THE PREVALENCE AND RISK FACTORS OF VENTILATOR – ASSOCIATED PNEUMONIA IN INTENSIVE CARE UNITS IN HOSPITAL SULTANAH BAHIYAH KEDAH MALAYSIA

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THE PREVELANCE AND RISK FACTORS OF VENTILATOR ASSOCIATED PNEUMONIA IN INTENSIVE CARE UNIT IN HOSPITAL SULTANAH BAHIYAH, KEDAH MALAYSIA

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Introduction: Ventilator associated pneumonia (VAP) is the commonest nosocomial infection in intensive care unit (ICU). We conducted a first study to collect local data on prevalence and risk factors of VAP in Hospital Sultanah Bahiyah (HSB), Kedah.

Methodology: This prospective cohort surveillance was conducted on patients admitted to an adult medical-surgical ICU of a tertiary hospital from 1st August 2104 to 31st July 2105. VAP was diagnosed using Malaysia Registry of ICU (MRIC) criteria which included clinical manifestation, imaging and investigations.

Results: In total, 297 patients were enrolled in this study. The prevalence of VAP was 22.0%. The most common causative pathogen was Acinetobacter sp. (31.8%). Multivariate analysis using simple logistic regression showed that risk factors for VAP were elderly patients (P=0.02; OR 1.02; 95% CI 1.00, 1.04), increase duration of ventilation (P<0.001; OR 1.49; 95% CI 1.35, 1.63), length of stay in ICU (P<0.001; OR 1.45; 95% CI 1.33, 1.59), length of stay in hospital (P<0.001; OR 1.07; 95% CI 1.04, 1.09), respiratory diseases (P=0.02; OR 2.25; 95% CI 1.17, 4.33), lung malignancy (P<0.001; OR 22.35; 95% CI 6.24, 80.09), previous antibiotic within three months (P=0.02; OR 2.25; 95% CI 1.17, 4.33), tracheostomy (P<0.001; OR 18.42; 95% CI 9.36, 36.23), reintubation (P<0.001; OR 25.69; 95% CI 12.73, 51.82), transportation for remote procedure (P<0.001; OR 20.76; 95% CI 9.65, 44.76), central venous line (CVL) insertion (P=0.04; OR 2.22; 95% CI 1.04, 4.76), continuous sedation (P=0.03; OR 1.85; 95% CI 1.04, 3.26) and without venous thromboprophylaxis (P=0.03; OR 2.05; 95% CI 1.09, 3.87).

Conclusion: The prevalence and risk factors in our study were comparable to national and international data. We identify one new risk factor which is CVL insertion.

Dr Laila Abdul Mukmin: Supervisor

Professor Mahamarowi Omar: Co-Supervisor

Dr Ahmad Shaltut bin Othman: Co-Supervisor

CHAPTER 1: INTRODUCTION AND LITERATURE REVIEW

1.1 INTRODUCTION

Hospital acquired infections or nosocomial infections can be defined as those occurring within 48 hours of hospital admission, 3 days of discharge or 30 days of an operation. They affect 10% of hospitalized patients and are important causes of morbidity and mortality throughout the world (1). The critically ill patients are at particular risk of developing intensive care unit (ICU) acquired infection as they were mostly immuno-compromised, mechanical ventilated and have multiple invasive procedures done. Nosocomial infections can affect multiple sites such as the lungs, urinary tract, surgical sites and the bloodstream. Of all the sites, lung is the most vulnerable to develop nosocomial infection. Nosocomial pneumonia occurring after 48 hours of mechanical ventilation is referred to as ventilator associated pneumonia (VAP).

The incidence of VAP varies from 9% to 27% all over the world. In the United States of America it ranges from 9.3% to 15% while in Europe is 8% to 28%. In Asia it was documented to be 2% to 40%. In Malaysia, the incidence was found to be 26.5%. The mortality rate varies between 30% to 70% (2) and can be as high as 90% in some centers. However, not all deaths among affected patients are the direct result of infection; rather, VAP is a marker for severity of illness.

