S., M.P.H. (Urban Health), M.Sc. (Medical Epidemiology)

ตำแหน่งทางวิชาการ รองศาสตราจารย์

ภาควิชาระบาดวิทยา คณะสาธารณสุขศาสตร์ มหาวิทยาลัยมหิดล

กรรมการผู้ควบคุมวิทยานิพนธ์

รศ. กนกรัตน์ ศิริพานิชกร

คุณวุฒิ B.Sc.(Physiotherapy), M.D., M.P.H.

ตำแหน่งทางวิชาการ รองศาสตราจารย์

ภาควิชาจุลชีววิทยา คณะสาธารณสุขศาสตร์ มหาวิทยาลัยมหิดล

กรรมการผู้ควบคุมวิทยานิพนธ์

พญ.สุธัญญา บรรจงภาค

คุณวุฒิ พ.บ. วว.กุมารเวชศาสตร์

ตำแหน่ง นายแพทย์ 8

สถานที่ปฏิบัติงาน กลุ่มงานกุมารเวชกรรม โรงพยาบาลนครปฐม จังหวัดนครปฐม

วัตถุประสงค์ของโครงการ

1. เพื่อศึกษาอุบัติการการติดเชื้ออะซินิโตเบาแมนนิไอที่ดื้อต่อยาปฏิชีวนะหลายชนิดในผู้ป่วยที่ใส่ท่อช่วยหายใจ
2. เพื่อศึกษาปัจจัยด้านผู้ป่วย, ปัจจัยด้านการรักษา, และปัจจัยด้านสิ่งแวดล้อมที่มีผลต่อการเกิดอุบัติการณ์การติดเชื้ออะซินิโตเบาแมนนิไอที่ดื้อต่อยาปฏิชีวนะหลายชนิด ในผู้ป่วยที่ใส่ท่อช่วยหายใจ

วิธีดำเนินการวิจัย

เป็นการศึกษาแบบติดตามไปข้างหน้า (Follow up study) ผู้ป่วยทุกรายในหอผู้ป่วยอายุรกรรม, หอผู้ป่วยศัลยกรรม, หอผู้ป่วยวิกฤติอายุรกรรม, หอผู้ป่วยวิกฤติศัลยกรรมและหอผู้ป่วยพิเศษที่ใช้เครื่องช่วยหายใจในโรงพยาบาลนครปฐม โดยใช้เครื่องมือที่ใช้ในการดำเนินการวิจัยประกอบไปด้วยแบบบันทึกการเฝ้าระวังการติดเชื้อในผู้ป่วยทุกรายที่ใส่ท่อช่วยหายใจและใช้เครื่องช่วยหายใจ, แบบบันทึกข้อมูลจำนวนผู้ป่วยและจำนวนการใช้เครื่องช่วยหายใจต่อวัน

เหตุผลที่เชิญชวนให้ผู้ยินยอมตนให้ทำการวิจัยเข้าโครงการวิจัย

เนื่องจากผู้เข้าร่วมการวิจัยได้รับการใส่ท่อช่วยหายใจและใช้เครื่องช่วยหายใจมีโอกาสเสี่ยงต่อการเกิดอุบัติการณ์การติดเชื้ออะซินิโตเบาแมนนิไอที่ดื้อต่อยาปฏิชีวนะหลายชนิด

ระยะเวลาที่ต้องทำการทดสอบในผู้ยินยอมตนให้ทำการวิจัย

ผู้เข้าร่วมวิจัยจะได้รับการบันทึกข้อมูลเกี่ยวกับตัวผู้เข้าร่วมวิจัยและปัจจัยที่ผู้เข้าร่วมวิจัยได้รับเมื่อเริ่มต้นการศึกษาคือเมื่อได้รับการใส่ท่อช่วยหายใจและใช้เครื่องช่วยหายใจมีการเฝ้าติดตามสังเกตอาการ การเปลี่ยนแปลง เฝ้าระวังการติดเชื้อปอดอักเสบที่สัมพันธ์กับการใช้เครื่องช่วยหายใจจนกระทั่งถอดเครื่องช่วยหายใจ