VAP is a common condition but it is difficult to diagnose and expensive to treat. Modifiable risk factors for VAP have influence on patient treatment. Thus with better

understanding of the risk factors of VAP and the implementation and awareness of ventilator bundle for ventilated patient, the mortality rate can be reduced to 50%. This is important as it not only reduces the cost of health care in Malaysia, but also reduces the length of stay in ICU. As in Malaysia the ICU bed is always shortage and limited, it is a concern that VAP depletes the limited resources in our ICU.

The outcome indicators of VAP can be used in benchmarking the quality of patient care in Malaysia. Therefore, surveillance of VAP received a high level of attention. Since 2000, the Malaysian surveillance has targeted three site-specific, device-associated infections, including ventilator-associated pneumonia, central-line-related bloodstream infection (CR-BSI), and catheter-related urinary tract infection (CR-UTI). The Malaysia Ministry of Health, Malaysian Registry of Intensive Care (MRIC) also produces a yearly report and recommendation on VAP. MRIC (3, 4) has also outlined and advised VAP bundle for our local hospitals.

1.2 LITERATURE REVIEW

1.2.1 Ventilator Associated Pneumonia

Ventilator associated pneumonia (VAP) is defined as nosocomial pneumonia occurring in a patient after 48 hours of mechanical ventilation via a tracheal or tracheostomy tube (5).

1.2.1.1 Pathogenesis

VAP has been suggested to be related to the interaction between endotracheal tube (ETT), host immunity, infecting microorganism and the presence of risk factors. The presence of ETT will more or less impaired the cough and gag reflex. This will cause microaspiration around the cuff of the ETT. The presence of ETT also caused the mucociliary functions to be impaired causing reduction in clearance of the mucous flow and thus increase the chance to get VAP. Critically ill patients are mostly immunocompromised as there may be impaired of phagocytosis. Furthermore the severity of underlying diseases, the used of previous antibiotic and previous surgery will also contribute to lowering the host immunity. The infecting microorganism can get access to the lower respiratory tract via microaspiration as describe previously. It can also form a biofilm laden with bacteria and bacterial colonization within the ETT. Last but not least, the trackling and pooling of secretion around the cuff of ETT also plays as a risk factor in VAP. These secretions have high bacteria load and subsequently they will have access to the pulmonary parenchyma and cause pneumonia. All these microorganisms can be pushed further by the positive pressure that is used for in mechanical ventilation.

Many risk factors for the development of VAP have been identified. They can be differentiated into modifiable and non-modifiable risk factors and into patient-related and treatment related risk factors.

Table 1. Risk factors for ventilator-associated pneumonia (6)

Nonmodifiable risk factors
1. Patient-related risk factor
• Chronic Obstructive Pulmonry Disease (COPD)
• Organ System Failure Index of > 2
• Age of > 60 years
• Coma
• Acute Respiratory Distress Syndrome (ARDS)
• Head trauma
• Male sex
2. Intervention-related risk factor
• Neurosurgery
• Thoracic surgery
• Intracranial Pressure (ICP) monitor
• Transportation out of ICU
• Reintubation

Modifiable risk factors

1. **Intervention-related risk factor**

- Use of H2-antagonist
- Use of antacids
- Use of sucralfate
- 24-h circuit changes, compared with 48-h circuit changes
- Use of antibiotics
- Supine position
- Receive of enteral nutrition
- Failed subglottic aspiration
- Intracuff pressure of < 20 cm H2O
- Tracheostomy
- Aerosol treatment

It is important to identify the risk factors for VAP as it provides a basis in the implementation of prevention strategies.

1.2.1.2 Microbiology

The type of microorganisms that cause VAP can be suspected by the duration of mechanical ventilation. Generally, VAP is divided into early onset (within the 1st 4 days) and late onset (day 5 onwards). Early onset VAP are usually cause by gram negative

bacteria that are sensitive to antibiotic while culprit of the late onset VAP are usually microorganisms that have higher level of antibiotic resistant.

1. Early onset VAP
    - *Streptococcus pneumoniae*
    - *Hemophilus infl uenzae*
    - *Methicillin-sensitive Staphylo coccus aureus (MSSA)*
    - *Escherichia coli*
    - *Klebsiella pneumonia*
    - *Enterobacter species*
    - *Proteus species*
    - *Serratia marcescens*

2. Late onset VAP
    - *Methicillin-resistant S. aureus (MRSA)*
    - *Acinetobacter*
    - *Pseudomonas aeruginosa,*
    - *Extended-spectrum beta-lactamase producing bacteria (ESBL)*

However the types of multidrug resistant (MDR) organisms are different from hospital to hospital. So it is important to know our local microbiological data as the treatment of VAP is mainly early empirical antibiotic based on the suspected organism. It can be de-escalated once the full culture and sensitivity is available.

1.2.1.3 Diagnosis of VAP

Over the years, there have been several criteria proposed for diagnosing VAP in clinical settings, such as clinical manifestations, imaging, bronchoalveolar specimens and others, but none of these has the needed sensitivity and specificity to accurately diagnosed VAP. As a result, there is still lack of acceptable gold standard in diagnostic criterion for VAP. The lacking of gold standard diagnostic criteria will cause a delay in diagnosis and subsequently delay in initiating appropriate therapy which will cause the patients' prognosis became worsen. Having say that, an inappropriate or inaccurate diagnosis will lead to unnecessary treatment and this will not only cause complications secondary to the treatment but also not economical. Therefore an accurate diagnosis for VAP is fundamental.

Johanson et al. (7) in year 1972 have suggested new or progressive consolidation on chest radiology plus at least two of the following variables:

1. fever greater than 38°C
2. leukocytosis or leucopenia
3. purulent secretions

as a diagnosis of VAP. Although the sensitivity was only 69% and specificity 72%, this criteria is the most acceptable and most widely used in our country currently as it was recommended by the American Thoracic Society Consensus Conference on VAP.

Another criterion is the National Nosocomial Infection Surveillance (NNIS) system (8). The NNIS system was developed in the 1970s by the Centers for Disease Control (CDC) as

a tool to describe the epidemiology of hospital-acquired infections. It includes radiological signs, clinical signs and microbiological criteria.

1. Radiology signs

   Two or more serial chest radiographs with at least 1 of the following:

   - new or progressive and persistent infiltrate
   - consolidation
   - cavitation

2. Clinical signs

   At least 1 of the following:

   - fever (temperature > 38 C)
   - leukopenia (< 4000 WBC) or leukocytosis (> 12000 WBC)
   - altered mental status, for adults 70 years or older, with no other recognized cause

3. Microbiological criteria

   At least one of the following:

   - positive growth in blood culture not related into another source of infection
   - positive growth in culture or pleural field
   - positive quantitative culture from bronchoal aveolar lavage (> 10^4) or protected specimen brushing (> 10^3)
   - five percent or more of cells with intracellular bacteria on direct microscopic examination of Gram-stained bronchoal aveolar lavage fluid
   - histopathological evidence of pneumonia

   Plus at least 2 of the following:-

   - new onset of purulent sputum, or change in character of sputum

- increased respiratory secretions, or increased suctioning requirements
- new-onset or worsening cough, or dyspnea, or tachypnea
- rales or bronchial sounds
- worsening gas exchange
- increase oxygen requirement

This NNIS system has a slightly higher sensitivity (84% versus 69%) if compare to the Johanson's recommendation but the specificity was only 69%.

Pugin et al. in 1991 also developed the Clinical Pulmonary Infection Score (CPIS) which was based on six variables such as fever, leukocytosis, tracheal aspirates, oxygenation, radiographic infiltrates, and semi-quantitative cultures of tracheal aspirates with Gram stain. Each variable has score from 0 to 2. Total score of > 6 points suggests ventilator-associated pneumonia.