ประโยชน์ที่คาดว่าจะเกิดขึ้นทั้งต่อผู้ยินยอมตนให้ทำการวิจัย และต่อผู้อื่น

1. เพื่อศึกษาปัจจัยที่มีความเกี่ยวข้องและมีผลต่อการเกิดอุบัติการณ์การติดเชื้ออะซินิโตเบาแมนนิไอที่ดื้อต่อยาปฏิชีวนะหลายชนิด ในผู้ป่วยที่ใส่ท่อช่วยหายใจ
2. เพื่อใช้เป็นแนวทางในการวางแผนเพื่อลดปัจจัยเสี่ยงต่อการเกิดอุบัติการณ์การติดเชื้ออะซินิโตเบาแมนนิไอที่ดื้อต่อยาปฏิชีวนะหลายชนิด ในผู้ป่วยที่ใส่ท่อช่วยหายใจ

ความเสี่ยงที่คาดว่าจะเกิดขึ้นกับผู้ยินยอมตนให้ทำการวิจัย

การศึกษาวิจัยครั้งนี้ เป็นการศึกษาในผู้ป่วยที่ใช้เครื่องช่วยหายใจทั้งหมด ซึ่งโดยส่วนใหญ่ผู้ป่วยอยู่ในภาวะหมดสติ ขาดสติสัมปชัญญะ ไม่สามารถตัดสินใจในการยินยอมให้ทำการวิจัย ผู้วิจัยจึงให้ผู้แทนชอบด้วยกฎหมาย หรือผู้ปกครอง หรือญาติที่ใกล้ชิดที่สุดเป็นผู้ลงนามยินยอม

ขอบเขตการดูแลรักษาความลับของข้อมูลต่างๆของผู้ยินยอมตนให้ทำการวิจัย

โดยผู้ยินยอมหรือผู้แทนโดยชอบด้วยกฎหมาย/ผู้ปกครอง/ญาติที่เข้าร่วมการวิจัยจะเข้าร่วมการศึกษาโดยความสมัครใจ ผู้วิจัยรับรองว่าข้อมูลของท่านจะได้รับการพิทักษ์สิทธิ์ไม่เปิดเผยเป็นรายบุคคล และจะเปิดเผยได้เฉพาะในรูปที่สรุปผลการวิจัย การเปิดเผยข้อมูลเกี่ยวกับตัวท่านต่อหน่วยงานต่างๆที่เกี่ยวข้องกระทำได้เฉพาะกรณีที่จำเป็นด้วยเหตุผลทางวิชาการเท่านั้น

ผู้วิจัยรับรองว่าหากมีข้อมูลเพิ่มเติมทั้งด้านประโยชน์และโทษที่เกี่ยวข้องกับการวิจัยครั้งนี้ ผู้วิจัยจะแจ้งให้ผู้ร่วมโครงการวิจัยทราบอย่างรวดเร็วโดยไม่ปิดบัง

ผู้ร่วมโครงการวิจัยหรือผู้แทนโดยชอบด้วยกฎหมาย/ผู้ปกครอง/ญาติ มีสิทธิ์ของดการเข้าร่วมโครงการวิจัยโดยไม่ต้องแจ้งให้ทราบล่วงหน้า โดยการงดการเข้าร่วมโครงการวิจัยนี้ จะไม่มีผลกระทบใดๆต่อสิทธิ์ที่ผู้ร่วมโครงการวิจัยจะได้รับต่อไป

ผู้รับผิดชอบที่ยินยอมตนให้การวิจัยสามารถติดต่อได้โดยสะดวก กรณีมีความจำเป็นหรือฉุกเฉิน

นางพัฒนา เลอศักดิ์สมบัติ

นักศึกษาหลักสูตรวิทยาศาสตรมหาบัณฑิต

สาขาเอกโรคติดเชื้อและวิทยาการระบาด

คณะสาธารณสุขศาสตร์ มหาวิยาลัยมหิดล

โทรศัพท์ 081-7052966, 034-254150-4 ต่อ 1094

เอกสาร จธ 4.2

หนังสือยินยอมให้ทำการวิจัย

การวิจัยเรื่อง ปัจจัยที่มีผลต่อการติดเชื้ออะซินิโตเบาแมนนิไอที่ดื้อต่อยาปฏิชีวนะหลายชนิด ในผู้ป่วยที่ใส่ท่อช่วยหายใจ ในโรงพยาบาลนครปฐม จังหวัดนครปฐม

วันที่ให้คำยินยอม วันที่.....เดือน.....พ.ศ. .....