1. Temperature
    - 0 point: 35.5-38.4 degree celcius
    - 1 point: 38.5-38.9 degree celcius
    - 2 point: < 36 or > 39 degree celcius
2. Blood leukocytes (cells/µL)
    - 0 point: 4000-11000
    - 1 point: < 4000 or > 11000
    - 2 point: > 500 band form
3. Oxygenation
    - 0 point: PaO_2/FiO_2 > 240 or acute respiratory distress syndrome

- 2 point: PaO_2/FiO_2 < 240 and no evidence of acute respiratory distress syndrome

4. Pulmonary radiography
    - 0 point: no infiltrate
    - 1 point: diffuse or patchy infiltrate
    - 2 point: localized infiltrate
5. Tracheal secretions (score)
    - 0 point: < 14
    - 1 point: > 14
    - 2 point: purulent secretion
6. Culture of tracheal aspirate
    - 0 point: minimal or no growth
    - 1 point: moderate or more growth
    - 2 point: moderate or greater growth

The initial description by Pugin (9) showed high sensitivity of 93% and specificity of 100%. However that sample size of the study was small and only included 28 subjects. Furthermore, the CPIS was compared to quantitative culture of BAL fluid using a 'bacterial index' defined as the sum of the logarithm of all bacterial species recovered, which is not considered an acceptable gold standard for the diagnosis of VAP. Later research compared the CPIS with the pathological diagnosis showed that the CPIS had sensitivity between 72 and 77% and specificity between 42 and 85%.

There are also many other studies evaluated the role of bacteriological data in improving the accuracy of a clinical diagnosis of VAP. These studies showed that bacteriological data

such as bronchoalveolar lavage (BAL), protected specimen brush and tracheobronchial aspiration did not superior to clinical diagnosis of VAP (10-12). However, these bacteriological data might be useful in identifying the infecting microorganism and assist in initiating the appropriate therapy.

Recently, there are increasing in interest in researchers regarding the role of using biological markers in diagnosing VAP. The proposed pathophysiology is that when the protective mechanism that prevent microorganism from reaching the alveoli are overwhelmed, the alveolar macrophages will be activated and release all the endogenous mediators. Biomarkers such as C-reactive protein, procalcitonin, elastin fiber, endotoxin and others are being studied. C-reactive protein and procalcitonin seems like promising biomarkers in diagnosis of VAP while elastin fiber and endotoxin are of limited value. However, large scale studies are still needed in evaluating the usefulness of biological markers in diagnosing VAP.

1.2.1.4 Prevention Strategies

Base on the pathogenesis and risk factors of VAP, prevention strategies can be implemented to reduce the incidence of VAP. There are several preventive strategies introduced by multiple sites and journals. Among them are American Thoracic Society (ATS), New England Journal of Medicine (NEJM) and Critical Care (CC). Below are guidelines of VAP bundles from ATS (13).

1. General prophylaxis

- Effective infection control measures such as staff education and hand hygiene.

- Surveillance of ICU infections.

2. Intubation and mechanical ventilation.

- Avoid intubation and reintubation if possible.
- Whenever possible, used noninvasive ventilation rather than invasive ventilation.
- Orotracheal intubation and orogastric tubes are preferred over nasal tubes as nasal tubes can cause nosocomial sinusitis and increases risk of VAP.
- Reduce early onset VAP by continuous suction of subglottic secretion.
- Maintain the endotracheal cuff pressure > 20cmH2O as it will prevent bacterial from trackling down to the lower respiratory tract.
- Contaminated condensate should be prevented from entering the ETT.
- Heat moisture exchanger (HME) is not VAP prevention tools.
- Reduce the day of intubation and early extubation if possible.
- Adequate staffing as 1 to 1 nursing if possible.

3. Aspiration, body position, and enteral feeding.

- Prop up patient 30-45 degree to prevent from aspiration.
- Enteral feeding is preferred over parenteral feeding.

4. Modulation of colonization: oral antiseptics and antibiotics.

- Antibiotic prophylaxis for HAP will reduce but not recommend for antibiotic if suspected colonization of MDR pathogens.
- Prior systemic antibiotic will reduce the risk of nosocomial pneumonia but we should suspect MDR pathogen if history of prior antibiotic administration is present at the time of onset of infection.
- Not recommend to use prophylactic antibiotic for 24 hours following intubation.

- Use of oral chlorhexidine in post CABG patient has shown to reduce VAP but its routine use not recommended.
- Sedation vacation and not using paralytic agent will preserve patient cough and gag reflex which is good for prevention for VAP.