ข้าพเจ้าขอทำหนังสือนี้ไว้ต่อหัวหน้าโครงการเพื่อเป็นหลักฐานแสดงว่า

ข้อ 1 . ก่อนลงนามในใบยินยอมให้ทำการวิจัยนี้ ข้าพเจ้าได้รับคำอธิบายจากผู้วิจัยให้ทราบถึงวัตถุประสงค์ของการวิจัย วิธีการวิจัย อันตราย หรืออาการที่อาจเกิดขึ้นจาการวิจัย หรือจากยาที่ใช้ รวมทั้งประโยชน์ที่จะเกิดขึ้นจากการวิจัยอย่างละเอียด และมีความเข้าใจดีแล้ว

ข้อ 2. ผู้วิจัยรับรองว่า จะตอบคำถามต่างๆที่ข้าพเจ้าสงสัยด้วยความเต็มใจ ไม่ปิดบัง ซ่อนเร้นจนข้าพเจ้าพอใจ

ข้อ 3. ข้าพเจ้าเข้าร่วมโครงการนี้โดยสมัครใจ และข้าพเจ้ามีสิทธิ์ที่จะบอกเลิกการเข้าร่วมในโครงการวิจัยนี้เมื่อใดก็ได้ และการบอกเลิกการเข้าร่วมวิจัยนี้จะไม่มีผลต่อการรักษาโรคที่ข้าพเจ้าจะพึงได้รับต่อไป

ข้อ 4. ผู้วิจัยรับรองว่า จะเก็บข้อมูลเฉพาะเกี่ยวกับตัวข้าพเจ้าเป็นความลับ และจะเปิดเผยได้เฉพาะในรูปที่เป็นสรุปผลการวิจัย การเปิดเผยข้อมูลเกี่ยวกับตัวข้าพเจ้าต่อหน่วยงานต่างๆที่เกี่ยวข้อง กระทำได้เฉพาะกรณีจำเป็นด้วยเหตุผลทางวิชาการเท่านั้น

ข้อ 5. ผู้วิจัยรับรองว่าหากเกิดอันตรายใดๆอันเนื่องจากการวิจัยดังกล่าว ข้าพเจ้าจะได้รับการรักษาพยาบาลโดยไม่คิดมูลค่าตามมาตรฐานวิชาชีพ และจะได้รับการชดเชยรายได้ที่สูญเสียไประหว่างการรักษาพยาบาลดังกล่าว ตลอดจนเงินทดแทนความพิการที่อาจเกิดขึ้น

ข้อ 6. ผู้วิจัยรับรองว่าหากมีข้อมูลเพิ่มเติมที่ส่งผลกระทบต่อการวิจัย ข้าพเจ้าจะได้รับการแจ้งให้ทราบโดยไม่ปิดบัง ซ่อนเร้น

ข้าพเจ้าได้อ่านข้อความข้างต้นแล้วมีความเข้าใจดีทุกประการ และได้ลงนามในใบยินยอมนี้ด้วยความเต็มใจ

ลงชื่อ.....ผู้ยินยอม
(.....)
ลงชื่อ.....พยาน
(.....)
ลงชื่อ.....พยาน
(.....)

ในกรณีที่ผู้ยินยอมตนให้ทำการวิจัยมาสามารถอ่านและเขียนหนังสือได้ จะต้องได้รับการยินยอมในขณะที่ยังมีสติสัมปชัญญะ และระบุข้อความไว้ตามนี้ ข้าพเจ้าไม่สามารถอ่านหนังสือได้ แต่ผู้วิจัยได้อ่านข้อความในใบยินยอมนี้ให้แก่ข้าพเจ้าฟังจนเข้าใจดีแล้ว ข้าพเจ้าจึงลงนาม หรือประทับลายนิ้วหัวแม่มือของข้าพเจ้าในใบยินยอมนี้ด้วยความเต็มใจ

ลงนาม.....ผู้ยินยอม
(.....)
ลงนาม.....พยาน
(.....)
ลงนาม.....พยาน
(.....)

ในกรณีที่ผู้ยินยอมตนให้ทำการวิจัยยังไม่บรรลุนิติภาวะ จะต้องได้รับการยินยอมจากผู้ปกครองหรือผู้อุปการะโดยชอบด้วยกฎหมาย

ลงนาม.....ผู้ปกครอง/ผู้อุปการะ
(.....)โดยชอบด้วยกฎหมาย
ลงนาม.....พยาน
(.....)
ลงนาม.....พยาน
(.....)