5. Stress bleeding prophylaxis, transfusion, and hyperglycemia.

- Stress ulcer prophylaxis with either H2 antagonists or sucralfate.
- Transfusion of packed cell should follow a protocol and leukocyte-depleted red blood cell should be used in selected patient populations.
- Maintain capillary blood sugar between 80-110mg/dl.

1.2.2 Bronchoscope and Bronchoscopy

Bronchoscope is an endoscope specially designed for passage through the trachea to permit inspection of the interior of the tracheobronchial tree. We can use bronchoscope to carry out endobronchial diagnostic and therapeutic maneuvers such as taking specimen for culture and biopsy and removal of foreign bodies. Bronchoscopy is the procedure we perform using a bronchoscope.

1.2.2.1 History of Bronchoscope

Gustav Killian was the father of bronchoscope. He was born on June 2, 1860. He studied medicine at the University of Strassburg then continued clinical education at Freiburg, Berlin and Heidelberg. He became head of the section of rhinolaryngology at Freiburg later. In 1889, he attended a meeting of Society of South German Laryngologists in Heidelberg. In that meeting, he learned about Kirstein who intentionally started to intubate the larynx with the esophagoscope after he accidentally passed the scope in the tracheal. He also learned about the experiences of Krakow who introduced direct lower tracheoscopy via tracheostomy without any complications. Thus in 1896, he began his experimental work. He performed the first direct endoscopy via the larynx in a volunteer and was able to introduce the scope into the bronchus and bronchi until the lobar level easily. So in year 1897, bronchoscopy was born. After he successfully removed 3 foreign bodies with his new direct bronchoscope, he presented his findings at the sixth meeting of the Society of South German Laryngologists in Heidelberg on May 29, 1898, and in the same year his first publication on direct bronchoscopy was printed (14).

During the early years, the indications for the using the bronchoscope was mainly for therapeutic purposes. It was used to remove foreign bodies and dilation of strictures from tuberculosis and diphtheria. In the early part of the 20th century, Chevalier Jackson, further advanced bronchoscopic techniques and designed modern rigid bronchoscopies (15). Fibreoptic bronchoscopy (FOB) was then developed in the late 1960s by S. Ikeda.

1.2.2.2 Indications, Contraindications and Complications of Bronchoscopy

Bronchoscope can be divided into rigid bronchoscope and flexible bronchoscope. Flexible bronchoscope nowadays gains more popularity since it was introduced in 1968. This is because compare to rigid bronchoscope, flexible bronchoscopes are more easily inserted, better tolerated by patient and can be used on critically ill patients. Furthermore, the flexible bronchoscope allows one to examine significantly more of the tracheobronchial tree including those of the upper lobes.

Indications for bronchoscope can be divided into diagnostic and therapeutic purposes (16)
For diagnostic purposes:-

- Identify suspicious lung pathology
- Examine patient with recurrent or persistant atelactasis
- Assessment of airway patency
- Investigate for hemoptysis**,** persistent cough, localized wheeze or stridor
- Obtain specimens for cytologic, histologic and microbiologic evaluation such as for diagnosis of lung carcinoma

- Obtain specimen for suspicious or positive sputum cytology results
- Identify the extend of airway injury from toxic inhalation, burn or aspiration
- Evaluation of problems associated with endotracheal or tracheostomy tubes such as tracheal damage, airway obstruction or to confirm tube placement

For therapeutic purposes:-

- Aspiration of retained secretions as in condition that mucus plug causing lung collapse or atelactasis
- Bronchoalveaolar lavage
- Resection of tumor by using laser
- As one of the management of bronchopleural fistula
- Photodynamic therapy
- Placement of airway stent for tracheomalacia
- For intubation in difficult situation
- Removal of foreign body usually by using rigid bronchoscope

Having discussed about the indications of bronchoscopy, we should also know about the contraindications for this procedure. However, until recently, there are still no control studies as to which factors causing patient unfit to do the bronchoscope. So we have to weigh the risk and benefit of doing bronchoscopy on individual patient.

High risk for bronchoscopy:-

- patient not cooperative
- unstable cardiovascular disease
- tracheal obstruction or stenosis
- moderate to severe hypoxemia

- hypercapnia
- uremia
- immunosuppression
- severe asthma
- bleeding disorders or coagulopathy
- respiratory failure

We have to note that lack of adequate staff and facilities are also considered as contraindications for bronchoscopy.

Bronchoscopy, particularly flexible bronchoscopy is an extremely safe procedure as long as we take the basic precautions. Credle Jr et al.(17) and Suratt et al. (18) reported a mortality rate of 0.01% and a major complication rate of 0.08% in a series of 24 521 procedures, and a 0.02% mortality and 0.3% major complication rate in a series of around 48 000 cases, respectively. Complications of bronchoscopy are divided into minor and major (19)

Minor complications (not life threatening):-

- vasovagal reactions
- febrile
- cardiac arrhythmias or dysrhythmias
- bleeding
- airway obstruction
- pneumothorax
- nausea and vomiting

Major life threatening complications:-

- hypoxia or respiratory depression
- infection to the lung or pneumonia
- pneumothorax
- airway obstruction
- cardiorespiratory arrest
- arrhythmias
- pulmonary congestion

The complications rate and whether it is a major or minor complication depend on the procedures and patients. For example, the transbronchial biospsy is associated with pneumothorax (5%) and hemorrhage (9%) (20). However the hemorrhage are usually mild and not life threatening. The uremic and immunosuppresed patients are also more prone to bleeding. Hypoxeamia are usually associated with BAL and if larger fluid volume given for the lavage.

1.2.3 Bronchoaveolar Lavage

BAL is obtained by infusion and aspiration of a sterile physiologic solution usually normal saline that is given through a flexible bronchoscope introduced into a bronchial subsegment (21). Warming the fluid to body temperature before injecting cause less irritation to the airway and thus reduce coughing and improves fluid recovery. Occasionally, to break up the thick secretions, mixture of normal saline and N acetylcysteine can be used. BAL can be both diagnostic and therapeutic.

The amount of BAL fluid needed to be given for assessment of the lungs has not been standardized. The BAL Cooperative Group Steering Committee has recommended using 240 ml for the evaluation of patients with interstitial lung disease. BAL for bacterial cultures, including patients who are mechanically ventilated, several studies showed that amounts of BAL fluid ranged from 100 to 150mls. Usually 50%-70% of this fluid will be recovered during aspiration.

BAL samples cells and debris from alveolar space. In order for our specimen to be valid and accurate, do not do suction through the scope 1st. After we inject the fluid, suction is done. The 1st bit is discarded as it is highly contaminated. Then we send the remaining sample for anylasis. The most accurate sample is from the middle lobe and lingual.

The BAL samples from non smoker and smoker are different. The table 3 below shows the BAL sample for non smoker. While for smoker there are decrease in lymphocytes (less than 7%) and an increase in neutrophils (more than 10%) if compare to non smoker.

Table 2: BAL sample for non smoker (22)

Normal Adults (Nonsmokers) Alveolar	BAL Differential Cell Counts
Macrophages	> 85%
Lymphocytes (CD4+/CD8+ = 0.9–2.5)	10–15%
Neutrophils	< 3%
Eosinophils	< 1%
Squamous epithelial / ciliated columnar epithelial cells	< 5%

There are several disorders that we can differentiate from BAL sample according to the increase percentage of specific BAL cells type. For examples, increase in percentage of lymphocytes > 15% might suggest of sarcoidosis, hypersensitivity pneumonitis, collagen vascular disease and lypmhoproliferative disorder. Increase in eosinophils can be seen in asthma, bronchitis, bacteria, fungal and pneumocystic infections, while increase in neutrophils >3% might be caused by aspiration pneumonia, bacterial and fungal infection and ARDS.

Beside from the normal cells, we can also obtain some abnormal findings from BAL. Some diagnosis also can be derived from these findings. Infectious organism cultured from BAL most probably is due to lower respiratory tract infection while malignant cells from BAL are due to cancer. Bloody fluid points to pulmonary hemorrhage or diffuse alveolar damage while milky fluid is caused by pulmonary alveolar proteinosis.