ในกรณีที่ผู้ยินยอมตนให้ทำการวิจัยยังไม่สามารถตัดสินใจเองได้ (เช่นกรณีผู้ยินยอมตนให้ทำการวิจัยอยู่ในภาวะหมดสติ) ให้ผู้แทนโดยชอบด้วยกฎหมาย หรือผู้ปกครอง หรือญาติที่ใกล้ชิดที่สุดเป็นผู้ลงนามยินยอม

ลงนาม.....ผู้แทน/ผู้ปกครอง/ญาติ
(.....)
ลงนาม.....พยาน
(.....)
ลงนาม.....พยาน
(.....)

APPENDIX

Data collection form ID.....

Part 1. General characteristics

1.1 Gender [ ] male [ ] female [ ]

1.2. Age……..…years [ ]

1.3. Ward admission (before diagnosis of VAP) [ ]

[ ] Intensive Care Unit [ ] General ward [ ] Private ward

1.4 Principle diagnosis…….. [ ]

1.5. Hospital Department [ ]

[ ] Medical [ ] Surgical [ ] Orthopedic [ ] Other

1.6 Admission date……/……/……..…Discharge date……/……/……..

Length of hospital……days

1.7 Date on intubation……/……/…….Date off intubation……/……/…….

Total ventilator days……days

Part 2. The medical characteristics

2.1 Severity of illness [ ]

[ ] SIC 1. [ ] SIC 2. [ ] SIC 3. [ ] SIC 4. [ ] SIC 5.

2.2 Underlying disease [ ] yes [ ] no [ ]

[ ] HT [ ] DM [ ] Head injury [ ] Chest injury [ ]

[ ] COPD [ ] TB [ ] IHD [ ] Respiratory failure

[ ] Cancer [ ] Renal failure

2.3 Prior antibiotic usage [ ] yes [ ] no [ ]

2.4 Presence of wounds [ ] yes [ ] no [ ]

[ ] surgery [ ] decubitus ulcer [ ] laceration [ ]

2.5 Co-infection [ ] yes [ ] no [ ]

[ ] UTI [ ] BSI [ ] SKIN [ ] SSI [ ]

2.6 Prior-infection [ ] yes [ ] no [ ]

[ ] UTI [ ] BSI [ ] SKIN [ ] SSI [ ]

Part 3. Treatment factors

3.1 Aerosol nebulizer [ ] yes [ ] no [ ]

3.2 Central venous line [ ] yes [ ] no [ ]

3.3 Tracheostomy tube [ ] yes [ ] no [ ]

Date on tracheostomy tube .. …..…/…..…/……. .

Date off tracheostomy tube …… /…..…/……. .

Total tracheostomy……days

3.4 Inter costal drainage [ ] yes [ ] no [ ]

3.5 Stress ulcer prophylaxis (before diagnosis of VAP) [ ] yes [ ]no [ ]

[ ] H2 receptor antagonist [ ] Antacid [ ] Sulcralfate [ ]

3.6 Treatment with antimicrobial drug before diagnosis of VAP

[ ] Penicillin on……off…… [ ]

Total……days

[ ] Anti - psuedomonal penicillins

on……off…… [ ]

Total……days

[ ] Cephalosporin on……off…… [ ]

Total……days

[ ] Aminoglycoside on……off…… [ ]

Total……days

[ ] Carbapenem on……off…… [ ]

Total……days

[ ] Vancomycin on……off…… [ ]

Total……days

[ ] Fluoroquinolone on……off…… [ ]

Total……days

[ ] Macrolides on……off…… [ ]

Total……days

Part 4. Out come

4.1 Presence of VAP [ ] yes [ ] no [ ]

Diagnosis of VAP date…….

Time of intubation until presence of VAP……days

4.2 Organism of VAP [ ]

[ ] *MDRAB* [ ] *A. baumannii* [ ] *P.aeruginosa* [ ] *MRSA*

[ ] *K.pneumoniae* [ ] *E.coli* [ ] *Enterococcus spp.*[ ] Other

BIOGRAPHY

NAME PATTHANA LERSAKSOMBAT

DATA OF BIRTH 5 August 1967

PLACE OF BIRTH Saraburi, Thailand

INSTITUTIONS ATTENDED Saraburi Nursing College,
Saraburi, 1989
Diploma in Nursing and Midwife

Mahidol University, 2008
Master of Science(Public Health)
Major in Infectious Diseases and
Epidemiology

POSITION & OFFICE Nakhon Pathom Hospital
Nakhon Pathom, Thailand
Position : Nurse
Tel 034-254150-4

HOME ADDRESS 18/3 tumbol srisathong,
Nakhonchaisri, Nakhon Pathom,
Thailand, 73120
Tel 034-227429-30