In the absence of a gold standard for the diagnosis of VAP, the value of BAL in diagnosis of VAP remains controversial. However there are studies that showed in patient with suspected VAP, the usage of BAL to directly sample a suspected area and quantitative cultures to distinguish infecting microorganism from colonizing microorganisms improved the survival rate, decreased antibiotic use, and was associated with fewer organ failures (23). Sanchez-Nieto et al. (24) reported that VAP patients who are managed with invasive strategy such as BAL have no significant influences on the mortality but it significantly modified the initial antimicrobial therapy.

In our ICU setting in HSB, it is difficult to adhere to invasive strategy such as BAL in all VAP patients as there is limited unit of FOB and not all staffs are trained in assisting bronchscopy. However, in this study, we used FOB for BAL sampling after the patients were diagnosed to have VAP.

1.3 INTENSIVE CARE UNIT HOSPITAL SULTANAH BAHIYAH

In this study, we take ICU HSB as having 24 beds (12 beds from ICU; 12 from high dependency ward (HDW) which function is exactly same as ICU). Total staff nurses are 83 (43 from ICU and 40 from HDW). There are 3 shift per day; AM shift which is from 7am-2pm, PM shift from 2-9pm and night shift 9pm to 7am. There are 16 staff nurses per shift (8 in ICU and HDW each). Each staff nurse will be assign to 1 to 2 patients depends on the severity of illnesses of the patients' in charge.

1.4 METHODOLOGY

1.4.1 Study Type

This is an observational study.

1.4.2 Study Design

This was a prospective, cohort study. The primary end point was to determine the prevalence of VAP in ICU HSB. The other objectives were the risk factors for VAP and the identification of organism involved in VAP.

1.4.3 Study Setting

This study was conduct in Intensive Care Units Hospital Sultanah Bahiyah.

1.4.4 Study Period

The duration of study was 12 months, started from 1st August 2014 to 31st July 2015.

1.4.5 Study Population

The study population was patients admitted to ICU HSB during the study period and who fulfill the inclusion and exclusion criteria.

1.4.6 Diagnosis

In Hospital Sultanah Bahiyah, Alor Setar, Kedah, the diagnosis criteria for VAP is based on MRIC. It is a modified version of those mentioned above based on the combination of clinical manifestation, imaging and laboratories results. (Appendix I)

- Diagnosis of VAP based on
  - (i) Suspicion of VAP
  - (ii) Chest X-rays shows new and or progressive pulmonary infiltrates
  - (iii) Presence of either 2 of the following 4 criteria
    - Fever $\geq$ 38.5^{o}C or < 36^{o}C within 24 hours
    - Total white cell count >12 000/mm^{3} within 24 hours
    - Purulent tracheobronchial secretions within 24 hours
    - Reduction of $PaO_2/FiO_2 \geq$ 15% in the last 48 hours

1.4.7 Selection Criteria

1.4.7.1 Inclusion Criteria

- Intubated patient
- Admitted to ICU
- Age more or equal to 12 years old

1.4.7.2 Exclusion Criteria

- Intubated less than 48 hours
- Patients that planned for end of life care

1.4.8 Sample Size Calculation

Sample size calculation was guided by Encik Shahrul Aiman Bin Soelar, statistician in Clinical Research Center (CRC) HSB Alor Setar. We used the calculator by Niang L, Winn T, Rusdi BN. Sample Size Calculator for Prevalence Studies, Version 1.0.01, (25) which is available at the below link. Http: // www.kck.usm.my/ppsg/statistical_resources/SSCPSversion1001.**xls**. The formula is as below.

Formula without Finite Population Correction

$$n = Z^2P (1-P) / d^2$$

Where

n = sample size

Z = statistic for a level of confidence

P = expected prevalence or proportion (if the expected prevalence is 20%, then P = 0.2)

d = precision (if the precision is 5%, then d = 0.05)

Formula with Finite Population Correction

$$n' = NZ^2P (1-P) / d^2 (N-1) + Z^2P (1-P)$$